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Aggressive angiomyxoma: clinical case and bibliography review

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Introduction

The term aggressive angiomyxoma was proposed by Steeper and Rosai in 1983 to define a slow growth myxoid mesenchymal neoplasm that appears fundamentally in the pelvic, genital and/or perineal region of women in their reproductive years[1].

The aggressive angiomyxoma is a rare neoplasia, almost exclusive to the female sex. It is theorized with a possible hormonal dependency given the expression of estrogen and progesterone receptors, in addition to their rapid growth during gestation. The treatment is principally surgical, having described various adjuvant treatments whose usefulness is not entirely established[2].

Clinical case

37 years of age nulliparous patient suffering from pain in medial region of right lower limb root and vulva since 1 year appears at private center after history of cervical conization in 2011 with biopsy confirming high-grade squamous intraepithelial lesions (HSIL). A pelvic MRI is performed with a diagnosis consistent with complex Bartholin cyst. The patient is referred to the Gynecological Service of our center for evaluation.

In the physical exploration at the level of the vaginal recess or right anterior ischioanal fossa, a tumor of approximately 2 cm at maximum diameter is detected, with regular margins, without contralateral equivalence that would correspond to the tumor under study. A thick needle biopsy is performed in which tissue compatible with skeletal muscle, cavernous bodies and minimal presence of loose connective tissue insufficient for the anatomopathological diagnosis are observed.

After a second opinion in our external MRI center, a diagnosis of a suspected tumor of mesenchymal origin is presented, compatible with angiofibroma or angiomyxoma.

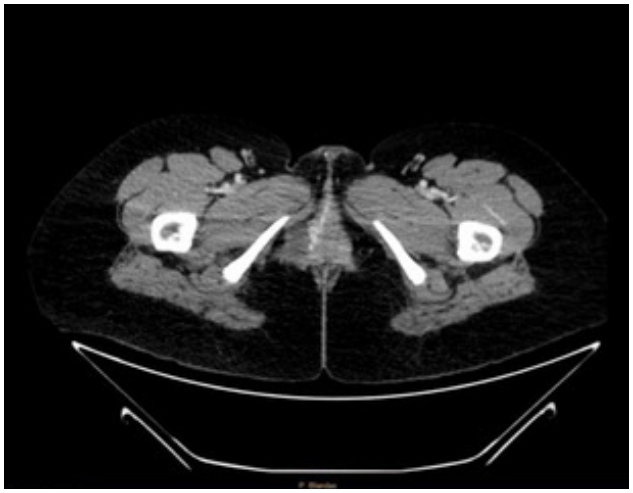

Image 1: CAT scan axial cut that shows hypodense lesion at the right paravaginal level.

Given the findings, a chest, abdominal, pelvic CAT scan is requested to study the extension, which reveals a tumor of hypodense and hypocaptant soft parts with poorly defined margins of 46 x 26 mm, located at the right paravaginal level in intimate contact with the right internal obturator and pubococcygeal muscles, without appreciation of lymph node or distant dissemination *(→ Image 1)*. In addition, a dynamic MRI was performed that showed a tumor of soft parts in the anterior recess of the right ischioanal fossa, with mixed polylobate and infiltrative margins of 4.7 x 2.8 x 3.7 cm. Said tumor infiltrates the anterior fibers of the pubococcygeal muscle contacting the external wall of the vagina to the introit and the fibers of the right internal obturator on the lateral margin.

The dynamic study showed a striated pattern with hyperintense lineal areas, hyperintense central zones and a centripetal collection *(→ Images 2A, B + C)*. Due to the radiological characteristics and the location of the tumor the diagnosis of aggressive angiomyxoma was considered the most plausible.

Serum tumor markers (CA 125 and CA 19.9) were requested that resulted to be negative. A second biopsy was carried out using echo guided CNB, which was unsuccessful, so it was decided to perform a surgical therapeutic excision of the lesion for diagnosis.

A vaginal and perineal approach was used, with a longitudinal incision with lateral concavity of 10 cm, situated 2 cm lateral of the right labium major. Dissection in layers to reach the anterior portion of the ischiorectal and ischioanal fossa. A dissection of the vascular spaces present in said compartments was performed, until the complete ischioanal fossa could be observed, as well as the ischiopubic pelvis and pubic bone. In this way, the right retro pubic space. the elevating muscle of the right anus and the internal obturator muscle were reached. In addition, a complete dissection of the lateral face of the vagina and the rectum was performed without observing a continuous solution for any of these structures during the procedure.

A well-defined tumor of a gelatinous aspect of 4 x 2 cm was exposed, in this way a complete excision of the tumor was achieved. The procedure continued to widen the margins at the internal level (paravaginal-pararectal), external (internal obturator muscle) and depth (elevator of the anus and perirectal fat). With the intention of obtaining an improved hemostatic control and diminishing the appearance of

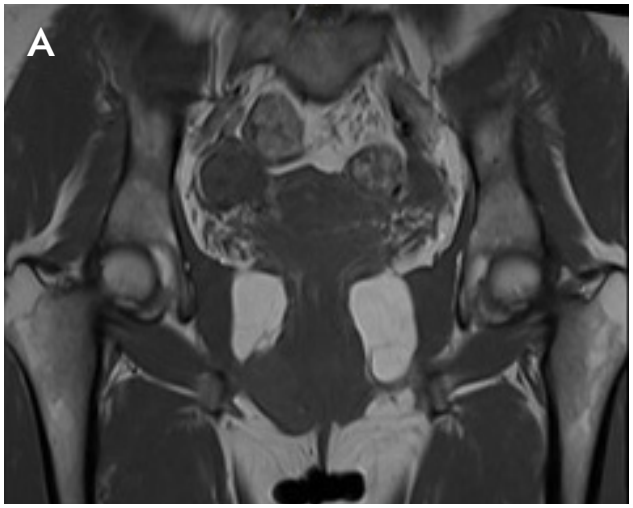

Image 2A: MRI. T1 Sequence in coronal section.

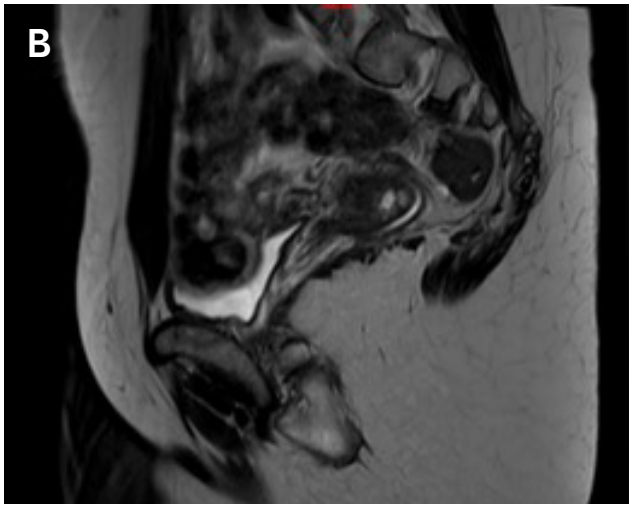

Image 2B: MRI. T2 Sequence in sagittal section.

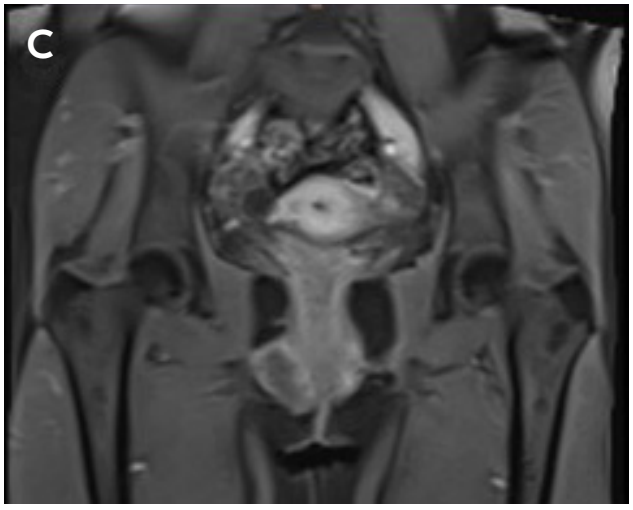

Image 2C: MRI. Dynamic study.

postoperative hematoma, it was decided to apply a local hemostatic (TachoSil®), which also eliminated the need to use surgical drains in the bed. After closure by layers, an intradermic suture was carried out on the skin with a slow reabsorbing suture *(→ Image 3D)*.

The anatomopathological study showed a paucicellular lesion of mesenchymal lineage that sits on a markedly edematous stroma of 4.1 x 2 cm. The nuclei were spindle- or stellate-shaped, of finely granular chromatin and with blunt and/or spiculated borders, with scarce and inappreciable cytoplasm. Cells with atypia, mitosis figures and necrosis phenomena were not observed. In the stroma abundant vascular structures were identified, with thin walls and curvilineal disposition. The lesion had poorly defined external margins, intermixed with the peripheral adipose tissue. The surgical margins were negative. The immunohistochemical study showed an intense expression for estrogen receptors (intensity 3+. Score 270 % of positive cells: 90 %), progesterone receptors (intensity 3+. Score 270, % of positive cells: 90 %) and focally for Smooth Muscle Desmin and Actin The nuclear proliferation index Ki 67 is <1 %. On the contrary, CDK4 and MDM2 immunostains were negative.

These anatomopathology characteristics were compatible with aggressive angiomyxoma of the vulva.

Discussion

Aggressive angiomyxoma is a benign mesenchymal tumor. In published literature approximately 300 cases of this tumor have been described[3]. It has slow growth and tends to be located in the pelvic-perineal region, although these tumors have been found in other parts of the body such as the diaphragm, retroperitonea or knee[4,5]. It appears most frequently in the female sex than in the male, with a relationship of 6:1[6]. Although cases have been described from infancy to the elderly, it is most frequent in the 4th decade of life, in women of child-bearing age[2,7]. Its histological origin and pathogenesis are not completely established, but it is believed that their origin are fibroblasts[5]. Although it is a benign tumor, it is denominated as aggressive due to its high rate of infiltration at the local level, that implies a high index of local recurrence. Distant metastasis, however, are exceptional[8].

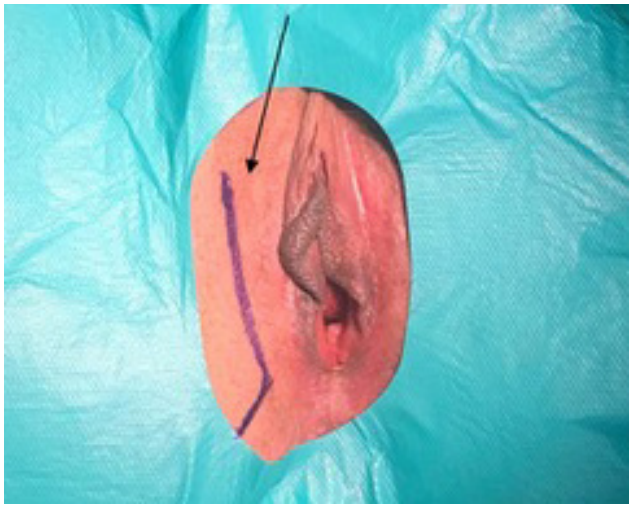

Image 3A: Surgical incision delimitation.

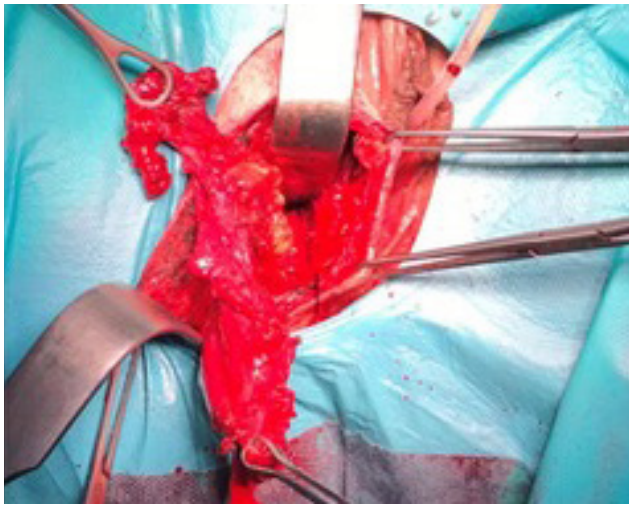

Image 3B: Tumor dissection.

Clinical overview

Clinically, the aggressive angiomyxoma can be asymptomatic, being diagnosed when, during a clinical exploration, a soft tumor is found, or as an accidental finding when an imaging technique is performed. In symptomatic cases, these tend to be non-specific, such as dysuria, abdominal bloating, dysmenorrhea or dyspareunia. It is worth noting that, as previously mentioned, during gestation their growth can be rapid[7].

Diagnosis

Since it is an infrequent tumor, it is not widely known and it is not included among possible presumptive diagnoses, commonly being confused with Bartholin cyst, vulvar cyst, abscess, lipoma or hernia.

To complete the diagnosis different complementary explorations can be carried out, among those recommended is a sonogram. This will show a tumor with well-defined margins, heterogeneous, iso or hypoechogenic that, due to its soft consistency, it is deformed during the exploration. It can be seen that it appears to have a swirling layout, or in layers and has abundant vascularization[10].

On the other hand, the CAT scan will show a homogeneous and hyperdense mass with respect to the muscle, although some of these tumors can also be cysts with a solid component[4,6].

The MRI is the imaging test of excellence. It will show a hypointense tumor in T1 sequence and hyperintense in T2 sequence. The most characteristic radiological pattern will be seen after administration of a contrast. In the dynamic study a mass with an intense and heterogeneous enhancement will appear, in addition to a distinctive swirling pattern because it has an abundant myxoid matrix and high water content[4,10].

Histology

The definitive diagnosis will be histological. Arriving at an anatomopathological diagnosis of an angiomyxoma prior to surgical intervention is difficult since performing a biopsy is difficult due to its soft consistency and because of its low cellularity. It is recommended taking the biopsy using aspiration from different directions and sections of the tumor, although this method doesn't increase the success rate either.

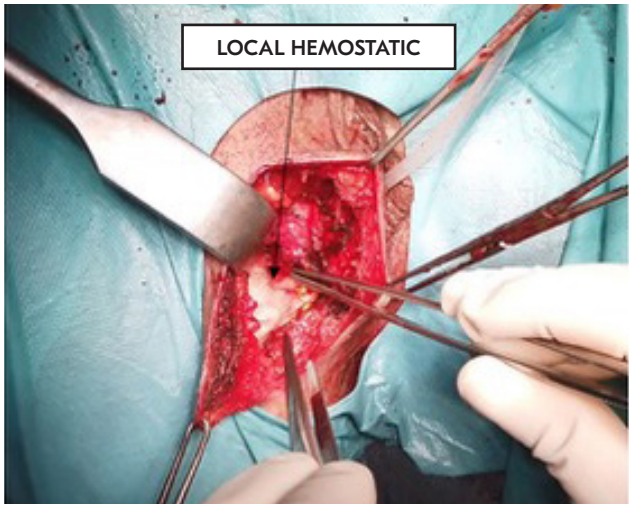

Image 3C: Surgical bed with local hemostatic.

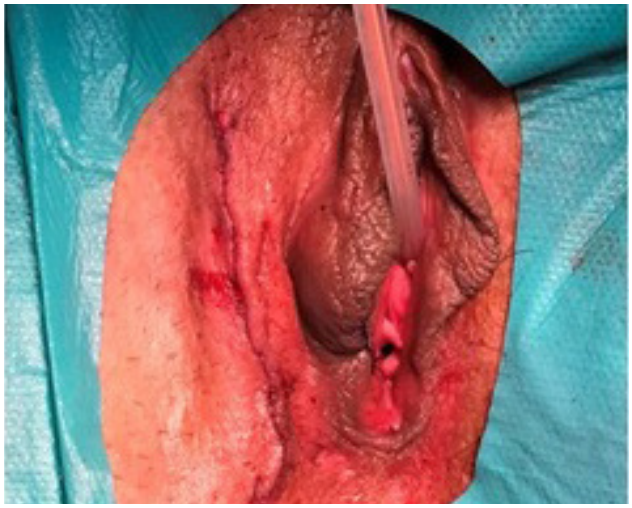

Image 3D: Intradermal suture after closure by layers.

At the macroscopic level, the mass will be a pinkish color, not encapsulated, with abundant vascularization and a gelatinous or rubbery feel. It will have a shiny appearance, although there may be fibrous areas, vascular congestion and even bleeding[6].

At the microscopic level, it will appear as a scarcely cellular tissue whose cells are spindle shaped with poorly defined cytoplasmatic borders, on a, pale myxoid-eosinophilic stroma. The cellular atypia is minimal or none, presenting a low rate of mitosis. Given its high vascularization, there will be abundant blood vessels and, occasionally, smooth muscle fiber can be found[11].

In the immunohistochemical study, there will be a high positivity of estrogen and progesterone receptors. Also, it may be positive in a diffuse form for vimentin and desmin. The CD34 marker is positive but the S-100 is negative. Presents a low proliferation rate (Ki-67 <1).

A characteristic marker is HMGA2. The HMGA2 gene (high mobility group AT-Hook2) participates in the regulation of the transcription of various cellular processes and its mutation has been described in other tumors of mesenchymal origin[12].

Treatment

Treatment for aggressive angiomyxoma is surgical. It is recommended that the tumor be excised with margins of 1cm, given its behavior of filtration at the local level[4,13]. However, if the surgery may entail comorbidities for the patient, a partial resection of the tumor is acceptable[14]. It is not recommended that a lymphadenectomy be performed, due to their lack of lymph node dissemination. In addition to surgical treatment, adjuvant hormone treatment with GnRh agonists may be administered. Control of the localized illness during its treatment has been objectified, which is usually temporary and conditioned to maintaining the treatment. With this objective, the use of aromatase or tamoxiphen inhibitors has been described, although the effectiveness of these treatments is controversial[6,15].

Arterial embolization constitutes another treatment option, even though performing an exclusive treatment with this technique is difficult, given the high vascularization of the tumor. Therefore, embolization treatment prior to surgery is preferred, with the intention of reducing the surgical bleeding or for the treatment of local recurrences[6].

Previously chemotherapy and radiation treatment were not considered useful for the treatment of aggressive angiomyxoma due to its low proliferation rate, but good results have been described after the use of radiation, especially in recurring cases. Its use has also been recommended when the rest of the adjuvant treatments weren't successful o when radical surgery is not possible, be it due to medical incompatibility or for causing important adverse effects[6].

Prognosis

Angiomyxoma has a high rate of recurrence at the local level (45—66 % of the cases). The principal factor is excision with positive margins (negative margins: 30—70 %, positive margins 50—70 %). The recurrence tends to appear within the first 2—3 years, although recurrences have been described after as much as 15 years after surgery. The most frequent location of recurrence tends to be in the isquiorectal fossa[9].

Distant metastasis is exceptional. Of the approximately 300 cases described in the literature, 3 cases of distant metastasis have been reported, all of them being at the pulmonary level[5].

Given the reported characteristics, long term follow-up is recommended for patients with a background of aggressive angiomyxoma[7].

Conclusion

Aggressive angiomyxoma is a benign mesenchymal tumor with a high incidence of local recurrence, frequently located in the pelvic-perianal region of women in their child-bearing years. The gold standard complementary test for its diagnosis is MRI. Obtaining an anatomopathological diagnosis prior to its excision is difficult. The treatment is fundamentally surgical, although other options may be considered (radiation therapy, embolization of GnRH analogs) to diminish the size of the tumor or the treatment of the recurrences. The recurrence of the tumor is frequent, and it is associated principally to the presence of positive margins in the resection. It tends to appear 2—3 years after the excision. Given the fact that long term recurrences have been described, it is recommended to carry out long term follow-up through physical exploration and MRI.

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2

Squamous cell breast cancer T2N1M0 treated with round-block type oncoplasty, axillary lymphadenectomy and Axillary Reverse Mapping (ARM)

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Introduction

From the Gynecological and Functional Breast Unit Service of the Hospital Universitari de Bellvitge in collaboration with the Catalonian Institute of Oncology (ICO for its Spanish acronym), we present the 2021 SEGO-CORZA competition*, a clinical case from our normal clinical practice in which we use the TachoSil® product as a hemostatic matrix in the surgical bed of an axillary lymphadenectomy.

It concerns a patient of 73 years of age with a diagnosis of squamous cell carcinoma of the breast, a subtype of metastatic carcinoma, very infrequent in its breast location, with negative response to conventional chemotherapy treatments.

After staging as cT2N1M0, with subrogated molecular study: Triple negative, primary treatment with conservative surgery was carried out through a right breast lumpectomy and round-block unilateral oncoplasty (or oncoplastic technique); right axillary lymphadenectomy using associated Axillary Reverse Mapping (ARM) technique.

Pending the presentation of the case in the tumor committee, the adjuvant treatment proposed will probably consist of breast radiology therapy and adjuvant chemotherapy.

After the presentation of the clinical case, during the discussion we presented subjects we found of interest such as squamous breast carcinoma, breast oncoplastic surgery (concretely the round-block technique), the Axillary Reverse Mapping technique in the axillary lymphadenectomy, and the use of hemostatic matrices in the surgical bed of an axillar lymphadenectomy.

* Contribution to the Spanish Society of Gynecology and Obsetrics (SEGO) of 2017. CORZA case competition

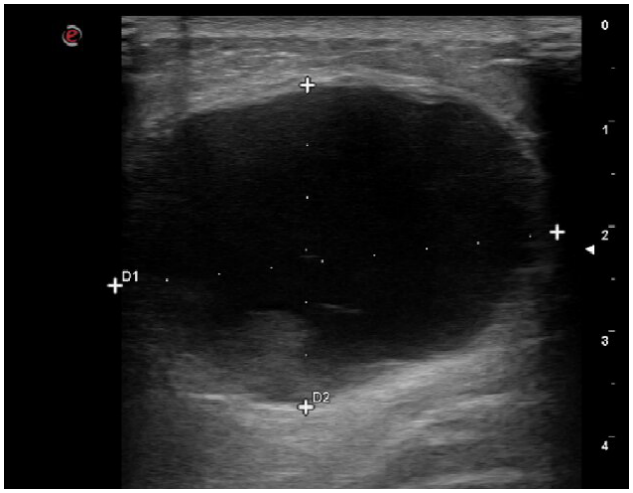


Image 1: Breast ultrasound. Image of the cystic lesion of the right breast.

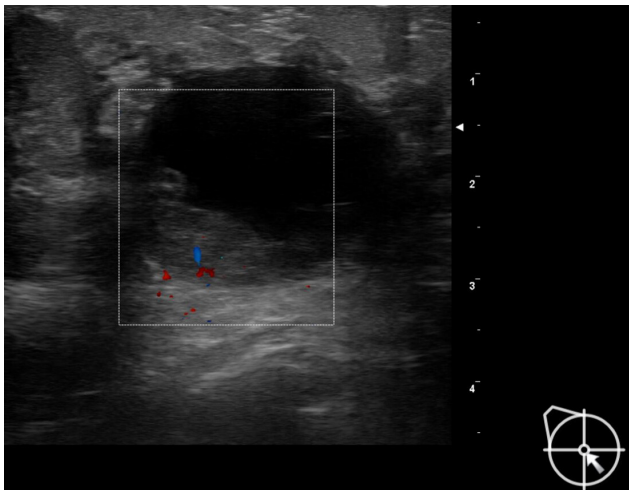


Image 2: Breast ultrasound. Image of the cystic lesion of the right breast.

Clinical case

Patient of 73 years of age referred to the Functional Breast Unit of the Hospital Universitari de Bellvitge —Catalonian Institute of Oncology (ICO), originating from their Primary Attention Center.

Motive for consultation: the presence of a palpable nodule in the junction of the inferior quadrants/inner-inferior quadrant of the right breast, under study for approximately one year.

Pathology background: Diabetes mellitus type 2 under treatment with Metformin, Sitagliptin and Dapagliflozin, high blood pressure under treatment with Lisinopril, dyslipidemia under treatment with Simvastatin, atopic dermatitis in follow-up, depression syndrome in follow-up and treatment with Venlafaxine; surgical history of excision of left axillary ectopic tissue at 30 years of age.

Family history

Among the familiar medical history are two brothers with lung cancer diagnosed at 60 and 65 years of age, respectively, a brother with pancreatic cancer and a son that died of a brain tumor at 43 years of age.

Current illness

The patient consulted approximately one year ago in her primary care center about a nodule in her right breast during self-examination. At this time, a mammogram and a breast ultrasound were requested that concluded that the lesion corresponded to a mammary cyst of 2 cm without signs of associated malignancy (BIRADS 2).

In various posterior controls through physical exploration and complementary image tests (mammograms and breast ultrasounds) growth of the described lesion is observed. Various punctures to empty the cyst were performed, with benign cytology results compatible with cystic lesion with squamous metaplasia.

The patient comes to the external consult offices of the Breast Unit of our center for assessment, due to recurrence of the lesion, after various echo guided punctures to empty the intracystic content (the last puncture was performed the prior month).

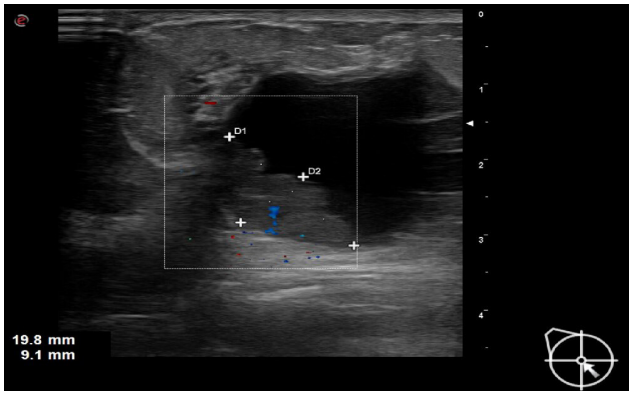


Image 3: Breast ultrasound. Image of the cystic lesion of the right breast.

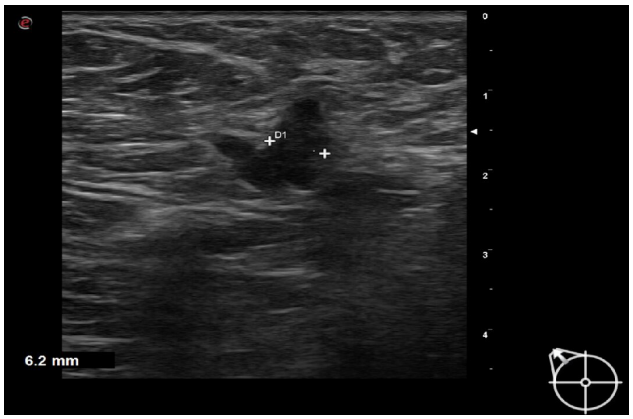


Image 4: Axillary ultrasound. Image of the right axillary adenopathy.

Physical exploration: medium size breasts, size 95 B cup. In our physical exploration a nodular area of 4 x 3.5 cm is palpable, with a hard, mobile consistency, located in the inferior quadrants of the right breast. A mobile lymphadenopathy is palpable in the right axillary. No other axillary lymphadenopathies are found, supraclavicular nor in the region of the internal mammary chain. The left breast shows no signs of alteration in the exploration.

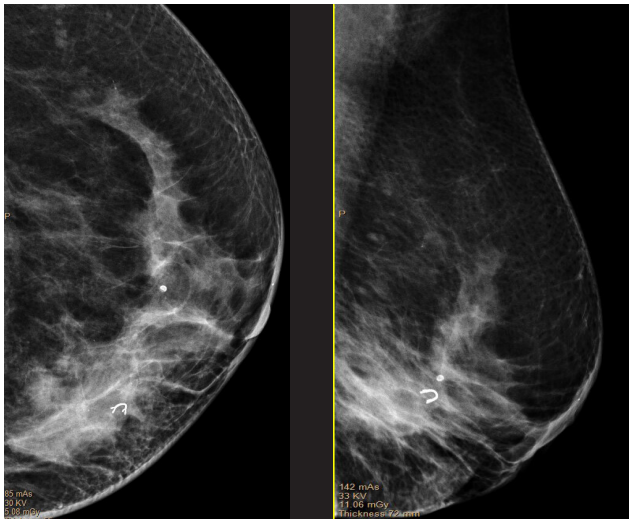
Radiology studies: the same day breast *(→ Images 1 to 3)* and axillary *(→ Image 4)* ultrasounds were performed that report: "Presence of a complex cystic lesion of 40 mm with 3 solid exophytes on the wall of 20 x 9 mm, 5 mm and 3 mm (BIRADS 4)." A CNB of a larger size is performed, obtaining 3 cylinders of 15 mm 14 g that are sent for study. At the right axillary level an image suggesting a lymphadenopathy with thickened cortex is observed (BEDI 4). PAAF is performed. In CSE of MI a hypoechoic nodule is observed with well-defined contours of 13 mm (BIRADS 2), visible in the mammogram and without change since 2015.

Pathology study

The anatomopathological results of the breast biopsy that was performed showed no evidence of malignancy, but due to the lack of radio pathological correlation a vacuum needle-assisted biopsy (VNB) was performed, after a prior Fine Needle Puncture Aspiration (FNA), to reduce the size of the wound and improve the procedure. Finally, the lesion was marked with a clip marker *(→ Images 5 and 6)*.

The anatomopathological study of the VNB demonstrated the lesion studied at the mammary level is a squamous cell carcinoma. The immunohistology study revealed negativity for estrogen and progesterone receptors, Her2/neu negative, Ki67 40 %, GATA-3 positive, p40 positive, p16 negative, Cytokeratin 5/6 positive, Pax-8 negative, the HPV detection study is negative. With this data is was concluded that from the pathology perspective it was not possible to establish if it was a primary case of breast cancer or a metastatic carcinoma.

The cytology of the axillary lymph node is positive for malignant cells, and compatible with carcinoma metastasis.



Images 5 + 6: Mammogram. Figure 5 (left) is a cranio-caudal (CC) projection, figure 6 (right) is the oblique mediolateral projection (OML). Control of clip marker in the area of the wound, placed after VNB.

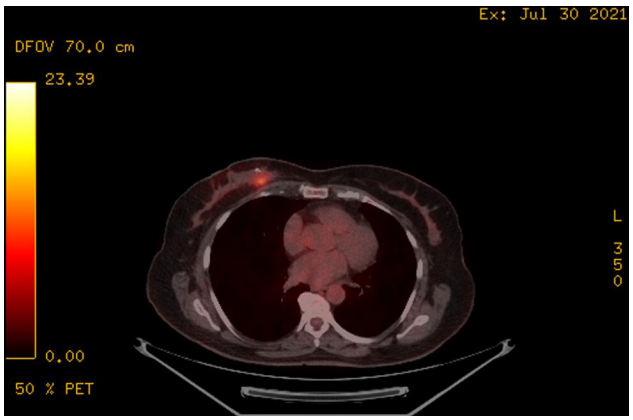


Image 7: PET-CT. In this cut the presence of a hypermetabolic pseudo nodular lesion at the junction of the internal quadrants of the right breast is observed, with the clip marker, related to the known neo proliferative process.

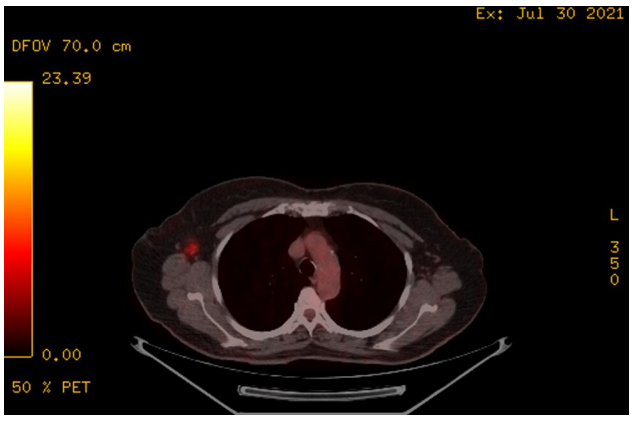


Image 8: PET-CT. In this cut, the presence of a hypermetabolic adenopathy in the right axillary suggestive of malignancy is observed.

Extended study: An extended study through PET-CT *(→ Images 7 and 8)* that inform the presence of a pseudo nodular hypermetabolic lesion in the junction of the internal quadrants of the right mammary gland, with a marking clip, in relation to the known neo proliferative process, a right axillary hypermetabolic lymphadenopathy suggesting malignancy, and no evidence of other significant lesions. In the blood analysis the CA 15.3, alkaline phosphatase transaminases nor the calcium were outside of the normal range.

Diagnostic orientation and staging: the case is oriented as a primary mammary squamous cell carcinoma and is staged as squamous breast carcinoma cT2N1M0, with a subrogated molecular study: Triple negative.

Primary treatment: the case is presented to the tumor committee and the initial treatment approved is conservative surgery through a right breast lumpectomy and round-block unilateral oncoplasty; right axillary lymphadenectomy using associated Axillary Reverse Mapping (ARM) technique.

Surgery

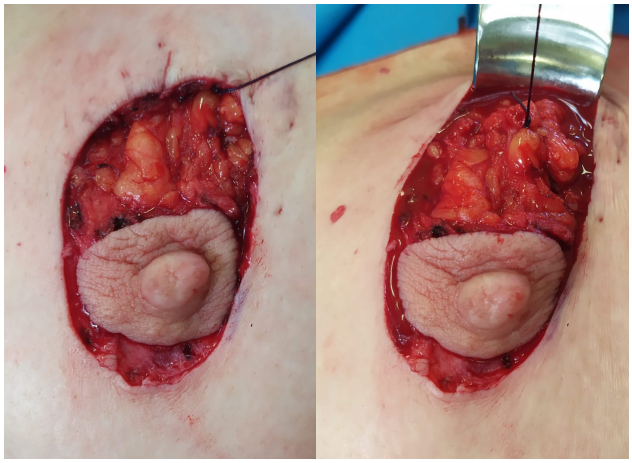
The surgery begins using the round block technique without reaching the nipple.

The lumpectomy is completed reaching the fascia of the pectoralis muscle and the sample is sent for intraoperative study. The pathologists inform that there is contact with a grainy area with a probability of an in situ component in the external margin. Said margin is increased and the material obtained is sent for differed study *(→ Images 9 + 10)*.

The breast is reconstructed using the round block technique, leaving the clips in the tumor bed.

The axillary approach is initiated with an italic S incision at the axillary level. Using the Axillary reverse Mapping technique 6 lymph nodes are identified with Indocyanine Green and SPY Fluorescence probe.

The axillary lymphadenectomy is completed including levels 1 and 2, and carefully verifying the long thoracic nerve (Bell's nerve) and the vasculo-nerve pedicle of the latissimus dorsi muscle. All of the material is sent to anatomopathology for differed study *(→ Images 11 to 19)*.



Images 9+10: Round-block design mammoplasty and mammary lumpectomy.

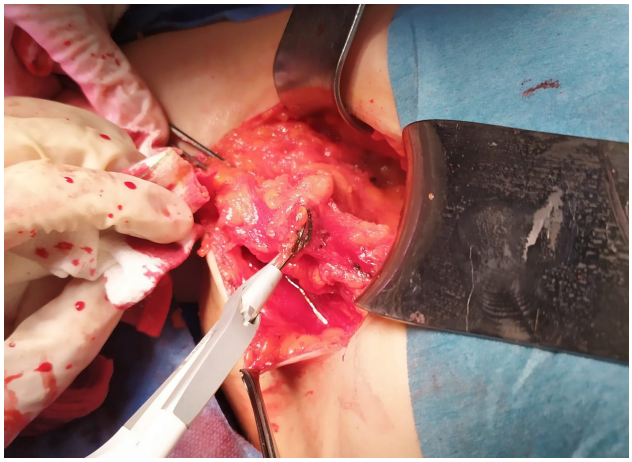


Image 11: Right axillary lymphadenectomy.

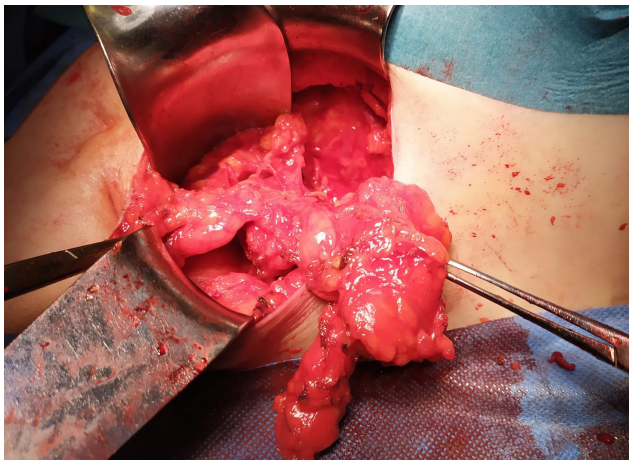


Image 12: Right axillary lymphadenectomy.

Once the procedure is finalized careful hemostasis of the axillary surgical bed is performed, and a hemostatic patch (TachoSil®) is placed in the most friable area; it is an adhesive collagen matrix coated with human fibrinogen and thrombin *(→ Images 20 to 22)*.

Postoperative pathology study

The anatomopathological results of the surgical piece conclude:

- Right breast lumpectomy: Invasive metaplastic squamous cell carcinoma (95 %) and non-specific (ductal) (5 %) with associated intraductal carcinoma of the intraductal cribriform type (95 %) and associated squamous (5 %). Tumor size: 21 mm. Histology degree: G3. Free definitive margins.
- Lymphadenectomy (14 lymph nodes): 3 affectations (2 micro metastasis, 1 macro metastasis).
- ARM study detected 1 lymph node, of 6 lymph nodes studied, with micro metastasis.
- Stage: pT2pN1a. Estrogen Receptors 0 %, Progesterone Receptors 0 %, Her2/neu negative, Ki67 40 %. Subtype Triple negative.

Adjuvant treatment

After the first line of treatment, that also permits a more definitive anatomopathological diagnosis and a post-surgical staging, the case will be presented to the committee again to jointly evaluate the indicated complementary and/or adjuvant treatment.

Due to a lack of a collective decision, the adjuvant therapeutic approach will probably be complementary breast radiation therapy and chemotherapy. The scheme of chemotherapy to be used will be a point of discussion since due to the fact that it is a metaplastic squamous cell carcinoma treatment through cisplatin may be proposed, but having the non-specific (ductal) component, although at a low percentage, another option would be to treat with a combination of Adriamycin and Cyclophosphamide.

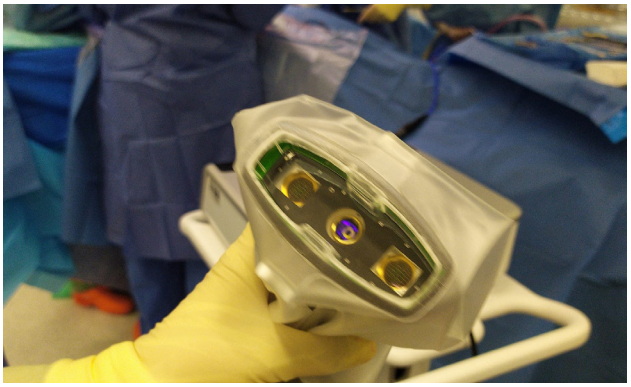


Image 13: Portable SPY image system. Permits the visualization of lymphatic vessels using infrared fluorescence imaging. Axillary Reverse Mapping technique.

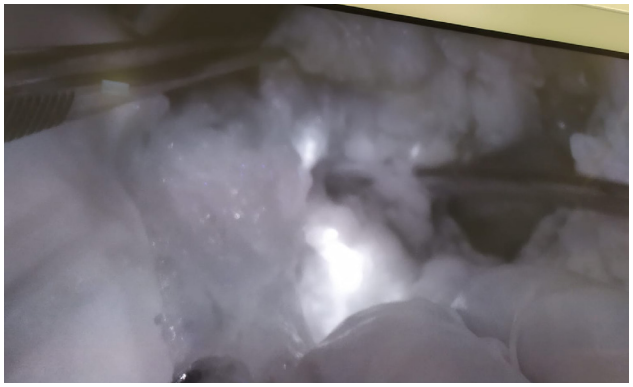


Image 14: Axillary Reverse Mapping technique. Detection of lymphatic node ARM marked with Indocyanine Green (SPY Fluoresence Mode).

Image 15: Axillary Reverse Mapping technique. View of lymphatic canaliculi marked with Indocyanine Green (SPY Fluoresence Mode).

Discussion

Squamous cell breast cancer is an infrequent breast cancer, constituting less than 0.1 % of all breast cancers[1].

From the pathological point of view, the tumor should include >90 % of squamous cells in its cell count. To be considered a primary breast tumor, the presence of another squamous cell carcinoma in a secondary location and the absence of affected adjacent cutaneous tissue must be excluded[2].

Among its clinical characteristics it is notable that it presents large nodes (usually >4 cm) in general and cysts in >50 % of the cases, as is the clinical case being presented.

Squamous cell breast cancer is a subtype of metaplastic cancer. These are usually triple negative or basal tumors, but have a poorer prognosis than other forms of triple negative tumors. This signifies therefore that it has no expression of hormonal receptors, estrogen nor progesterone, nor does it present an overexpression of the Her2/neu gene. They tend to have a high histological degree. These characteristics cause them to be considered tumors with aggressive behavior and associated with poor prognosis, with a tendency for recurrence, little response to conventional chemotherapy schemes (a differentiating aspect with respect to triple negative tumors), and without the possibility of hormone treatment[3].

Due to the aforementioned comments, neoadjuvant chemotherapy is not considered recommendable in this type of tumor in spite of appearing as a locally advanced tumor. This is why, in the clinical case presented, in spite of being in clinical stage cT2N1M0 and being classified as triple negative, the initial therapy was not neoadjuvant chemotherapy as would be appropriate, considering only the stage according to the clinical guides[4], but instead the case was directed to primary surgery.

Also, with respect to the surgical approach to the breast there is a disparity of opinion among the authors. Some studies are shown to be in favor of a mastectomy instead of conservative surgical treatment, alleging a greater risk of locoregional recurrence in spite of complementary breast radiotherapy, but the existence of a clear superiority has not been demonstrated.

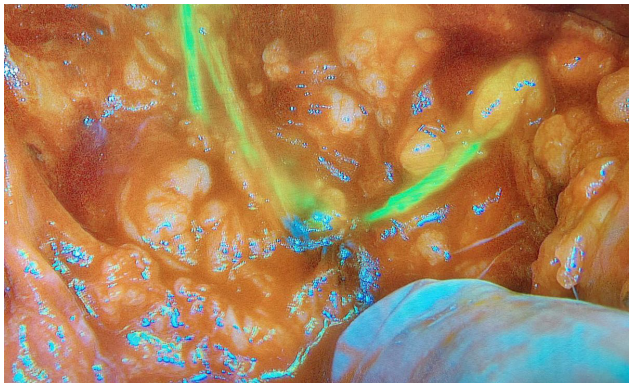


Image 16: Axillary Reverse Mapping technique. View of lymphatic canaliculi marked with Indocyanine Green (Overlay Mode).

Image 17: Axillary Reverse Mapping technique. View of lymphatic ganglions marked with Indocyanine Green (SPY Fluoresence Mode).

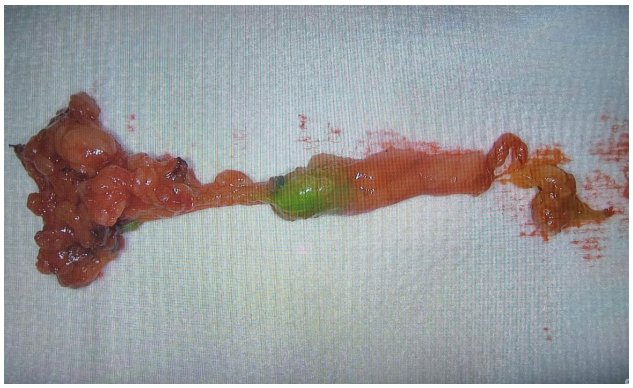


Image 18: Axillary Reverse Mapping technique. View of lymphatic ganglions marked with Indocyanine Green (Overlay Mode).

On the other hand, other studies referring to metaplastic breast cancer exist, that demonstrate that no significant difference exists, in terms of global survival, between conservative surgery or mastectomy in metaplastic breasts[5].

In the case of our patient, we opted for the choice of a conservative oncoplasty in the same surgical act, due to the size of the tumor, the relation between the size of the tumor and the breast, and the localization in the internal quadrants.

Conservative breast surgery is the gold standard for treatment of breast cancer in early stages. From the oncological point of view, the conservative surgery presents equal global survival with a discreet increase in local recurrence, with respect to a mastectomy, and presents lower morbidity and better aesthetic results. The excision margins are a determining factor for the control and prognosis of the illness. The aesthetic results, however, will depend on the volume of tissue extracted, the localization of the tumor and the adjuvant radiotherapy.

The oncoplastic surgery combines the oncological principals with plastic surgery and reconstructive technique with the objective of achieving good results both from the oncological and aesthetic perspectives.

The round-block mammoplasty, described by Benelli[6], is a technique that is based on displacing the mammary tissue, to remodel the quadrant where the tumor was, after the demolitive surgery. This is indicated in small to medium size breasts without significant ptosis; and preferably in tumors located in the upper quadrants. However, it is not such an appropriate option for superficial tumors or those that are in contact with the skin.

The surgical procedure is based on performing two concentric incisions at the peri areolar level, taking into account that the distance between them will be slightly wider in the opposite quadrant to where the tumor we are extracting is located, to prevent a deviation of the areola nipple complex (APC). The skin between the two incisions is de-epithelialized.

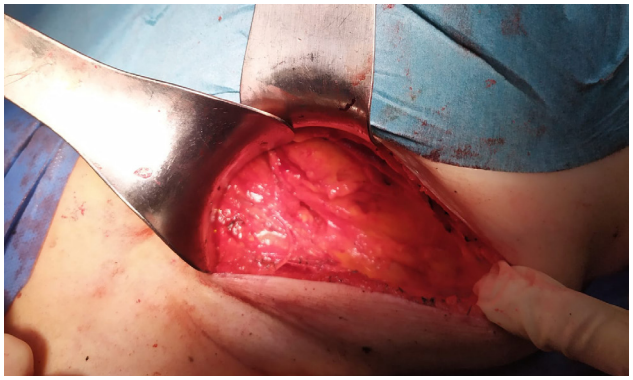


Image 19: Completed right axillary lymphadenectomy.

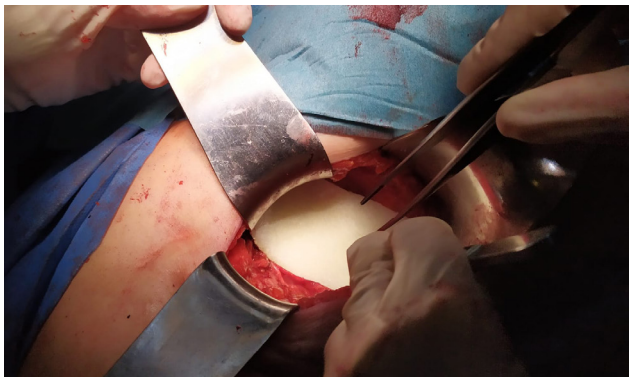


Image 20: Application of TachoSil® on the axillary lymphadenectomy surgical bed.

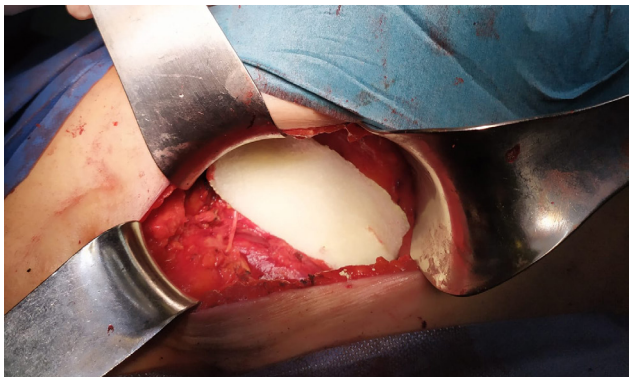


Image 21: Application of TachoSil® on the axillary lymphadenectomy surgical bed.

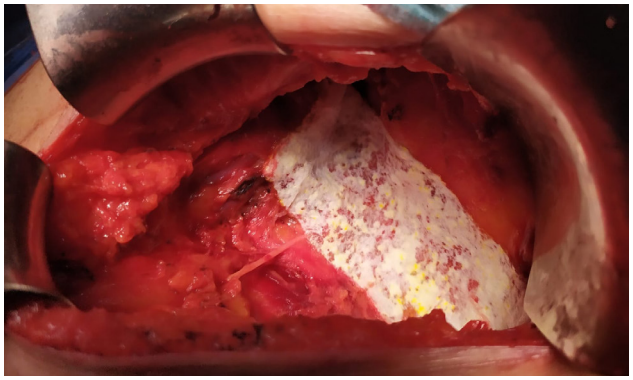


Image 22: Application of TachoSil® on the axillary lymphadenectomy surgical bed.

The dermis can only be cut in the region closest to the tumor (conventional round-block) to maintain the vascularization of the APC originating from the posterior glandular base and the dermic vessels that have not been cut; or, the dermis may be cut around the entire circumference of the APC (modified round-block), such that the APC maintains its vascularization originating only from its posterior portion. This second technique is indicated for tumors situated more peripherally to the APC to facilitate the movement of the mammary tissue and the excision of the tumor. Finally, and after the extraction of the tumor, the flaps of the mammary tissue will be moved to prevent dead space (gaps between the wound bed and the dressing)[6,7].

Oncoplastic breast surgery has demonstrated a control of the illness equivalent to the conservative surgery, an improvement in the aesthetic results and the patient's satisfaction[6,7].

The round-block type mammoplasty is a simple oncoplastic technique (level I oncoplasty), that permits good access to perform an oncology tumor resection surgery with safety and to displace the mammary tissue and as such prevent gaps between the wound bed and the dressing and consequently deformities in the breast. It presents few postoperative complications, does not usually require the use of drains in the surgical bed nor the need for contralateral symmetrization[7].

The disadvantages of this technique are that it does not achieve good breast projection, it can affect the sensitivity of the nipple, and may produce widening of the neo-areola[7].

With respect to the axillary approach, it is worth mentioning that the axillary affectation is one of the most important factors in prognosis of breast cancer. The axillary lymphadenectomy was historically the classic method for staging the axillary, being as well another procedure associated with less morbidity: the selective biopsy of sentinel nodes (SLNB). However, even though the treatment of patients with breast cancer has varied notably in recent years, in a substantial percentage of patients the indication to perform an axillary lymphadenectomy for the staging and optimization of the locoregional control of the illness still exists.

Axillary lymphadenectomy is associated with a significant risk of complications, such as the appearance of lymphedema, paresthesia and/or reduction of range of movement of the upper extremity. Among all, the most important adverse effect is the appearance of ipsilateral lymphedema after the performance of the procedure, that severely conditions the quality of life of these patients. There exists, as a result, a considerable percentage of patients that suffer these adverse effects associated with breast cancer[8].

In 2007, the first studies on the "axillary reverse mapping" (ARM) technique were published. This is a procedure that permits the discrimination and identification of the lymphatic drainage of the upper extremity with the purpose of preserving it. The fundamental concept of this procedure is based on the hypothesis that the upper extremity and the breast possess independent lymphatic drainage paths through the axillary, such that, by preserving the corresponding path of the upper extremity (ARM lymph nodes), it is possible to prevent the appearance of lymphedema after axillary surgery[9].

The technique described in the literature consists of subcutaneous injection, in the medial intermuscular zone of the upper extremity, of a tracer that permits us to identify the drainage pathways and its lymphatic nodes during the axillary surgery. With respect to the tracer that is used, the use of patent blue, Tc-99 or fluorescence (indocyanine green)[9]. With the use of indocyanine green, according to prior studies[9], a rate of visualization of the lymph nodes ARM of 88 % is established, similar to the rest of the techniques (patent blue 39—90 % and Tc-99 90 %). Some of the advantages it presents with respect to the rest of the techniques are: no systematic allergic reaction to the tracer have been reported and the "green tattoo" disappears quickly[9].

Studies exist that have shown a significant reduction in the percentage of patients that develop lymphedema associating the ARM technique to axillary lymphadenectomy. Abdelhamid et al.[10] have published a rate of lymphedema of 6.5 % in this group of patients, compared to 20.9 % observed in those in which a conventional axillary lymphadenectomy was performed. As well as in a study by Ahmed et al.[11], that showed a rate of 2 % among those patients in which the lymph node drainage paths of the upper extremity were identified and preserved.

However, the concern exists that the preservation of these lymph nodes, that could have a lymphatic drain crossed between the arm and the breast, could be affected and, therefore, leaving them during the surgery would lead to poorer control and/or treatment of the illness[11]. Beek et al.[9] conclude that the metastatic lymph node involvement of the ARM lymph nodes in patients with breast cancer in early stages only represent a small percentage (2.9 %), without further conditioning the appearance of locoregional recurrences of the illness during follow-up (in this case, of 24 months). On the contrary, other studies, show greater rates of affectation when dealing with patients with advanced local illness (27 %), therefore this technique would not be recommended for this group of patients.

In our center, the Hospital Universitari de Bellvitge, we are developing a pilot study with the principal objective being to validate the ARM technique with indocyanine green (fluorescence) in the treatment of breast cancer patients that are subjected to an axillary lymphadenectomy for the identification of lymphatic drainage of the ipsilateral upper extremity (ARM lymph nodes); and this way be able to determine the percentage of metastatic ARM nodes and identify predictive factors of their being affected, and select the patients in which this surgical technique could be applied.

Finally, once the axillary lymphadenectomy is finalized, and to guarantee a better hemostasis of the surgical bed we used an adhesive matrix made of collagen and covered on the active face (yellow) with human fibrinogen and thrombin: TachoSil®.

TachoSil® is indicated as support treatment in surgery to improve hemostasia, promote tissue sealing and as a reinforcement for sutures in vascular surgery when the standard techniques prove to be insufficient; among other indications.

The active ingredients of TachoSil®, fibrinogen and thrombin, are proteins extracted from blood that participate in the physiological process of coagulation. Thrombin acts by breaking the fibrinogen into smaller units known as fibrin, that is then added to form clots.

When TachoSil® is applied on a bleeding surface during an intervention, the moisture causes the reaction between the active ingredients achieving the rapid formation of clots.

This permits a stronger adhesion of the patch on the tissue and in this way helps detain the bleeding and seal the wound.

The amount of TachoSil® to be used must always be established as a function of the patient's clinical needs and will be determined by the size of the wound. It is exclusively for epilesional use and should not be used in an intravascular route.

Concretely, in the axillary application after a lymphadenectomy, the effect of TachoSil® is being investigated in the prevention of the appearance of lymphocele and axillary seroma. The theoretical reasoning for this hypothesis is based on the fibrin patch adhering to the surrounding tissue and eliminating the gap between the wound bed and the dressing that favors the appearance of seroma, as well as seal the damaged or severed lymphatic vessels, in a way similar to how it does in blood vessels, and therefore it can be expected to diminish lymphatic morbidity.

However, to date no statistically significant results have been obtained, that permits the affirmation that TachoSil® is an effective preventative measure in the formation of axillary lymphocele. But studies do exist that confirm that TachoSil® applied to the axillary after a lymphadenectomy, reduces the volume of axillary drainage, the average axillary drainage time, and the symptomatic collections, quantified in terms of the reduction of evacuation punctures required[12]. It is necessary to continue studying if the reduction of secretions can prevent the need for placement of axillary drainage.

Conclusion

- The diagnostic process, consensual decision making in expert committees and treatment in multidisciplinary Breast Centers, permit the individualization of therapeutic options for each patient, improving the quality of assistance and the oncological results.
- Squamous cell breast cancer is an infrequent breast cancer, aggressive and with poor response to chemotherapy. It is fundamental, to discard that it is a metaplastic lesion of a different origin and plan an individualized and directed treatment.
- The objectives of conservative surgery are to obtain a tumor excision with free margins, to minimize an eventual local recurrence and a correct aesthetic result.
- Oncoplastic surgery is the application of plastic surgery techniques to oncological surgery to prevent deformities and reach a proper aesthetic result.
- It is fundamental to promote new lines of research that permit the reduction of morbidity of the oncological treatments in favor of our patients.
- The use of drug matrices destined for control of the hemostasis and/or tissue sealing, such as TachoSil®, have demonstrated their efficacy in different surgical environments. The axillary level may have a relevant role in the control of hemostasis and the formation of axillary seromas.

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3 Primary cytoreductive surgery in advanced-stage ovarian clear cell carcinoma

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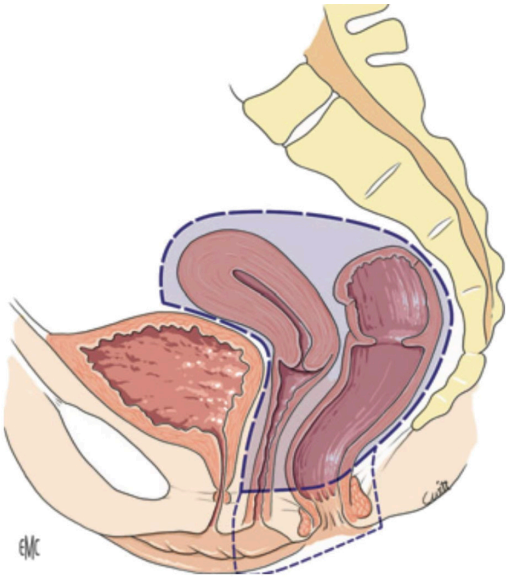

Image 1:
Modified posterior exenteration scheme.

Introduction

Ovarian cancer is the seventh most common cancer among women worldwide. It is estimated that the global index is 6.3 per 100,000 women and it is higher in developed countries[1].

More than 50 % of ovarian cancers are diagnosed in advanced stages and the 5-year survival rate is only 44 %[2].

Approximately 90 % of ovarian cancers are carcinomas (malignant epithelial tumors) and, based on the histopathology, the immunohistochemistry and the genetic molecular analysis, at least five principle subtypes are distinguishable: high-grade serous carcinoma (70 %), endometrioid carcinoma (10 %), clear cell carcinoma (10 %), mucinous carcinoma (3 %), and low-grade serous carcinoma (<5 %)[1].

In the treatment of epithelial ovarian cancer, the only independent factors related to survival that maintain statistical relevance are the size of the residual tumor after the surgery and the chemosensitivity to platinum. The response to chemotherapy and survival are directly related to the residual illness after the surgery, as such, the importance of obtaining a complete primary cytoreduction. The surgery varies in function of the stage of the illness and of the comorbidities of the patient.

The staging of ovarian cancer in the initial stage includes a hysterectomy with double adnexectomy, a complete pelvic and para-aortic lymphadenectomy up to the left renal vein and the supra and inframesocolic omentectomy; in addition to the peritoneal cytology and taking peritoneal biopsies. In other cases where the illness is found in a more advanced stage, the treatment of choice is primary cytoreduction surgery or neoadjuvant chemotherapy if the patient doesn't fit the criteria for surgical treatment[3].

Frequently patients with advanced ovarian cancer present widespread involvement of different abdominal regions, including the large and small intestines. In these cases, the sigmoid colon is one of the most frequently affected areas. This implies that in many occasions it is necessary to resect the intestines to reach the principal objective, which is the complete cytoreduction. One of the procedures performed most frequently in these patients is a radical retrograde oophorectomy or modified posterior exenteration *(→ Image 1)*. In this surgery an opening is made in the retroperitoneal space to later tie the vascular pedicle to the ovary. Continuing with the dissection of the parametrium and tying of the uterine vessels. After which the retrograde colpometry is performed to access the recto-vaginal space. Finally, the mesorectum and the proximal part of the rectum are dissected. The sigmoid colon is resected from above the tumor using wedge resection. Once the descending colon is mobilized, the intestinal bypass is performed by means of an anastomosis or colostomy[4].

Due to the impact in the quality of life the protective stomata have, after the rectosigmoid resection procedure in the cytoreduction for ovarian cancer, direct anastomosis is attempted if the conditions are optimum for performing the surgical technique without increasing the risk of dehiscence.

This surgery is historically associated with an elevated postoperative morbimortality. However, the results in recent publications highlight that it is a procedure that is becoming safer thanks to the advances of imaging tests, a careful selection of the patients, multidisciplinary participation, the neoadjuvant treatments and the improvement in the surgical technique[5].

The incidence of anastomotic dehiscence varies in different series between 1.24 % and 9 % in patients with ovarian cancer[6]. This complication worsens the short- and long-term prognosis and represents one of the principal causes of postoperative mortality and morbidity increasing the hospital stay and its cost. Additionally, it assumes the delay of adjuvant chemotherapy that the majority of these patients require.

Numerous risk factors have been documented in the anastomotic dehiscence in preceding studies: age, nutritional state, neoadjuvant treatment and the experience and technique of the surgical team[6].

For this reason different preventative methods have been studied during the surgical procedure. One of these is the use of hemostatic materials applied to the colorectal anastomosis. The presence of fibrinogen and thrombin around the suture favors the sealing of the suture, and establishes biological bridges that favor healing reducing in this way the risk of anastomosis leaks and fistulas between adjoining organs.

A clinical case of a modified posterior exenteration surgery in the context of a complete primary cytoreduction of an ovarian clear cell carcinoma in advanced stage IIIC is shown below.

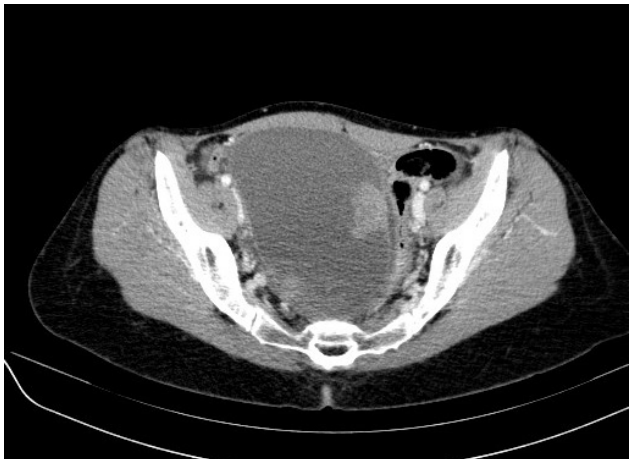

Image 2: Giant adnexal mass.

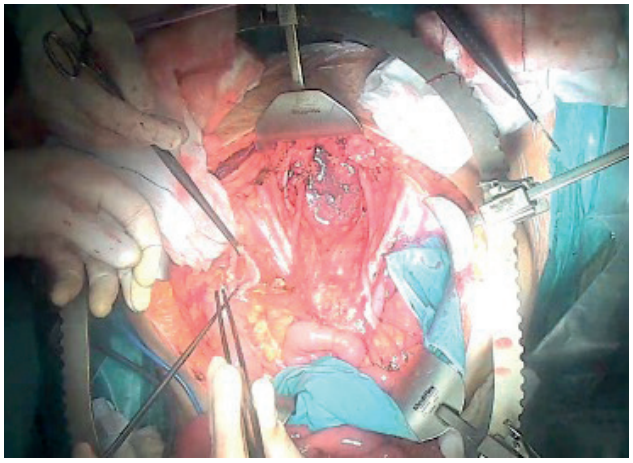

Image 3: Resection of 12 cm of recto sigma. In the image proximal end of left colon after resection.

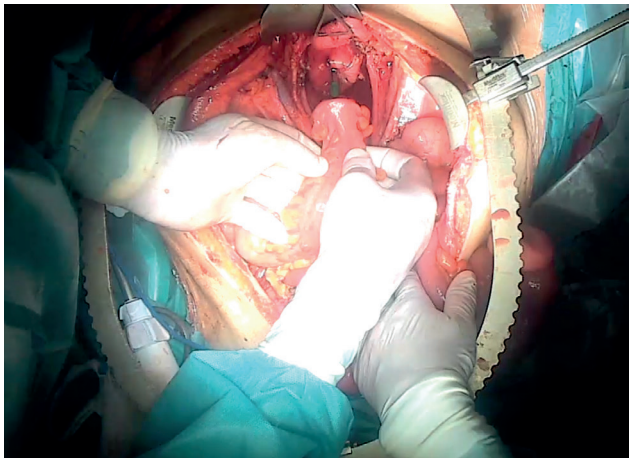

Image 4: End-to-end colorectal anastomosis with CEEA.

Clinical case

Female of 44 years of age, with history of deep ovarian endometriosis. During a routine examination in the Endometriosis Unit, growth of a known cystic lesion is observed with increased tumor markers. The size of the cyst at the last measurement performed 9 months prior was 27 x 32 mm with tumor markers within normal range.

Physical exploration

Uterus in anteversoflexion, not very mobile, with retraction at the level of the retrocervix, very painful to the touch. Anexial mass reaching the umbilical level that appears to depend on the right annex.

Complementary tests

Tumor markers: CARCINOEMBRYONIC ANTIGEN <0.5 ng/ml (0 – 5), CA 125 147.6 (UI/ml) U.I./ml, HE-4 110.9 pmol/l (0 – 108.4), CA 15.3 50.7 U.I./ml (0 – 32), CA 19.9 <1.2 U.I./ml (0 – 37).

High resolution ultrasound: Uterus in anteversoflexion with histerometry of 8 cm. Regular homogenous endometrium of 9 mm. Well-defined endometrial-myometrial line. A small uterine myoma is observed. In the left ovary two endometriomas of 31 mm and 25 mm are observed. In the right annex an image of 12 cm at widest diameter is observed with a score of high risk for malignancy with vascularized papillae. Thickening of torus and left LUS. No skin dilatation.

Abdominal-pelvic CAT scan: Retroperitoneal tumor located in the pelvis, probably dependent on the right ovary, predominantly of cysts with solid poles. Cyst images are observed with Douglas sack bottom highlighting edges, unable to discard relationship to said tumor. Image in left hypochondrium suggestive of peritoneal implant. Probable necrotic interaortocavity adenopathy. Partially loculated free fluid of slightly higher attenuation than water in left parietocolic gutter and pelvis. Nodular lesion with a solid appearance in the left kidney.

MRI: Pelvic cystic mass with solid nodules, partially included, compatible with primary ovarian neoformation. Subscapular hepatic cystic lesions in segments 3 and 6 suggesting simple hepatic cysts.

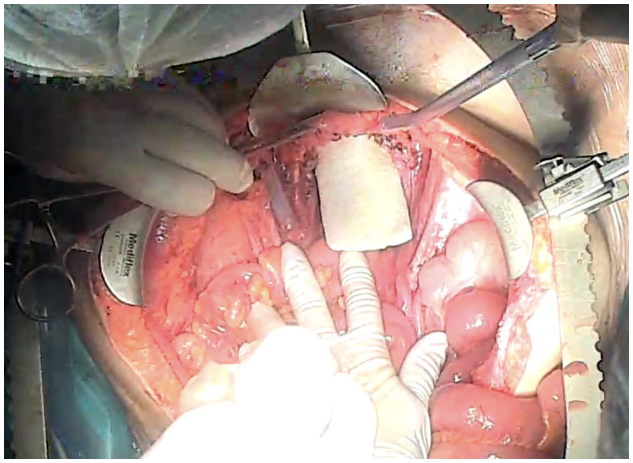

Image 5: Placement of hemostatic material like TachoSil® in colorectal anastomosis.

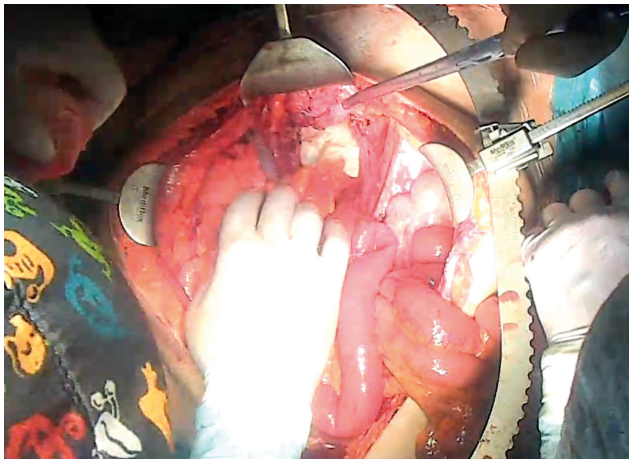

Image 6: Placement of hemostatic material in colorectal anastomosis.

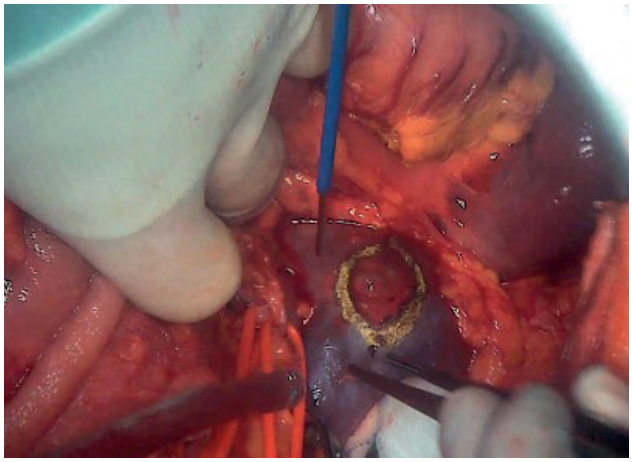

Image 7: Resection of lesion in superior renal pole.

Nodule in left hypochondrium that may be related to the small accessory spleen, less probable implant. Solid hypo vascular neoformation in anterior cortical cortex of the left renal middle third that does not show signs that suggest the presence of macroscopic fat.

PET-CAT examination: Pelvic mass with intense increase of metabolism of possible ovarian origin, suggestive of neoplasm, to be correlated histologically, with possible ganglion affectation in the left external iliac chain and possible millimetric implants in both hypochondrium *(→ Image 2).*

After presenting the case to the multidisciplinary committees it is decided to perform surgery with an interoperative biopsy of the adnexal mass and complete the definitive surgery based on its results.

Surgery – Findings

Tumor in right ovary of 12 cm attached to sigma and Douglas with blocked pelvis. Lymph nodes suspicious of malignancy in the right and left external iliac of 2 cm each. Multiple millimetric implants in the pelvic peritoneum (Douglas and vesicouterine plica). Implant in sigma rectum of 1 cm. Millimetric implants in omentum. Accessory spleen in omentum of 1.5 cm in diameter. Area of carcinomatosis of the right diaphragmatic dome of 6 x 6 cm, left diaphragmatic dome clean. Solid tumor of 2 x 2 cm in superior pole of left kidney.

Surgical technique

Bilateral opening of the retroperitoneum at the level of the psoas, identification of both ureter and external iliac vessels. Resection of adenopathy in territories of both external iliac arteries is performed. Followed by dissection of the bladder plica that is difficult due to the infiltration of the peritoneum tumor. After excision of tumor tissue reinforcement sutures are made in the detrusor muscle. Following this, the bladder sealant is tested without visualization of leakage points. The radical retrograde oophorectomy continues, resecting 12 cm of rectosigmoid (at 15 cm of the anal margin) *(→ Image 3).* Closure of the vaginal dome with continuous suture. End-to-end colorectal anastomosis with CEEA is performed *(→ Image 4).* TachoSil® is left at the level of sigmoid rectum anastomosis *(→ Images 5 and 6)* and rectal sealant test is performed.

Subsequently continuing with supramesocolic omentectomy including accessory spleen and implant on splenic surface. Hepatic mobilization through round and sickle ligament sections and peritonectomy of right diaphragmatic dome with bipolar scissors. Finally a partial left anterior open nephrectomy and removal of lesion of 2 x 2 cm in upper renal pole is performed, previously clamping the left renal artery *(→ Image 7)*.

The following are achieved: Complete Cytoreduction.

Postoperative evolution

Without complications. Hospital discharge after six day stay on gynecology ward.

Anatomy pathological results

Radical oophorectomy: Bilateral ovarian clear cell carcinoma with extensive necrosis associated with endometrial ovarian cysts. Infiltration of tube, peritoneum, uterine serosa and large intestine serosa. Pathological staging: pT3b N0 Mx (pTNM 8th edition AJCC). Stage IIIC of the FIGO (2018 FIGO Cancer Report).

Omentum: Fibroadipose tissue infiltrated by bilateral ovarian clear cell carcinoma.

Diaphragmatic peritoneum: Fibroadipose tissue infiltrated by bilateral ovarian clear cell carcinoma.

Renal node: Renal oncocytoma.

Adjuvanted

Chemotherapy scheme with Carboplatin + Paclitaxel x 6 cycles. 1 cycle every 21 days.

Currently disease free. Posterior examinations without findings.

Discussion

Ovarian cancer continues to be the most lethal form of gynecological cancer. Approximately 70 % of the patients are diagnosed when the disease is found in an advanced stage[3]. Treatment of patients with advanced stage ovarian cancer is based on surgery and adjuvant chemotherapy.

Multiple studies have demonstrated an inverse relationship between the quantity of residual illness after cytoreduction surgery and the illness free interval and survival[7], converting it into the current paradigm of treatment for patients with advanced stage ovarian cancer. This is why it is important to obtain a complete cytoreduction.

To achieve optimum surgical results with a higher survival in advanced stages of the illness, the surgical techniques include pelvic surgery with a bloc intestinal resection as well as surgeries extended to other abdominal structures such as the liver, pancreas, spleen, stomach and including the addition of a transthoracic approach in the case of supra diaphragmatic extension.

For these results to be possible it is essential that the surgical management be performed by an expert multidisciplinary team in gynecological oncology capable of approaching all of the visible illness in any of the abdominal regions.

The decision to perform a direct anastomosis or preventive colostomy is not completely standardized and is competency of the surgical team[8]. The infraperitoneal rectum is invaded in an exceptional way in some patients, which permits the performance of a colorectal anastomosis with healthy tissue in the majority of the cases, conserving good sphincter function[9]. The psychological impact and the quality of life[5] of a colostomy obligates the attempt to perform a direct anastomosis after the resection in selected patients and in those where the surgical technique is feasible.

Anastomotic dehiscence (AD) is one of the most serious complications related to intestinal surgery, especially in the sigmoid rectum resection with low anastomosis. The incidence of this complication oscillates between 2.8 % and 23 % of the colon cancer resections and between 0.8 and 6.8 % for gynecological cancers[10]. The lower rate of complications after gynecology surgeries may be due to a lower frequency of the so called low resections.

The AD after colorectal anastomosis has been associated with high rates of morbidity and mortality, with poorer results in ovarian cancer patients. The habitual absence of post operative complications allows the initiation of adjuvant chemotherapy as soon as possible[7]. The delay in the initiation of chemotherapy has a negative impact on the overall pathological response and significantly affects global survival[11].

Among the risk factors described, different pre-operative factors are found such as obesity (BMI N 30), malnutrition, neoadjuvant chemotherapy and other intraoperatives such as intraoperative bleeding greater than 1 L, reduction of vascularization, or a positive rectal sealant test, as well as factors derived from the surgical technique related to the colorectal anastomosis procedure such as excessive tension, bleeding, hematoma or anastomosis close to the anal border[12].

In advanced ovarian cancer surgery very limited evidence exists, extracted from small samples, that provides information about the risk of anastomotic leaks such as serum albumin ≤3 g/dL, multiple intestinal resections, the distance to the anal border, long operating times and bleeding in excess of 1 L 6.

To reduce the rate of anastomotic dehiscence and other complications such as infections, various methods have been proposed, such as antibiotic prophylaxis, intestinal preparation with antiseptic enema, fecal bypass to protect the high risk anastomosis and the biofragmentable anastomosis ring[11]. External coating of the anastomosis with diverse materials has been proposed as a measure to reduce the rate of leakage[11].

A study carried out in 2013 comprised of 188 patients that underwent laparotomic rectosigmoid surgery and with risk factors established for anastomotic dehiscence (over 70 years of age, neoadjuvant chemotherapy/radiotherapy and/or alteration of their nutritional state) confirmed the security and efficacy of the hemostatic matrix with fibrin as a protective factor in the prevention of anastomotic leakage[13].

In 2010, Huh and its team performed a prospective study in which 223 patients that underwent laparotomic rectal resection participated. One group underwent the surgery followed by the application of a fibrin sealant over the anastomosis, while the other group only underwent the surgery. The rate of clinical leaks was 5.8 % for the group with fibrin and 10.9 % for the other group[13].

The action mechanism of TachoSil® follows the principles of the physiological formation of fibrin clots. When it comes into contact with the surface of a bleeding wound or that has a leak, or it is activated by the presence of physiological saline solution, the collagen coating of the sponge dissolves and the following thrombin-fibrinogen reaction initiates the last step of the coagulation process: the fibrinogen is converted, by the action of the thrombin, into fibrin monomers, that spontaneously polymerize to form a fibrin clot. The thrombin can also activate the factor XIII endogen, that covalently cross-links fibrin to create a firm, stable fibrin network[7].

This stable fibrin clot leads to the sealing of the anastomosis in many ways: the physical barrier created by the fibrin clot, the facilitation of the tissue approximation, the promoting of the tissue healing on behalf of the components and the creation of adhesion to the surrounding tissues.

The security of TachoSil® in the sealing of gastrointestinal anastomosis with a collagen patch covered with fibrin components has been previously demonstrated in a study by Nordentoft et al.[14]. This study revealed an equal healing strength and complication rate after sealing with a collagen patch covered with components of fibrin glue in comparison to the unsealed anastomosis. In addition, no differences in the stenosis of the anastomosis were found. Another benefit of fibrin sealants that was reported is that they reduce intraabdominal adhesions[14]. Also, a study demonstrated that TachoSil® has no negative secondary physiological or histological effects[7]. In another study the viability of the application of TachoSil® for sealing colorectal anastomosis was demonstrated.

An average postoperative stay shorter than 7.2 days was observed in patients in which TachoSil® was applied, compared to 9.3 days for patients where TachoSil® was not used. This difference was principally related to the anastomotic insufficiencies registered in the group where TachoSil® was not used[14].

The use of medicated hemostatic matrices for the reinforcement of the intestinal anastomosis has been safe and efficient, contributing to a reduction in the risk of digestive fistula in patients with high risk of dehiscence because they are oncology patients, undergoing extensive, prolonged surgeries, almost all of whom were previously treated with systemic chemotherapy and were generally malnourished.

This suggests an improvement in the morbidity with the consequent reduction in the hospital stay and its costs[14].

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4 Control of active bleeding using TachoSil® in a radical abdominal hysterectomy

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Introduction

TachoSil® is a hemostatic preparation in the form of a matrix composed of human fibrogen and thrombin. By entering in contact with any fluid (blood for example) these compounds dissolve creating a fibrin clot that strongly adheres to the surface[1].

Initially, the technical use was exclusively for liver surgery. Today it has extended to other surgical disciplines including gynecology and urology surgery.

Diverse studies of different surgical areas exist that seek to demonstrate the additional benefits of the hemostatics of the use of this preparation, such as the prevention of fistulas due to iatrogenic lesions from aggressive surgeries and the reduction of the formation of secondary adhesions resulting from invasive surgical procedures.

Radical abdominal hysterectomy is part of the treatment of invasive cervical cancer. The indication for surgical treatment, will depend on the clinical condition of the disease, the age and health of the patient and the formation and experience of the gynecologist.

This technique comprehends the excision of the parametrial tissue and vaginal fornix.

The lateral parametrium, is a structure through which the tumor extends to the pelvic walls and tends to do so in a discontinuous way towards the lymph nodes and vessels. A partial resection implies the risk of leaving positive parametrial lymph nodes.

The vesicocervical, vesicouterine tissue and utero-sacral ligaments rarely participate in the extension of cervical cancer. The margin of the vaginal cuff must be 2—3 cm with respect to the tumor.

The intervention also includes a prior pelvic lymphadenectomy. Salpingectomy and bilateral oophorectomy do not necessarily form a part of this surgery, preserving it in younger patients. The radicality is established in function of the 2017 Querleu Morrow classification *(→ table 1)*, and references the quantity of vaginal and parametrial tissue removed (margin required with respect to the tumor), that will depend on the size of the tumor and the existence of signs of extension towards the parametrial and vaginal tissue[2].

Following is presented a case of control of active bleeding using TachoSil® in a radical abdominal hysterectomy performed in our center.

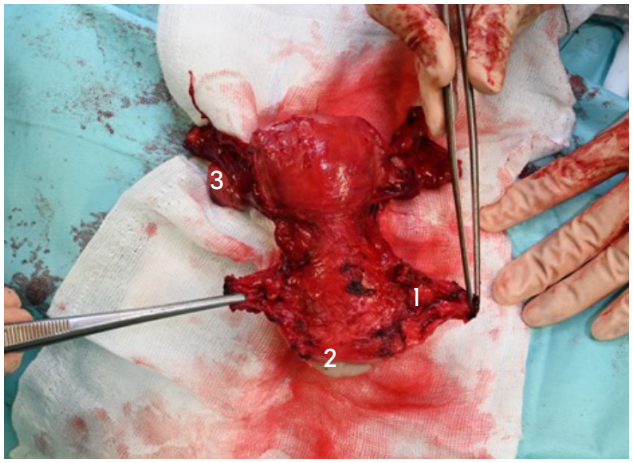

Image 1: Sample from radical hysterectomy with exposure of both lateral parametrium (1), vaginal cuff (2), and adnexectomy (3).

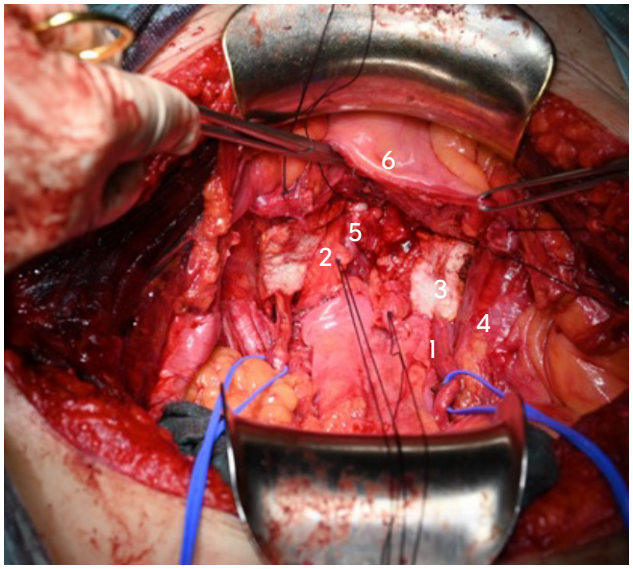

Image 2: Surgical bed after extraction of the sample. Ureter (1), uterosacral ligament (2) TachoSil® (3), psoas muscle (4), vagina (5), bladder (6).

Clinical case

The patient in the case presented, is a female of 45 years of age referred from primary attention by cytology with screening results of: High grade squamous intraepithelial lesion (HSIL) and presence of atypical lymph nodes PCR positive for the human papilloma virus (HPV) of high risk.

Background history of interest, highlights: eutocic delivery, smoking habit of 6 cigarettes a day. Non-user of barrier method. Genetic desires fulfilled.

The patient had not regularly carried out cytology screening control nor was vaccinated for HPV.
The only clinical manifestation was the presence of coitorrhagia.

In the first gynecology consultation visit, a colposcopy was performed describing: an area of transformation type III and an iodine negative lesion at 12 o'clock, having a glandular aspect, with extension into the canal, not able to define the limits. Atypical vessels were visible on the surface and brittleness upon touch. A biopsy of the lesion was taken and an endocervical and endometrial curettage were performed.

The posterior anatomopathological study, revealed the presence of squamous carcinoma both in the biopsy of the lesion as well as in the sample from the endocervical and endometrial curettage.

The posterior exploration described a unique center tumor of 1.5 cm with entrance into the endocervical canal without lesions in the exocervical epithelium. Upon touch, the cervix was mobile and free. It did not give the impression of parametrial infiltration, nor upon rectal exam.

The extension study, with pelvic magnetic resonance, described a tumor of 3 x 2 cm with penetration in the stroma of 18 mm. Not affecting the upper third of the vagina nor transmural to parametrial, FIGO stage IB2.

First, a bilateral pelvic lymphadenectomy was performed using laparoscopy for histological study of lymph node involvement that resulted negative for malignancy.

Second, a radical abdominal Wertheim hysterectomy with double adnexectomy was performed. A radical B1 type surgery with excision of the lateral parametrium (paracervix) was performed at the level of the ureter tunnel and partial excision of the recto-vaginal septum, sacral uterus and vesicouterine ligament (→ *Image 1).*

Querleu-Morrow Type	Paracervix or Lateral parametrium	Ventral parametrium	Dorsal parametrium
Type A Limited radical hysterectomy	Resection of the medial paracervix to the ureter without its mobilization from the ureter bed, but lateral to the cervix.	Minimal excission	Minimal excission
Type B1 Resection of the paracervic at the level of the ureteral tunnel	Lateral mobilization of the ureter and reseccion of the paracervix at the level of its tunnel.	Partial excision of the vesicouterine ligament	Parcial resection of the rectovaginal and utero-sacral septum
Type B2	Identical to the B1 with paracervical lymphadenectomy without resection of the vascular/nerve structures	Partial resection of the vesicouterine ligament	Partial resection of the rectovaginal and utero-sacral septum
Type C1 Section of the paracervix at the union of the vascular system of the internal iliac (Nerve preservation)	Complete mobilization of the ureter and lateralization of the same, with the section of the paracervix at the level of the internal iliac vessels, respecting the caudal portion.	Excision of the vesicouterine ligament in the bladder. Proximal section of the vesicovaginal ligament. Preserving vesical innervation	Excision up to the level of the rectum. Disection and preservation of the hypogastric nerve
Type C2 Section of the paracervix at the union of the vascular system of the internal iliac (No nerve preservation)	Complete mobilization of the ureter and section of the paracervix at the level of the iliac vessels, respecting the caudal portion.	Excision up to the vesical level, sacrificing the vesical innervation	Excision up to the level of the sacral, sacrificing the hypogastric nerve
Type D Extension of the lateral resection	Resection up to the pelvic wall, including resection of the internal iliac vessels and/or wall structures.	Excision up to the bladder Not applicable in case of exoneration	Excision up to the sacral. Not applicable in case of exoneration

Table 1: Querleu Morrow 2017 classification of the types of radical hysterectomies.

During the surgical procedure, numerous adhesions were observed at the level of the posterior and anterior uterine face, omentum and appendages, in addition to an intense fibrous parametrial, possibly secondary to prior surgery of lymph node staging. After the extraction of the piece in a single block, sheet bleeding in the surgical bed was observed, especially at the level of the roof of the ureters, posterior face of vesicouterine plica and both external iliac veins.

After several minutes of digital compression, persistent bleeding was identified, so two TachoSil® sponges were placed on both sides, with the objective of controlling it *(→ Image 2)*.

Discussion

The principal objective of radical hysterectomy in initial stages of cervical cancer is curative. The radicality of the technique demands that the surgeon have an exhaustive knowledge of the locoregional anatomy and of the different techniques to control the possible complications that can occur during the same[2,3]. This surgical technique implies the exposition of the noble structures such as the external iliac veins or the ureter.

Lower urinary tract dysfunction is the most frequent complication of this surgery. It occurs in 20–80 % of the patients, and one of the causes is the iatrogenic lesion of the ureter[4]. Which is why it is fundamental to know its route throughout the pelvis and identify any possible intraoperative lesion to avoid future complications.

Ureterovesical and vesicovaginal fistulas are rare, with an incidence of 2—0.9%, respectively. They are more frequent in aggressive surgeries of large tumors[4].

Arterial bleeding tends to be easy to solve. However, bleeding form the large trunk veins, can cause serious hemorrhaging that is difficult to control. Therefore, the surgeon must have a thorough knowledge of the exposed vascular structures and be very familiar with the fundamental techniques of hemostatic control, among which are found the hemostatic preparations such as TachoSil®[5,6].

In the case presented, the complexity and aggressiveness of the surgical technique was greater because it was a second surgery.

As such, in the first place, the presence of multiple adherences increased the risk of iatrogenic lesion to neighboring structures. This was due to the secondary anatomical alteration upon finding the uterus and its appendages joined en bloc to the vesical region and pelvic walls. This fact increased the difficulty in the identification and isolation of the limits of the intervention.

In the second place, the hemostatic control was more difficult due to the increase in the bleeding sites secondary to adhesiolysis, technique that was necessary at various points in the surgery, to adequately expose the structures to be resected.

Employment of TachoSil® in the case presented, was an effective and safe option for the control of the bleeding on the external iliac vein and ureter.

The knowledge and application of slightly invasive and fast acting hemostatic techniques such as TachoSil® seem to be a good alternative to situations similar to this, where the bleeding is produced on structures whose lesion with other hemostatic control technique such as electrocoagulation, can cause more harm than good[7].

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5

Dissecting subcutaneous hematoma post hysterectomy: use of a fibrin medicated matrix for vaginal vault hemostasis

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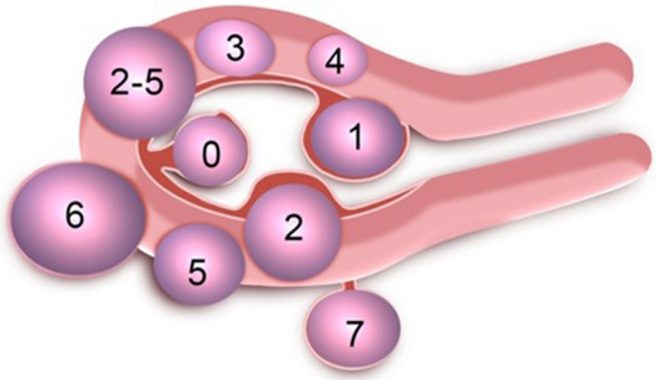

Image 1: FIGO classification of the uterine myomas taken by Munro M et al.[3]

type 0 = pedicled, intracavity;
type 1 = submucosa, < 50 % intramurals;
type 2 = submucosa, ≥ 50 % intramurals;
type 3 = contact with the endometrium, = 100 % intramurals;
type 4 = intramurals;
type 5 = subserosa, ≥ 50 % intramurals;
type 6 = subserosa, < 50 % intramurals;
type 7 = subserosa, pedicled;
type 8 = others (i.e. Paracervical).

When two numbers are combined (i.e. 2 – 5), the first number refers to the relation with the endometrium, while the second refers to the relation with the serosa.

Introduction

Hysterectomy is the most frequently performed gynecological surgery in the world both in benign and malignant pathologies. For consent, patients must be offered complete information about the benefits and potential risks during and after the procedure. In addition, each patient's characteristics must be taken into consideration (BMI, age, comorbidities...) as well as their pathology (uterine size, benign or malignant pathology...) to establish preoperative risk. The complications that may arise are those general to any surgical procedure, such as infection, bleeding or damage to neighboring structures, and those specific to a hysterectomy, the dehiscence or vaginal vault prolapse, pelvic abscesses and fistulas[1,2].

One of the indications of hysterectomy in benign pathology are myomas. This is a benign tumor that affects from 50 – 60 % of the women, and that is made up of smooth muscle. It is calculated that in perimenopause up to 70 % of women have them, but only 30 % demonstrate symptoms. Metrorrhagia and a heavy or tight pelvic sensation are the most frequent symptoms. Other clinical cases the patients may present are pelvic pain (especially when there is vascular degeneration), infertility and the sensation of an abdominal mass[3].

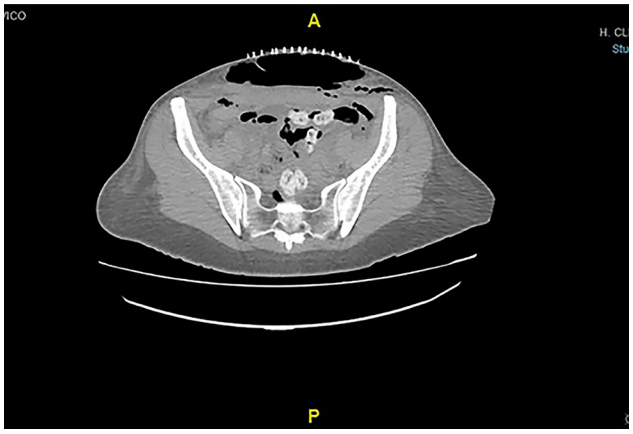

Image 2: Subcutaneous collection in transversal cut of the CAT scan at the level of staples.

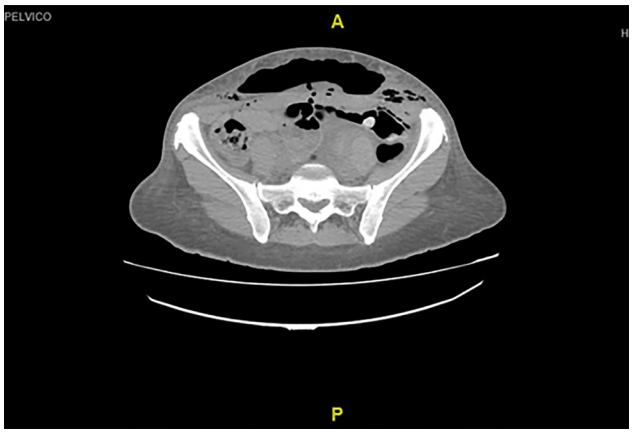

Image 3: Subcutaneous collection in transversal cut of the CAT scan and free liquid at the pelvic level.

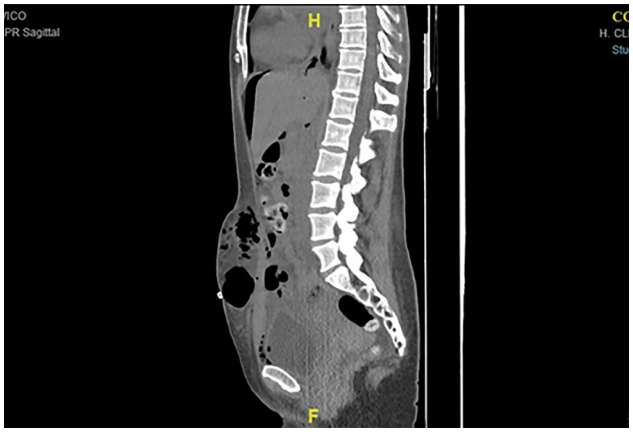

Image 4: Subcutaneous collection in sagital cut of the CAT scan and pneumoperitoneum.

There currently exists a classification of myomas that easily permits the characterization of their type and location. According to the classification of the International Federation of Gynecology and Obstetrics (FIGO for its Spanish acronym) there are currently 7 types of myomas, each of which differs with respect to its symptomology and therapeutic approaches[4] *(→ Image 1)*. The partial or total hysterectomy by laparoscopy or laparotomy is the treatment of choice in women whose genetic desires have been met, in some cases being performed through the vagina[5].

Among the possible complications of abdominal surgeries such as a hysterectomy, are subcutaneous hematomas. These consist of the accumulation of blood between the tissues that tend to separate them, which at the same time can cause an infection in the surgical wound. Their diagnosis can be immediately after the surgery or later, and classically cause pain, local swelling, and/or drainage of material. Small hematomas can be treated by observation, while large collections should be drained. Subcutaneous hematomas can also originate from deeper hematomas due to dissection of all of the layers until reaching the subcutaneous[6].

Since the beginning of the XX century different products known as hemostatic agents have been developed to prevent the appearance of these type of complications and their use has increased in recent years in multiple specialties, including gynecology.

We present a case in which the use of TachoSil® was necessary for the hemostasis of the vaginal vault.

Clinical case

Female of 45 years of age that had a total hysterectomy due to symptomatic myxomatous uterus. She was under ambulatory follow-up for two years after the incidental diagnosis of a FIGO type 2—5 myoma on the anterior side of the uterus of 90 x 70 mm. Personal background of interest highlights previous morbid obesity (intervened with bariatric and plastic surgery), appendectomy, and laparoscopic myomectomy. The patient was informed of the possibility of observation management while she remained asymptomatic, but after a year of observation, hypermenorrhea, short menstrual cycles (every 21 days) and pelvic pain began, so surgical treatment was requested.

The patient was programmed for a simple laparotomic hysterectomy, the intervention was carried out without interoperative complications, identifying during the surgery a uterus increased in size at the expense of the myoma on the anterior side, of 8 cm and macroscopically normal ovaries that were not removed. The closure of the vaginal vault was performed using loose double stitches identifying light bleeding that was solved with fulguration with electric scalpel and mechanical compression. No peritoneal closure or approximation of the rectus abdominis muscles was performed, the aponeurosis was sutured with two hemi continuous sutures and the skin with staples.

In the immediate post operative period (first 24 hours after the intervention) the patient appeared in overall good condition, adequate oral tolerance and gas expulsion. Constant monitoring reflected that she was apyretic and normotensive. The physical abdominal exploration was slightly painful, with the surgical wound in good condition. The urinary probe was withdrawn, and she was allowed to walk. However, between 24—48 hours of the surgery the patient upon standing suddenly presented an increase in the abdominal perimeter above the surgical wound accompanied by diffuse and intense pain.
The patient was re-examined observing pallid skin and distended abdomen on the upper left side painful to the touch. An abdominal ultrasound revealed aponeurosis apparently integral and abundant loops with pronounced peristalsis below it. The patient progressively complained of the pain and of the abdominal perimeter. The surgical wound was in good condition palpating a much softer abdomen below this which raised suspicion of eventration.

On auscultation, hydro area sounds were present. An urgent hemogram revealed hemoglobin of 7.3 g/dl and hemocrit of 22 %, indicating the urgent performance of a CAT scan and the transfusion of two red blood cell concentrates in case a possible surgical re-intervention was necessary. In the CAT scan no signs of eventration were observed, but there was abundant free intraabdominal liquid and large subcutaneous emphysema in the region of the surgical incision. Pneumoperitoneum was also described, normal in the context of the postoperative patient, and minimal bilateral pleural effusion *(→ Images 2, 3 and 4).*

Due to the clinical decline it was decide to re-intervene the patient. After the opening of the skin abundant clots were identified in the subcutaneous cellular tissue that dissected this plane with an extension of approximately 15—20 cm. During the review of the pelvic cavity a stitch with active bleeding in the vaginal vault was observed as the only possible origin of the hemoperitoneum and the subcutaneous hematoma. The angles of the vaginal vault were reinforced with sutures and the placement of a TachoSil®
(fibrin sealant patch) as a medicated hemostatic matrix on the same, checking the correct hemostasis upon finalization of the intervention.

After the surgery the patient presented an evident symptomatic improvement. The control hemogram showed a hemoglobin of 8.8 g/dl and hemocrit of 26 %. Patient was discharged three days later.

One month after the intervention, the patient appeared with a surgical wound in a good state of healing. A transvaginal ultrasound was performed where there were no findings suggestive of persistence of free liquid and in the anatomopathological report a uterus with benign leiomyoma was confirmed.

Discussion

The dissecting hematoma of the subcutaneous cellular tissue is a very infrequent entity whose diagnosis doesn't differ from other similar acute processes such as spontaneous hematomas in the muscles of the abdominal wall, the Morel-Lavallée syndrome or non-dissecting post operative subcutaneous hematomas. It should be noted that patients with hemorrhagic diathesis or chronic anticoagulation are more propense to these types of complications[7].

Currently, for the correct diagnosis of this pathology we have ultrasound and CAT scan. In the ultrasound the most common finding is the visualization of a lesion occupying the space, located in the soft parts, heterogenous and with hypoechoic areas alternating with other hyperechoic. The abdominal CAT scan can be carried out with or without contrast and permits the classification of the hematomas in different types according to the findings observed. The hematoma appears like a homogeneous or heterogeneous collection, contained within the subcutaneous cellular tissue, being possible to detect zones of hyper density in the initial hours[8].

The treatment of choice should initially be conservative and consist of rest, analgesics and anti-inflammatories. In cases where a postoperative active hemorrhage or hemodynamic repercussion are suspected, surgical treatment may be necessary to evacuate the hematoma and perform hemostasis of the bleeding vessel that originates it[8].

To avoid complications derived from hemostatic problems there are numerous products in the market approved by the U.S. Food and Drug Administration (FDA) that have the indication for surgical hemostasis. They can be divided into four subcategories: mechanical agents, biological agents, thrombin agents and fibrin agents. Each category differs in the action mechanism, the formulations available, the ease of use and the possible secondary effects. The mechanical agents are spread to stop active bleeding, activate the platelet aggregation and provide a framework to accelerate the inherent clotting functions. The biological agents provide thrombin that converts the fibrinogen of the patient in a fibrin clot. The thrombin agents can be combined with pH neutral mechanical hemostatics (ie: gelatin granules) to create the category of fluid hemostatics. As the gelatin spreads to mechanically stop the bleeding, the thrombin component converts the fibrinogen of the patient into fibrin triggering the clotting cascade. Finally, the fibrin agents, used in our clinical case, function by providing supraphysiological levels of fibrinogen and thrombin that when mixed, form a fibrin clot at an accelerated speed. The concentration of the fibrinogen determines the strength of the sealant, and the concentration of thrombin determines the velocity of the formation of the clot. These products can come already commercially packaged or they can be prepared in the operating room[9]. Concretely, TachoSil® is a device prepared to be used directly. The yellow side (active side) of the patch is applied over the clean surface of the area for hemostasis and it is pressured with a humid surgical pillow during 5 minutes. This produces the fibrinogen-thrombin reaction imitating the last phase of clotting that leads to the conversion of fibronogen into fibrin monomers[10].

The use of hemostatic agents in gynecological surgery has increased in recent years, making further investigation regarding the efficacy and risks of its use in benign cases necessary. Santulli et al.[10] evaluated the viability and efficacy of the use of TachoSil® in obstetric and gynecological surgery. They used this fibrin agent in 84 women, 21 of which had benign gynecological surgery as indication, 17 of them myomas. The application of Tachosil® resulted in a complete hemostasis in 81 of the patients with only 3 women requiring surgical reintervention. Their study design was based on two prior series. In the first the rate of intraoperative bleeding and transfusion of 1,460 women that had undergone total hysterectomy laparoscopic surgery for benign uterine pathology, where they observed an intraoperative bleed rate of 1.3 % and a transfusion rate of 0.6 %. In the second they analyzed a 5-year history of the incidence of postintervention bleeding in 167 women intervened for total hysterectomy by laparoscopy or vaginally, where the post intervention bleeding incidence was 0.85 %. Both authors postulate that these hemorrhaging complications could have been avoided with the use of a fibrin agent, as had already been demonstrated by Ochial et al in a previous study with TachoComb®, its predecessor[11]. This study evaluated the hemostatic control of 16 women intervened for myomas, cervical cancer, endometrial cancer, endometriosis or pelvic inflammatory disease where said material was used. In 14 of them the hemostasis was total, and the two remaining it was qualified as adequate.

In our case we could prove that the management of a hemorrhage that could not be resolved by only using selective vascular closing methods of hemostasis (sutures or electrosurgery), could benefit from other additional methods, such as the application of a hemostatic topical agent that helps to control the bleeding, even in a second instance. Their synergistic application from the first surgery could have prevented the reintervention, but in many cases these agents are used only when the first measures fail. Additional studies investigating whether its use from the first moment can be of benefit to the patient, when a higher risk of bleeding can be foreseen, would be of great interest to our area.

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6

Massive secondary hemoperitoneum in gestation in rudimentary horn of unicornuate uterus

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Introduction

The incidence of congenital uterine malformation is 1/200 – 1/600 women of child-bearing age. Although their prevalence is not well established, since the majority tend to appear asymptomatically[1,2].

The müllerian malformations are produced by alterations in the development of the Müller ducts during embryogenesis. Concretely the unicornuate uterus is the result of an incomplete development of one of the Müller ducts and an incomplete fusion of both. The incidence in the general population is 0.1%[3,4].

According to the American Fertility Society, there are 4 types of unicornuate uterus: those that present a rudimentary horn with a communicating cavity with the unicornuate uterus (class II A), those that have a rudimentary horn without a communicating cavity (class II B), those that only have a rudimentary horn without a cavity (class II C), and lastly, those that lack a rudimentary horn (class II D)[4].

Gestation in a rudimentary horn is considered as an extreme case of ectopic gestation. The prognosis is very bad. The most severe complication is the rupture of the rudimentary horn that tends to appear as a severe condition of massive hemoperitoneum in the second trimester of gestation, as in the case presented.

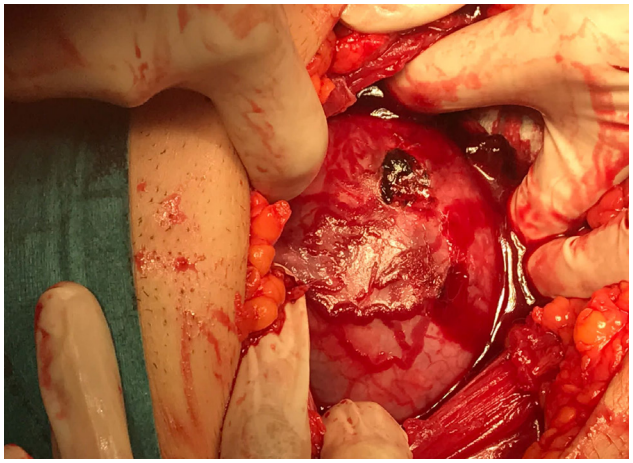

Image 1: Uterine surface with bleeding hypertrophic vessels causing the massive hemoperitoneum.

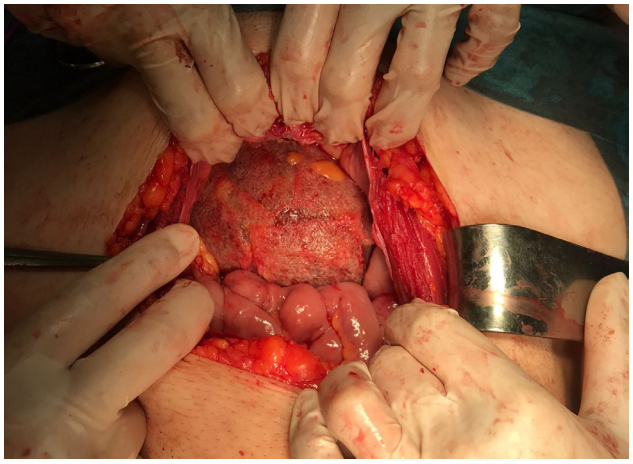

Image 2: Uterine surface covered with TachoSil®.

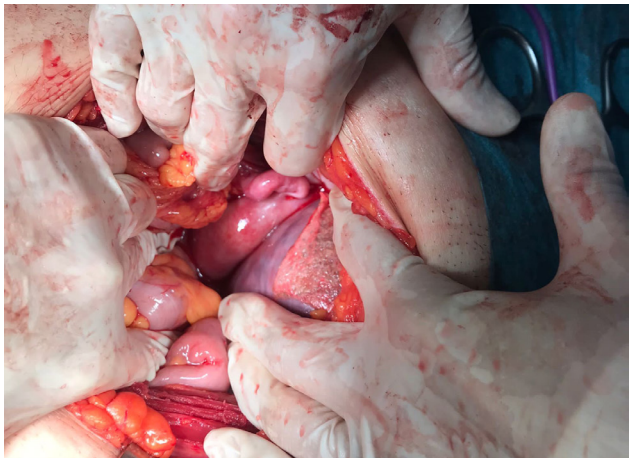

Image 3: Identification of normal left hemi uterus.

Clinical case

36 years of age woman, nuliparous pregnant of 15 weeks and 6 days, controlled in the external offices, comes to the emergency service of the Hospital Universitario Joan XXIII due to the sudden onset of pain in the right iliac fossa irradiating towards the ipsilateral lumbar zone. Without other associated clinical symptoms. No medical or surgical history of interest. Hemodynamically stable. Upon exploration, the abdomen shows signs of peritonitis. An obstetric ultrasound is performed identifying a uterus didelphys with viable gestation that corresponds with 16 weeks in the right hemi uterus and a moderate amount of free liquid in Douglas pouch, motivating an extended study with an abdominal ultrasound that reports abundant intra-abdominal free liquid of non-filial origin, without being able to identify the cecal appendix.

While in the emergency room, the patient presents a clinical decline and a progressive anemia, reason for which it is decided to perform an exploratory laparoscopy. A massive hemoperitoneum of approximately 2 liters is identified in the left hemi uterus with a normal appearance with a gestating right rudimentary horn with some hypertrophic and tortuous vessels on the surface with active bleeding. Attempts to perform hemostasis through monopolar and bipolar energy and hemostatic powders are unsuccessful, so a reconversion to laparotomy is performed, and finally satisfactory hemostasis is achieved covering all of the uterine surface with TachoSil® *(→ Images 1, 2 and 3).*
Three red blood cell concentrates are transfused intraoperatively and fetal viability is checked at the end of the procedure.

By controlling the bleeding, the hemodynamic stability of the patient is achieved who is awakened to inform, both her and her partner, of the diagnosis, of the therapeutic possibilities and the prognosis.

Afterwards, an MRI is performed that describes the presence of a left unicornuate uterus with a gestating communicating rudimentary right horn (class IIA/U4a) with a very thin wall, myometral thickness of < 2 mm, and signs of placental accretism *(→ Images 4 and 5).*
With the result and consensus of the couple, a differed excision of the gestating rudimentary horn is planned.

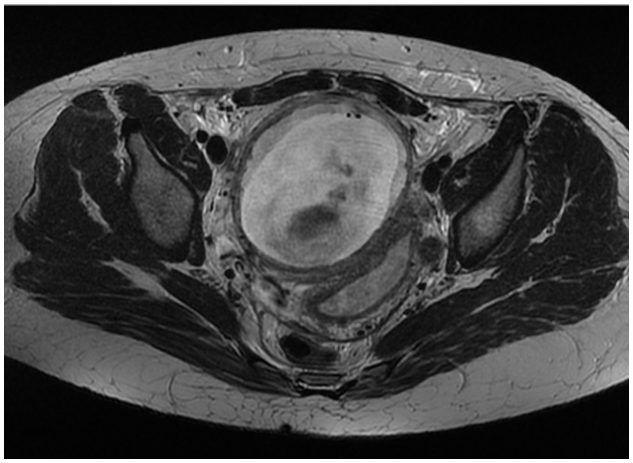

Image 4: Transversal MRI cut showing the existence of a left unicornuate uterus with a gestating right rudimentary horn with a thin myometrium and signs of placental accretism.

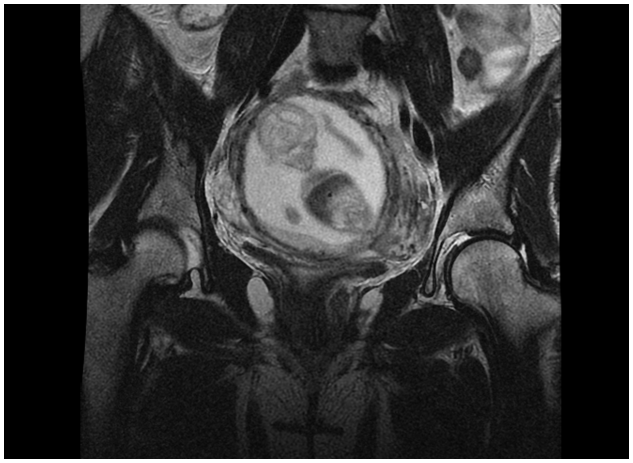

Image 5: MRI Vault cut where the gestation in the rudimentary horn can be seen with a thinning myometrium.

Finally, the patient is re-intervened. Previously a temporary occlusion is performed using a selective balloon of hypogastric arteries for improved control of the bleeding and, afterwards, the gestating rudimentary horn is excised with its ipsilateral tube, with minimal bleeding during the surgical intervention *(→ Images 6, 7 and 8).* The patient has a favorable postoperative evolution and is discharged after three days. The anatomopathological report informs of a 16-week gestation in the rudimentary horn with a maximum myometrial thickness of 13 mm and a placenta increta.

Currently, the patient is asymptomatic, satisfied and comfortable with the decision made. The patient has had posterior menstruations and in the posterior control ultrasound a normal left hemi uterus is observed.

Discussion

The unicornuate uterus associated with a rudimentary horn with communicating cavity, (class II A according to the American Fertility Society classification, class U4a according to the European Society of Human Reproduction and Embryology (ESHRE)/European Society for Gynaecological Endoscopy (ESGE) classification) constitutes 10 % of all cases of unicornuate uterus. One-third of these cases are associated with renal malformations[5,6].

It is estimated that pregnancy in a rudimentary uterus has an incidence of 1/76,000 – 1/160,000 pregnancies[1,3]. The importance of its early diagnosis is essential to reduce the maternal morbi-mortality, since the rate of rupture of the rudimentary horn is 80 % and is associated with mortality of 0.5 %[2,5,7]. It tends to appear with a massive secondary hemoperitoneum upon rupture of the wall and the rudimentary horn vessels, due to the thinning of the myometrium during the development of the gestation. The time of its appearance varies from 5 to 35 weeks of gestation, in function of the thinkness of the myometrium of the rudimentary horn, establishing a directly proportional relationship between the weeks of gestation and the thickness of the same[1,4]. It is estimated that in 70 – 90 % of the cases, the rupture occurs in the second trimester of gestation, as in the case presented[6,7].

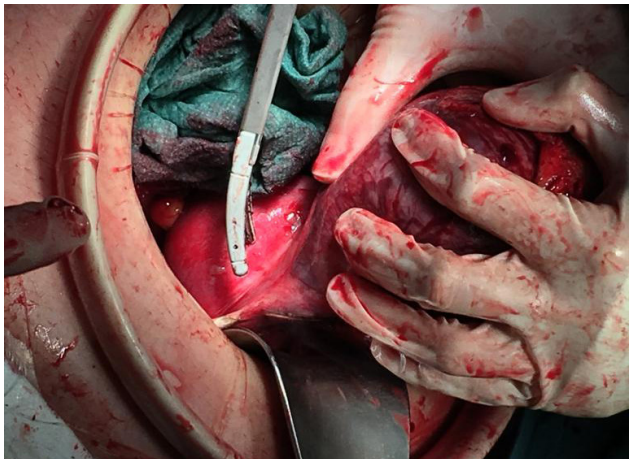

Image 6: Excision of gestating rudimentary horn and ipsilateral tube.

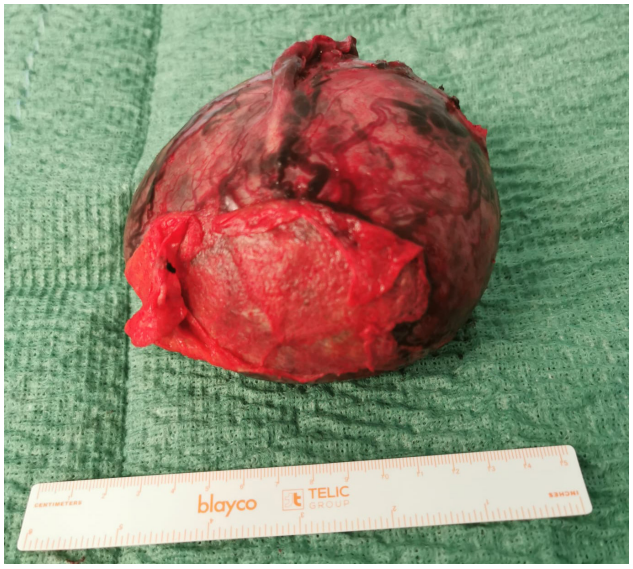

Image 7: Gestating rudimentary horn with previous TachoSil®.

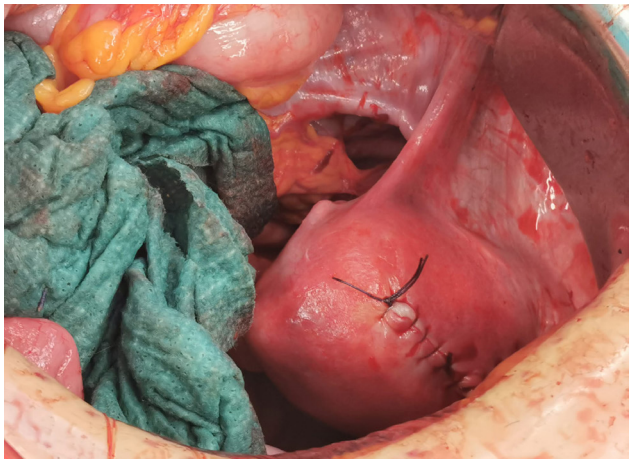

Image 8: Left hemi uterus on completion.

Reviewing the literature, there is a case described in which gestation to full term is achieved, with the rudimentary horn gestation being an accidental find during a cesearan[8]. The degree of development of the rudimentary horn is found to be closely related to the course of the gestation.

For this reason, the imaging tests such as ultrasound and MRI can be useful in order to prevent a rupture, since it has been shown that a myometrial thickness <2 mm presents a high probability of uterine rupture[7].

For early diagnosis, a series of criteria have been established such as: the presence of a bicorporal asymmetric uterus, the absence of continuity between the cervical canal and the cavity where the gestation is found, and the presence of myometrial tissue around the gestation sac. All of these evaluated by ultrasound, although the MRI can provide more information about the diagnosis. The incidence of placenta acreet is increased in the cases of rudimentary horn gestation[1,7].

The confirmation of the diagnosis is intraoperatory, since the majority of the cases require an urgent laparotomy due to the severity of the case with which they usually debut. In our case, the ability to control the bleeding with the use of Tachosil® in the first surgery, allowed us to be able to inform the mother of the diagnosis, and to be able to better plan a differed surgery. The treatment consists in the excision of the rudimentary horn along with the ipsilateral Fallopian tube. This conservative treatment will be the election in nuliparous women with the desire to become pregnant, although in some cases a total hysterectomy is the only possible treatment. The use of imaging tests and a correct diagnosis of the type of malformation is of great usefullness to the surgical approach. The way to approach the surgery will be determined by the severity of the case. After the surgery, the intergenesic period recommended for a new pregnancy is one year, and it should be considered a high risk pregnancy[2,5,6].

With respect to the management of the unicornuate uterus with a rudimentary horn with functional endometrium prior to gestation, some authors are partial to excising it to reduce future obstetric complications[8]. Although there is no solid clear evidence for its recommendation.

In conclusion, pregnancy in the rudimentary horn should be included as a differential diagnosis before the case of an acute abdomen in the second trimester of gestation. Its suspected diagnosis should be as early as possible in order to avoid the possible complications and reduce the associated risk of maternal mortality.

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7

New methods to achieve an adequate hemostasis in breast cancer

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Guadalajara University Hospital

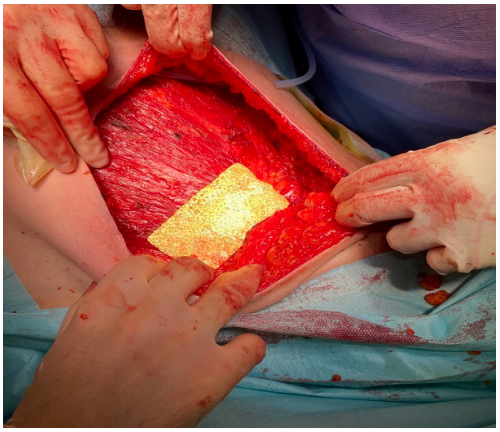

Image 1: Aspect after the immediate application of TachoSil® in the surgical bed of the mastectomy.

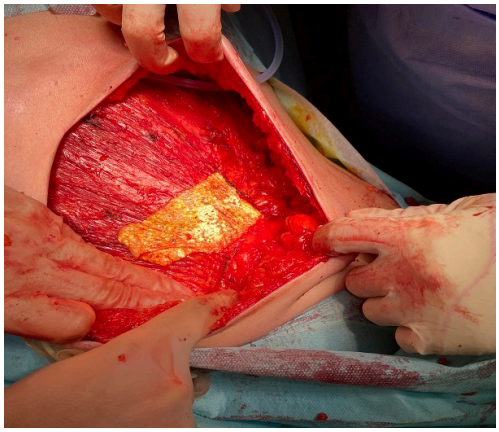

Image 2: Aspect of the drug treated matrix integrated in the tissue a few minutes after its application, observing the absence of bleeding in the surgical bed.

Introduction

Being consistent with the greater demands and performance that is expected of health professionals in the XXI century, we not only need to provide solutions to patient's health problems, but in addition, we must ensure that the techniques we perform are safe and have the least possible negative implication for the patients.

Surgery, a fundamental part of treatment, becomes more complex and technical every day, even more so in oncology patients, and therefore, must be based on achieving the therapeutic objective without inducing iatrogenesis.

The most relevant complications resulting from surgery are: infection and hemorrhage. Adequate hemostasis in the surgical bed is fundamental to prevent future complications and avoid the need for reintervention that can create higher morbidity for the patient.

Today we have tools available that help to obtain this desired hemostasis in an adequate way.

With this clinical case we want to show the benefit of the use of new hemostatics in patients operated for breast cancer.

Clinical case

We present a patient of 50 years of age, allergic to quinolones and asthmatic, without other personal history of interest and with family history of postmenopausal breast cancer in two of her cousins. During the population screening program she is diagnosed with an oncological process in the right breast. It is a case of a multicentric tumor of approximately 35 mm in the upper external quadrant of the right breast with a retro areolar component, that after biopsy returned a result of luminal infiltrating lobular carcinoma A.

In the operating room a modified radical mastectomy was performed on the right breast with a selective biopsy of right sentinel lymph nodes that resulted negative.

After extracting the surgical mass sheet bleeding was observed in the area in contact with the pectoralis major muscle, without an identifiable origin, that did not stop in spite of habitual measures. For this reason we decided to apply a local hemostatic (TachoSil®) in the surgical bed, placing the active side over the pectoralis muscle. After 3 to 5 minutes of compression on the same, adequate hemostasis was observed. The plastic surgery service inserted an expander to be able to insert a prosthetic breast and after this, finalized the intervention without further incidents.
A Blacke type drain was placed in the bed of the mastectomy to control the bleeding.

The postoperative phase passed without incident. The drainage debit was serohematic, being 250 cc on the first day and 200 cc on the second day. After 2 days from the intervention the patient was discharged due to overall good condition. Afterwards in her health center pertinent surgical wound care was applied and drainage was controlled until it could be removed.

In the control performed one month after the surgery, the patient was in good condition overall and the surgical would was healing well. In addition, the anatomopathology reports of the surgical mass were collected and she was informed that she would need to receive radiotherapy, hormone therapy and chemotherapy to complete the treatment.

Discussion

According to the TachoSil® technical specifications, this medicated matrix, composed of human fibrinogen and thrombin on its surface, is also indicated as a support treatment in surgery to improve hemostasis, to favor tissue sealing and as a reinforcement of sutures in vascular surgery when the standard techniques prove to be insufficient[1].

In the case of patients with breast cancer, not only is it important to excise the tumor, this surgery has a significant aesthetic impact as well, that today we are able to minimize with immediate mammary reconstruction techniques.

These procedures that take place after the surgery and that are so important for the patient, require an adequate hemostastis, without which they cannot be performed safely, with the impact that this supposes for the patient from the physical and psychological point of view.

Surgical techniques continue to advance and are more complex, which is why we cannot forget the development of hemostatic substances that minimize the possibility that these and other complications appear.

Different materials that help to obtain an adequate hemostasis are available, that result in greater benefits and safety for the patients.

It is, therefore, a route to explore in which investigation and innovation are fundamental.

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Hemostatic matrix in breast surgery for the prevention of post-surgical complications

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Introduction

Breast cancer is the most frequent neoplasm in women worldwide, with a global incidence of 2 million women per year, approximately[1], supposing a representation of 30 % of the tumors in the female population in Spain. Although it is true that the risk of developing breast cancer has increased in recent decades, currently in developed countries it has remained stable and even presents a declining trend[2]. Also, a reduction in the associated mortality has been identified, due both to early diagnosis of this pathology (associated to screening programs and public awareness), as well as to improvements in the treatments used and multimodal therapy. Once the diagnosis is established, the election of the therapeutic protocol to follow in this type of tumor will depend on factors such as the prognosis, the subrogate type and the stage, with the objective of individualizing and personalizing the treatment of each patient.

Surgical treatment is one of the pillars of treatment for breast cancer, with the objective of carrying out a local control of the illness, a complete study of the tumor and a lymph node staging of the illness. Whenever it is possible, conservative surgery is the choice, pursuing the objective of performing an excision of the tumor with free margins and an optimal aesthetic result, highlighting as well the line of oncoplastic surgery.

Nonetheless, these interventions are not exempt from complications, highlighting among them hemorrhaging, lymphorrhagia, abscesses and infections, seromas and nerve or vascular lesions.

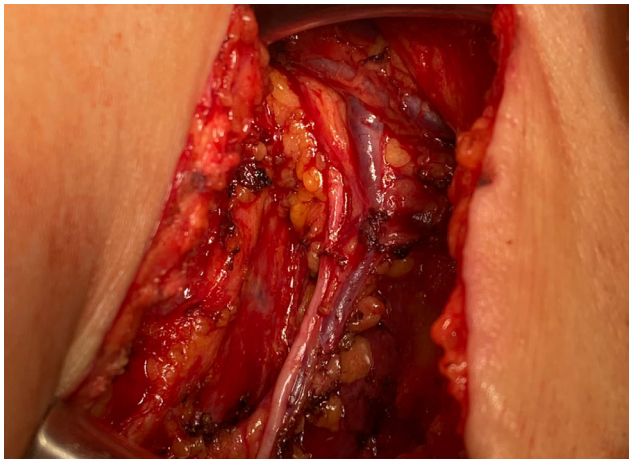

Image 1: Surgical bed after axillary lymphadenectomy, identifying the principle anatomical limits of the same: superior (axillary vein), deep (subscapular muscle), external (latissimus dorsi muscle) and internal (serratus muscle).

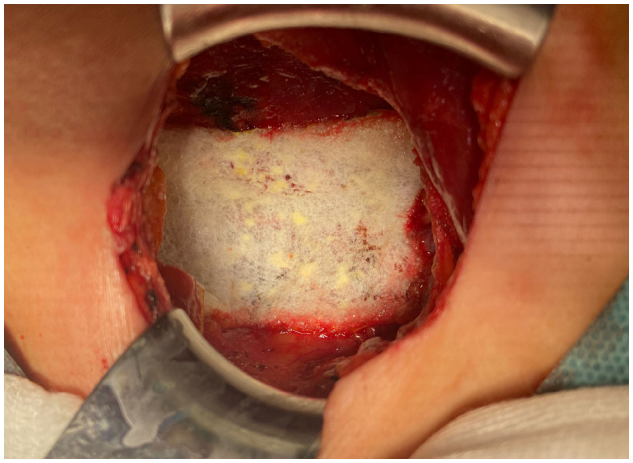

Image 2: Axillary lymphadenectomy surgical bed after application of local hemostatic (TachoSil®).

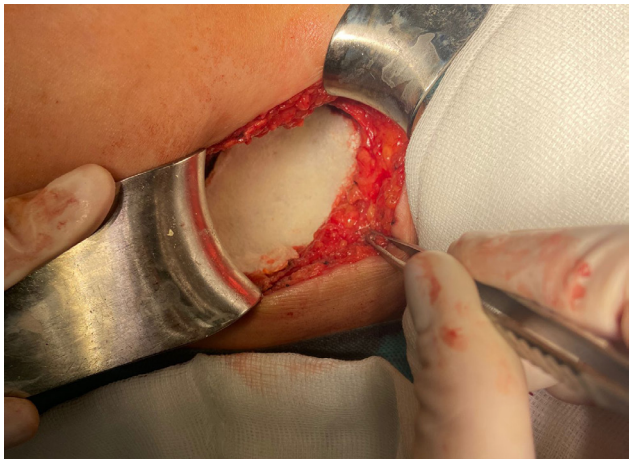

Image 3: Axillary lymphadenectomy surgical bed 3—5 minutes after the application of medicated matrix (TachoSil®), correct hemostasis.

Clinical case

Woman of 74 years of age, without known allergies to medications with personal history of high blood pressure and dyslipidemia under treatment with enalapril and simvastatin. Nulliparous, menopause at 54 years of age. Family history includes breast cancer in maternal grandmother.

The patient comes to the breast pathology offices at our center in June 2021, referred by Primary Care due to a suspicious mammogram. In the physical exploration of the breast, a suspicious nodule of 2 cm is palpated, with poorly defined borders, in the superior external quadrant of the left breast, without apparent axillary or supraclavicular lymphadenopathies.

Also, the bilateral mammogram with tomosynthesis showed a spiked nodule in the quadrant of reference, with some associated skin retraction, that in the complementary breast ultrasound, corresponded to a solid, hypoechogenic nodule, of irregular morphology and with bad sonic transmission of approximately 22 mm, with suspicious characteristics, resulting in a request for an echo guided biopsy and magnetic resonance with contrast. In this last diagnostic test, a new nodule with poorly defined spiculated margins of 22 x 20 x 18 mm appears in the superoexternal quadrant of the left breast (at 7.4 cm of the nipple and 10.5 cm of the pectoral muscle), isointense with parenchyma in power sequences in T1 and slightly hypertense in STIR. After intravenous administration of contrast, it shows a ring enhancement with type III dynamic curves. At the axillary level, a sub centimeter left axillary lymph node is identified, with a preserved fatty hilum and slightly increased cortical thickness, nonspecific, evaluated and biopsied by ultrasound as well.

Both the results of the breast and axillary biopsies resulted pathological, with diagnosis of micropapillary infiltrating carcinoma, with positive estrogen receptors (100 %), positive progesteron receptors (40 %), negative for Her-2 oncogene by immunohistochemistry and a tumor proliferation rate (Ki67) of 15 %. The left axillary lymph node shows extensive infiltration by carcinoma similar to the accompanying breast biopsy.

After confirmation of the diagnosis, an extension study is requested, without signs of distance dissemination, so the patient was programmed for a lumpectomy with marking and a left axillary lymphadenectomy.

The procedure took place without incidents, identifying marking harpoon, metallic clip and lesion in piece remitted for interoperative mammographic study, amplifying the superior and inferior external margins. The regulated axillary lymphadenectomy was performed in the same surgery *(→ Image 1)*, with correct hemostasis and placement of a local hemostatic in the form of a medical matrix (TachoSil®) *(→ Images 2 and 3)* in addition to placement of a Redon type axillary suction drainage.

Immediate postoperative results were favorable, with good looking surgical wounds, without observing collections nor hematomas and with axillary drainage with scarce debit, being discharged to her home 48 hours after the intervention.

The patient was controlled in the next five days by the breast pathology office, with surgical wound in the healing process, without hematomas or seromas and with axillary drainage debit serohematic (200 cc since hospital discharge), so it was removed. The anatomopathological study confirmed the initial diagnosis, with free surgical margins, and with neoplasic infiltration on one of the three axillary lymph nodes analyzed, with a final stage pT1c N1a.

Currently, the patient is undergoing chemotherapy treatment with carboplatin, finalyzing the fourth cycle, with good tolerance and waiting for the oncological radio and hormonal therapies.

Discussion

The surgical treatment of breast cancer is one of the principal therapeutic tools, always opting when possible for conservative surgery, maintaining the surgery minimally invasive, and improving the aesthetic results and emotional impact of the same in the patients.

Nonetheless, said procedure is not exempt of risks and complications, the majority of the cases appearing within few hours or days of the intervention.

One of the complications that we find most frequently is hemorrhaging, due to the intense vascularization of the mammary gland, which is why the dissection of the same must be performed with great care and with controlled hemostasis[3], resulting difficult on some occasions due to the limited surgical field.

In the majority of the interventions of the mammary gland it is advisable to place a drainage in the surgical bed (Redon type suction drainage is recommended, principally in axillary surgery), even if an adequate capitonage of the tissue has been performed, in this way trying to prevent hemorrhaging and a posterior reintervention.

In this respect, in recent years new hemostatic methods complementary to the drainage system have appeared, with the objective of minimizing these complications. In our case, a collagen adhesive matrix with a fibrinogen and thrombin association (TachoSil®) was used, performing its pre-coagulation function by entering in contact with the physiological fluids, in this way favoring the sealing of the tissue.

In the following days, the patient presented a postoperative without incidents, no hemorrhaging, seromas or other collections and with a scarce debit in the axillary drainage, being able to remove it five days following the intervention, 48 hrs. before the average of our center in this type of intervention.

In this way, the combined treatment of suction drainage and local hemostatics could be recommended as prevention for post-surgical hemorrhage and seromas, both to diminish these complications, as well as to try to perform an early removal of the drainages, minimizing the risk of infection and the physical discomfort for the patient.

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9 Other applications of hemostatic matrix in breast surgery

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Introduction

Breast cancer is the most frequent neoplasm in women worldwide, with a global incidence of 2 million women per year, approximately[1], supposing a representation of 30 % of the tumors in the female population in Spain. Although it is true that the risk of developing breast cancer has increased in recent decades, currently in developed countries it has remained stable and even presents a declining trend[2]. Also, a reduction in the associated mortality has been identified, due both to early diagnosis of this pathology (associated to screening programs and public awareness), as well as to improvements in the treatments used and multimodal therapy. Once the diagnosis is established, the election of the therapeutic protocol to follow in this type of tumor will depend on factors such as the prognosis, the subrogate type and the stage, with the objective of individualizing and personalizing the treatment of each patient. The most important prognosis factor is the affectation of the lymph nodes, with the most frequent being the axillary, followed by the internal mammary (the localization of the tumor at deep and medial level in the breast is associated to migration of the radiotracer of this region)[3].

However, selective lymph node biopsy of the internal mammary gland is controversial, and may be reserved for those cases in which the objective is to capture it at this level[4].

Surgical treatment is one of the pillars of treatment for breast cancer, with the objective of carrying out a local control of the illness, a complete study of the tumor and a lymph node staging of the illness. Whenever it is possible, conservative surgery is the choice, pursuing the objective of performing an excision of the tumor with free margins and an optimal aesthetic result, highlighting as well the line of oncoplastic surgery.

Nonetheless, these interventions are not exempt from complications, highlighting among them hemorrhaging, lymphorrhagia, abcsesses and infections, seromas and nerve or vascular lesions. Less frequently, we find nerve or vascular lesions, as well as lesions of neighboring structures, such as muscular or organic lesions[5].

Image 1: Preoperative lymphoscintigraphy, with radiotracer uptake in the region of the internal mammary chain.

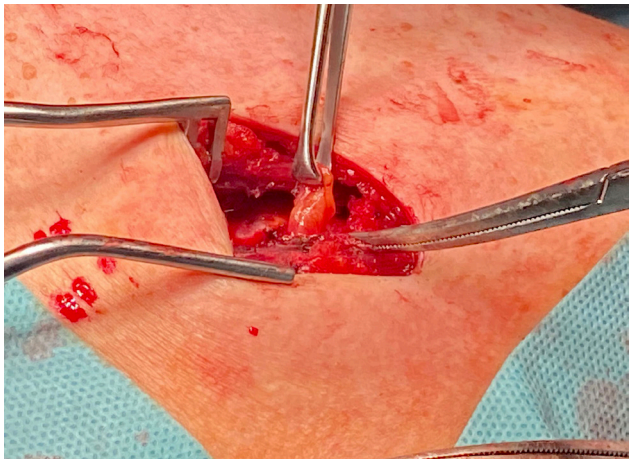

Image 2: Selective sentinel lymph node biopsy in the region of the internal mammary chain.

Clinical case

Woman of 46 years of age, without known medicine allergies, with personal history of high blood pressure under treatment with lisinopril and amlodipine, appendectomy and hemorrhoidectomy. Multiparous and without family history of interest.

The patient comes to the breast pathology offices at our center in September 2020, for consultation due to diagnosis of multifocal infiltrating ductal carcinoma of the right breast after self-examination of a suspicious nodule. In the mammography and ultrasound reports provided, diverse irregular hypoechogenic lesions of at least 25 mm in the infroexternal quadrant of said breast, is identified, without apparent axillary affectation.

A radical mastectomy was performed with selective biopsy of sentinel ganglion in July 2020, with final diagnosis of multifocal infiltrating ductal carcinoma (with the focus on the largest of 1.8 cm) of the right breast, with associated intraductal carcinoma, positive estrogen receptors (90 %), positive progesterone receptors (90 %), negative for Her-2 oncogene by immunohistochemistry and a tumor proliferation rate (Ki67) of 12 %. No axillary or lymphovascular invasion was identified (pT1N0). Patient began treatment with tamoxifen and was discharged from oncology due to the fact that it was a low-risk benign tumor, starting habitual controls with gynecology.

In the one-year control after the intervention, upon physical exploration a keloid scar in the right mastectomy region was detected, and in the lower third of the same, a nodule of 1 cm, slightly mobile and adhered to the deep planes, with no associated axillary or supraclavicular lymphadenopathies.

Due to the nodule in the mastectomy bed in a patient with personal history of breast cancer, an ultrasound and CNB were requested.

The ultrasound revealed that said nodule corresponded to a hipoechoic area with a slightly irregular contour of 10 x 8 mm in the junction of the inferior quadrants of the right breast (Breast Imaging Reporting and Data System/BIRADS 4C), and the anatomopathology confirmed tumor recurrence (infiltrating ductal carcinoma of 10 mm with positive estrogen receptors (10 %), positive progesterone receptors (10 %), negative for Her-2 oncogene by immunohistochemistry and a tumor proliferation rate (Ki67) of 60 %).

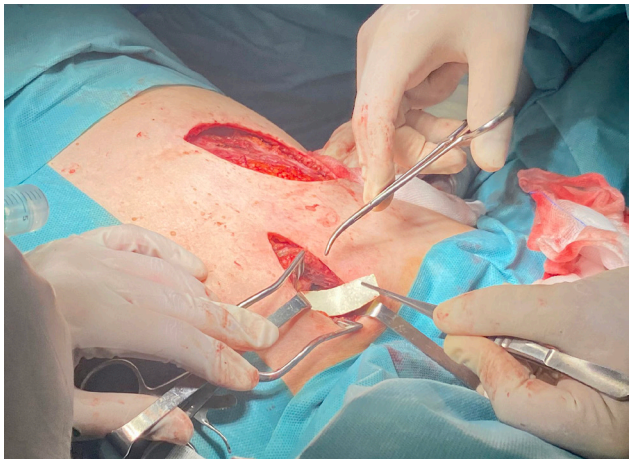

Image 3: Surgical bed with application of the medicated matrix (TachoSil®).

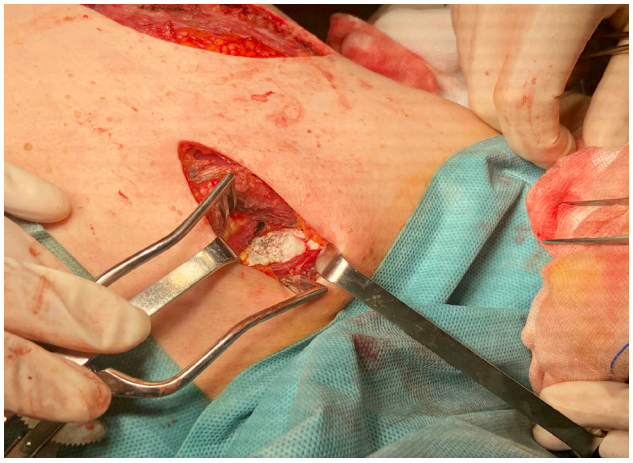

Image 4: Surgical bed with application of the medicated matrix (TachoSil®).

After confirmation of the diagnosis, an extension study is requested, without signs of distance dissemination, so the patient was programmed for a nodule resection on the surgical bed of the mastectomy and selective biopsy of right axillary sentinel lymph node. After performing the lymphoscintigraphy, in the anterolateral sequential image two capturing lymph nodes in the right axillary region were found, and two medials in the anterior projection, in the territory of the internal mammary artery *(→ Image 1)*, so a lymph node biopsy was performed on them as well.

The procedure takes place without incidents, with resection of the pathological nodule and selective biopsy of the axillary sentinel lymph node and in right internal mammary chain *(→ Image 2)*. During the latter procedure, a millimetric pleural lesion is produced, that is resolved with sutures and the application of a medicated matrix (TachoSil®) as a tissue sealant and reinforcement of the sutures *(→ Images 3 and 4)*. A sealant test is performed, without finding leaks and a negative pressure system is put in place.

The immediate post-operative period is favorable, with a chest x-ray clear for pneumothorax and surgical wounds healing well, without indications of collections or hematomas. The patient is discharged 48 hours after the intervention.

The patient was controlled in the next five days at the breast pathology office, with surgical wounds in the healing process, without hematomas or seromas and removal of the functioning vacuum system. The anatomopathological study confirmed the initial diagnosis, with free surgical margins, and without neoplasic infiltration on of the axillary or internal mammary lymph nodes.

Currently, the patient is undergoing chemotherapy treatment with doxorubicin, cyclophosphamide and taxanes, well tolerated and waiting for the oncological radiotherapy and subsequent chemical castration.

Discussion

The surgical treatment of breast cancer is one of the principal therapeutic tools, always opting when possible for conservative surgery, maintaining the surgery minimally invasive, and improving the aesthetic results and emotional impact of the same in the patients.

Nonetheless, said procedure is not exempt of risks and complications, the majority of the cases appearing within a few hours or days of the intervention.

Hemorrhaging, infection and seromas are the most frequent complications associated with breast surgery. Nonetheless, it is fundamental to evaluate and be aware of other possible complications that can arise and increase the difficulty of both the surgical procedure as well as the postoperative period. Pneumothorax is an infrequent complication during surgical treatment of breast cancer, primarily associated to the pleural lesion during the internal mammary lymph node biopsy.

In recent years new hemostatic methods complementary to the drainage system have appeared, with the principle objective of preventing and controlling the principle complications of breast surgery, such as hemorrhaging and seromas. Nonetheless, there exist other less known applications that are very useful for hemostasis, due to their tissue sealing function. In our case, a collagen adhesive matrix with a fibrinogen and thrombin association (TachoSil®) was used in the internal mammary lymph node region, on one hand performing its pre-coagulation function and on the other favoring tissue sealing and reinforcing the pleural suture, preventing posterior pneumothorax.

In the following days, the patient had a non-incidental post operatory, without clinical or radiological findings of pneumothorax.

Therefore, the application of said hemostatics could be recommendable not only as pre-coagulation agents, but also as tissue setters and sealants in these procedures with risk of leakage.

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10

Use of adhesive matrix for the prevention of lymphorrhagia-lymphoceles after axillary lymphadenectomy

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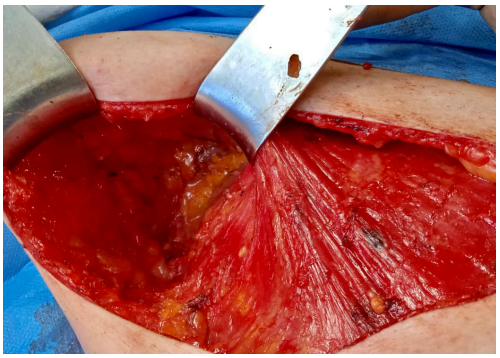

Image 1: Axillary after lymphadenectomy.

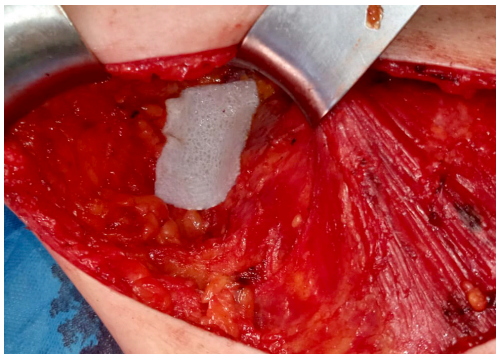

Image 2: TachoSil® on the surgical bed.

Introduction

Although currently the comorbidity and complications of breast surgery have declined considerably with selective biopsy of the sentinel lymph node, there continues to be a group of patients with advanced stages that require the performance of an axillary lymphadenectomy. Among these patients, the most frequent complication is the appearance of lymphorrhagia and lymphocele/seroma formation[1], This increases the risk of infection, dehiscence of the suture and necrosis of the tissue, increasing the discomfort of the patient and the time required to remove the suction drainage, prolonging the hospital stay and delaying the patient's return to normal life. It may also require an increase in medical visits due to need of manual drainage if this accumulates fluid.

To prevent this, multiple techniques have been proposed from closure of the space created by the dissection with sutures, electrocoagulation of the area, to the application of fibrin adhesives[2].

Various published studies exist proposing the use of equine collagen patches covered with human fibrinogen, TachoSil®, for the prevention of the formation of limphoceles[3].

A review of the available literature on this subject is presented in relation to a case in which this technique was used.

Clinical case

The case concerns a patient of 44 years of age, diagnosed with an infiltrating ductal carcinoma of the right breast, luminal B, cT3cN2 diagnosed and in follow-up by our unit. The patient does not have personal or family history of interest, is not overweight and was not a smoker. Given the stage of the disease, the patient was initially referred to the medical oncology service to initiate neoadjuvant chemotherapy, following the 4-cycle scheme of Adriamycin-cyclophosphamide, followed by 4 cycles of docetaxel. After completing the treatment, the patient showed a radiological response complete with magnetic resonance, without evidence of axillary lymphadenopathies. The patient is programmed for a modified radical mastectomy of the right breast. The lymphadenectomy was carried out to Berg level II *(→ Image 1),* conserving the pedicle of the dorsal muscle and the long thoracic nerve. After completing the axillary dissection, two TachoSil® patches were applied in the bed *(→ Image 2).* Two number 10 redone drains were left in, one at the axillary level and the other at the mammary level.

Both the surgery and the immediate post-operative period took place without incident, being discharged from the hospital after two days.

The patient returns five days after the intervention for control with 60 cc of sero sanguinolent fluid in each drain and the surgical wound in good condition. The mammary drain is removed. In the control eight days after the surgery, the patient has a total of 20 cc of serous liquid in the axillary drain, so it is removed. The average daily drainage was 10 cc. The patient had a good evolution without presenting lymphoceles in the successive controls.

Discussion

The lymphorrhagia and formation of lymphoceles and seromas after the performance of an axillary lymphadenectomy in breast cancer surgery is a multifactorial process, which depends both on the characteristics of the patient as well as the surgical technique. The physiological process that produces them includes, according to the studies realized, two mechanisms.

On one part an exudate is triggered secondary to inflammation caused by tissue aggression and on the other part, a section of the lymphatic vessels of the area is produced, with the consequent lymphorrhagia.

Between the different techniques employed for the prevention of this postoperative complication, there have been controversial results, without a clear advantage determining which is the concrete technique[2].

The use of collagen patches that associate coagulation factors assumes an advance, since it combines the mechanical support of the collagen, with the adhesive and hemostatic effect of the fibrinogen and thrombin.

Piñero-madron et al.[4] demonstrated in a prospective study a significant decline in the incidence of seromas with the use of collagen patches. The patients of this group also required during a shorter period of time the use of drains, with a reduced quantity of drainage liquid, although these results were not statistically significant.

In the same way, in a matched case-control study[5] obtained with the use of these patches, a reduction of the symptomatic collections was obtained, reducing the number of evacuation punctures to reduce the volume of accumulated liquid, compared to the group in which TachoSil® was not applied.

On the contrary, other studies exist with designs similar to these that did not obtain significant results when comparing between the use or not of this sealant matrix in the surgical bed after an axillary lymphadenectomy. This is why studies with larger sample sizes, prospective and multi center are required to find the best formula for the prevention of this frequent complication in breast cancer surgery.

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11

Use of TachoSil® in the control of hemostasis and sealing in breast cancer surgery, a clinical case report

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Introduction

The use of local hemostatics has become a habitual practice in the centers where they are available. The use of an adhesive matrix that contains fibrinogen and thrombin can help to control those hemorrhages of scarce quantity that do not have a unique origin, but rather appear as diffuse bleeding. Although this bleeding does not threaten the hemodynamic stability of the patient a priori, it requires strict control since it can cause secondary anemia and reinterventions, among other complications. Said hemostatics can be used in different locations and varied surgical procedures[1]. Besides the control of the hemostasis, their properties as a tissue sealant can provide additional benefits such as the reduction of seroma, a frequent complication in the case of lymphadenectomies.

The objective of this article is to present the use of this hemostatic tool applied in a clinical case of breast cancer.

Clinical case

Woman of 57 years of age, diagnosed with type 2 diabetes mellitus under treatment with oral antidiabetics, without other illnesses of interest. Does not present known medical allergies, nor previous surgical interventions. Gynecological history includes 3 euthyroid deliveries, menopause at 50 years of age. Does not have an oncological family history, only highlighting that her sister suffers from Sjogren syndrome.

The patient starts the breast cancer screening program at 45 years of age, according to the protocol currently in place at the Castilla La Mancha, having biannual mammography in the external hospital center for this purpose.

In the mammography, a suspicious nodule is visible, motive for which she is referred to our center (center of reference in the province), where the study is completed.

On clinical exploration no nodules suspicious of malignancy were palpated and the axillary exploration results were nondescript.

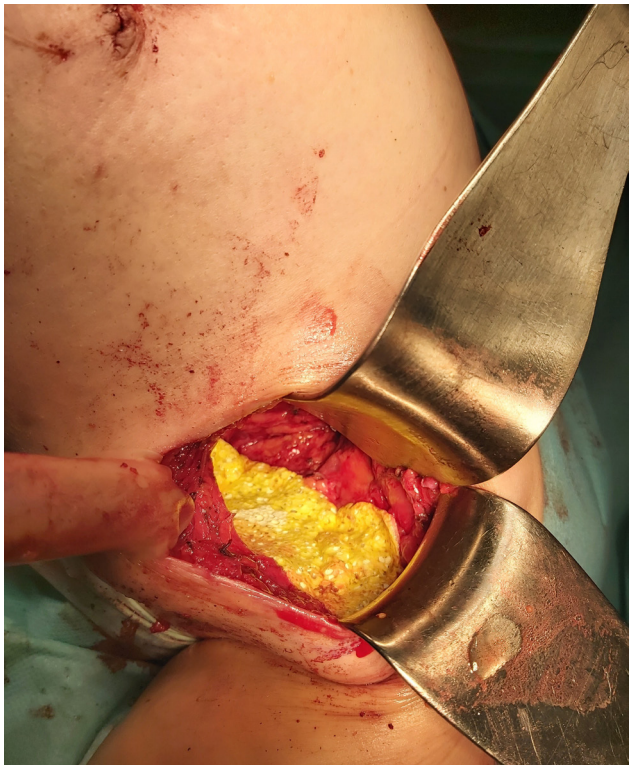

Image 1: Shows the surgical bed after the axillary lymphadenectomy, after the placement of TachoSil® Sealant Matrix.

The mammography performed in our center described an image with irregular borders of 8.3 x 4.2 mm located in the external superior quadrant of the left breast, juxta areolar. The study was completed with an ultrasound. No axillary lymphadenopathies suspicious of malignancy were detected. The lesion was classified as Breast Imaging Reporting and Data System/BIRADS 4C, performing a vacuum-assisted echo-guided biopsy.

The histological study informed of an infiltrating ductal carcinoma histological grade: 2 biomarker tests were performed resulting as a cytokeratin 19 positive. The immunohistochemistry study informed of a immunophenotype concordant with a carcinoma of type "Luminal B Her2 negative". As treatment a lumpectomy was performed guided by harpoon, as well as a sentinel lymph node selective biopsy, through two incisions in the skin (lumpectomy, peri areolar arch of 4 cm; and axillary access, transverse, 3 cm long, running parallel 2 cm below the insertion of the pectoralis major muscle).

The lumpectomy was performed guided by harpoon, with an interoperative study of the margins described as free. The intraoperative study of the sentinel lymph node informed by OSNA gave a result of 47,000 copies, completing the intervention with a left axillary lymphadenectomy following the protocol currently in force in our center, after amplifying the previously described incision to access the axillary.

During the intervention, the hemostasis of the bed of the lumpectomy was controlled with relative ease, however, in the bed of the axillary lymphadenectomy sheet bleeding without a clear origin could be seen, that could not be completely controlled exercising pressure over the area. In this situation, it was decided to use a local hemostatic, TachoSil® Sealant Matrix was used *(→ Image 1)*, applying the same according to the detailed instructions in the technical specifications. A correct seal of the tissue was obtained, and the bleeding stopped. The rest of the intervention took place without incidents. A Blake drain was placed in the axillary bed for control during the immediate postoperative period which took place without incidents.

The day after the intervention the patient was in a good general state and pain was controlled with analgesics. The control analysis that was performed showed a hemoglobin of 12 g/dl. The drainage showed a debit of 70 cc of serohematic characteristics. At 48 hours after the intervention the debit was 60 cc and at 72 hours at 20 cc, removing it at this time. Hematomas were not visible in the breast nor the axillary and given the positive postoperative evolution, it was decided to discharge the patient with daily controls of both surgical wounds on behalf of the nurse of the area.

The anatomopathological study confirmed the type of histology of the previously performed biopsy A single infiltrating neoplastic focus was evidenced in the lumpectomy piece, with a maximum size of 10 x 6 mm, informing free margins. The axillary lymphadenectomy obtained a total of 16 lymph nodes of which 15 reported as reactive and only one sentinel ganglion reported as affection. The stage according to the classification pTNM (8th Ed.) was pT1b pN1a Mx.

After debating the case in the multidisciplinary tumor committee it was decided to implement adjuvant treatment with radiotherapy, gene platform and hormone therapy.

It should be noted that the patient presented an infection in the mammary surgical wound that required oral antibiotic therapy, after which it healed without complications.

At 15 days after the intervention, the patient was evaluated by the rehabilitation service, initiating advice and activities for the prevention of lymphedema. The mobility of the left arm was completely preserved and did not show any type of limitation or stiffness, nor lymphedema at that time.

Discussion

TachoSil® is presented as a yellow-colored adhesive matrix that contains in its surface human fibrinogen in a concentration of 5.5 mg combined with 2.0 IU of human thrombin. In its technical specifications this product is indicated in adults and children from 1 month of age as support treatment in surgery to improve hemostasia, promote tissue sealing, as a reinforcement for sutures in vascular surgery when the standard techniques prove to be insufficient and as a complement for the sealing of the dura mater to prevent postoperative cerebrospinal fluid leakage after neurosurgery[1]. In the case described it was used as support in breast surgery to improve the hemostasis, being highly effective and achieving control of the bleeding.

The action mechanism of this compound consists in the reproduction of the final stages of the coagulation cascade, increasing the hemostasis. In addition, it also acts as a tissue sealant, increasing the cellular adherence, reducing the number of connections between small arterial and lymphatic vessels and promotes the growth of fibroblasts. These activities could reduce the rate of the formation of seromas and improve the healing of wounds[2,3].

In the case described an axillary lymphadenectomy was performed, among whose complications, in addition to severe bleeding in the surgical bed, are the formation of seromas, hematomas, infection of the surgical wound, prolongation of the hospital stay and nerve lesions[2] none of which occurred in our case.

The formation of seromas is the most frequent complication of lymphadenectomy, with an incidence of 15 to 80 % of the cases, which can also delay the healing of the surgical wound and increase the risk of infection of the same. Various methods have been used to prevent this complication, a suture over the axillary gap space, external compression, the use of a vacuum drainage device, the application of bovine thrombin and sclerotherapy with tetracyclines. However, the most efficient method to prevent seroma continues to be controversial[2].

Chang et al. in the year 2020 carried out a systematic review and a meta-analysis of the controlled randomized clinical studies published to date about the reduction in the incidence of seroma that these sealants could have in the cases of axillary lymphadenectomy. It concludes, that although standardized use of these is not recommended in this type of surgery, they can provide benefits in selected patients in terms of reduction of seromas and duration of drainage[2].

Other published studies report results in which the use of the fibrin sealants does not diminish the rate of seroma, although they may reduce the duration of the hospital stay[4,5]. Gasparri et al., 2021, adds the benefit of reducing the days of duration of drainage[6].

More studies will be necessary to establish the benefits that local hemostatics may have in axillary lymphadenectomy. However, in the case presented control of the bleeding was obtained and the patient did not present a seroma as a consequence of the surgery. It is worth noting, as well, that, in spite of the infection of the surgical wound of the breast, the axillary suture did not present local complications and the drainage was removed at 72 hours of the intervention, coinciding with the hospital discharge, so we can affirm that, in spite of our limited and not standardized experience with the use of these materials in this specific type of surgery, the postoperative results in the case described were satisfactory.

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Use of TachoSil® in bilateral adnexectomy via laparotomy, a clinical case report

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Introduction

The hemostasis is a process whose function is to limit the loss of blood through an injured vessel. Said process is comprised of different phases: vasoconstriction, platelet plug formation and fibrin formation. Thanks to scientific advances today we have local hemostatics that support hemostasis such as TachoSil®.

TachoSil® corresponds to an off-white sealant matrix. The active side of the matrix, which is coated with fibrinogen and thrombin By entering in contact with fluids the fibrinogen converts into fibrin monomers that polymerize to form a fibrin clot that stays adhered to the factor XIII creating a firm and stable network with adhesive properties that permit sealing[1].

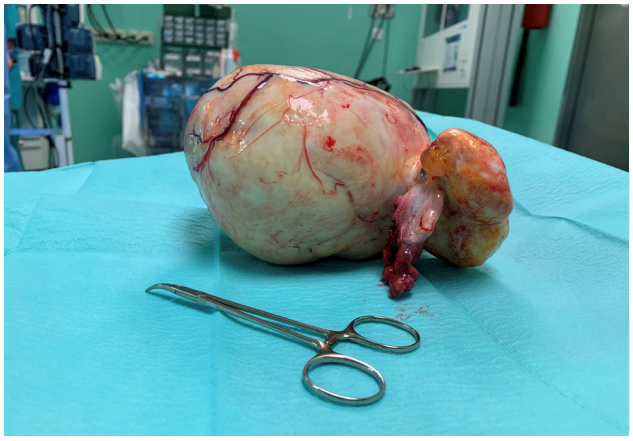

Image 1: Right adnexectomy piece.

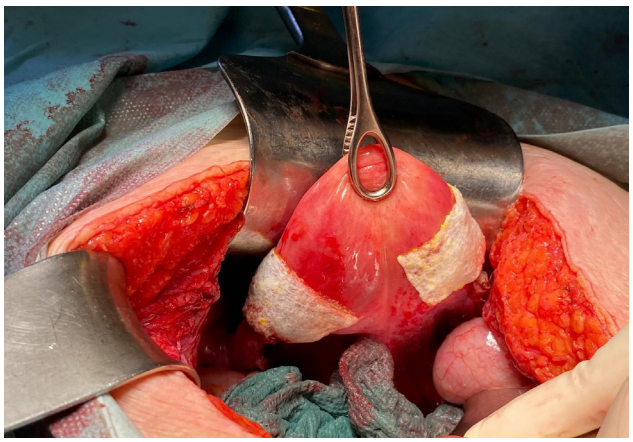

Image 2: Placement of 1 unit of TachoSil® in each surgical bed of the adnexectomy.

Clinical case

Woman of 88 years of age without medical or surgical history of interest comes for consultation at general surgery due to the appearance of an abdominal tumor of approximately 5 cm in the left iliac fossa of 4 months of evolution. Findings are confirmed and an abdominal CAT scan is requested in which a right center abdominopelvic mass of possible solid adnexal origin is observed, with well-defined borders, lobed of 112 x 171 x 121 mm with moderate quantity of ascitic fluid in the pelvis.

With the aforementioned data the patient is referred to gynecology for consultation where a ruled transvaginal ultrasound is performed finding at the right adnexal level a bilobed solid mass of measurements similar to those described with the central zone echo negative and scarce color map. The suspected diagnosis points to a possible myoma without ruling out sarcomatous degeneration or high risk cancer of the right ovary.

In the gynecological exploration an abdominal tumor is felt corresponding to a mobile mass, displaceable and slightly painful.

The case is presented in the surgical session deciding on an exploratory laparotomy due to the impossibility of reaching a clear diagnosis through the image tests and physical exploration.

In the operating room a tumor is identified of approximately 20 x 20 cm *(→ Image 1)* right annex dependent with a pearly aspect and peripheral vascularization indicating bilateral adnexetomy as well as taking a sample of the ascitic fluid for cytology. During the surgical procedure sheet bleeding was seen precedent from both surgical beds of the adnexectomy deciding to apply 1 unit of TachoSil® in each one of them according to the detailed recommendations of the technical specification with bleeding stopping at 3 minutes *(→ Image 2)*. The rest of the intervention takes place without incident and with the correct sealing of the tissues it is not considered necessary to insert intra-abdominal drainage.

The postoperative period transpires satisfactorily and the discharge is indicated 48 hours after surgery. In the clinical control 1 month after the intervention the patient is found to be asymptomatic and the wound has a good appearance.

The anatomopathological study of the piece of the right adnexectomy revealed the diagnosis: ovarian fibrotecoma The cytology of the ascitic fluid was negative for malignancy.

Discussion

The ovarian fibrothecoma is a benign neoplasm of the sex cord-stroma with typically unilateral localization. Patients tend to be asymptomatic or have pelvic pain secondary to the tumor. On occasions it is accompanied by pleural diffusion and ascites constituting the triad of Meigs Syndrome[2].

It is an infrequent tumor[3] which is why little evidence is found in literature evidencing the use of hemostatics in the laparotomy dedicated to the resection of the fibrotecoma. Nonetheless, the indications of TachoSil® are based on those situations that require support during surgery to improve the hemostasis. Therefore, the use of this medication is indicated in a perilesional form quickly sealing the vessels.

The success of any surgery is based on an adequate hemostasis. In spite of the existence of different mechanical, thermal and chemical procedures to maintain the control of bleeding sometimes not all achieve satisfactory results making occasional use of biomaterials useful to reach this objective[4].

Studies confirm that the use of TachoSil® in gynecological surgeries similar to that mentioned is efficient and well tolerated. As such, we must consider scenarios in which diffuse bleeding is produced in locations close to sensible structures such as the urinary tract and the pelvic nerves where the use of hemostatic agents are more justified than sutures and electro-cauterization[5].

In spite of the small amount of data found in the bibliography on the use of TachoSil® in similar surgeries, the case under study reveals a satisfactory intraoperative and postoperative result that could support the standardization of the method as long as it is indicated.

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13

Use of TachoSil® on active sheet bleeding in the context of an iterative cesarean

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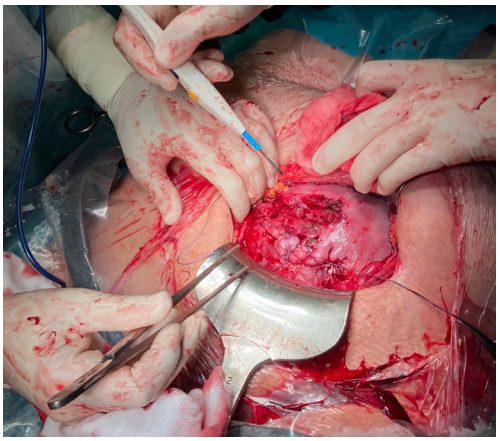

Image 1: TachoSil® on the surgical bed.

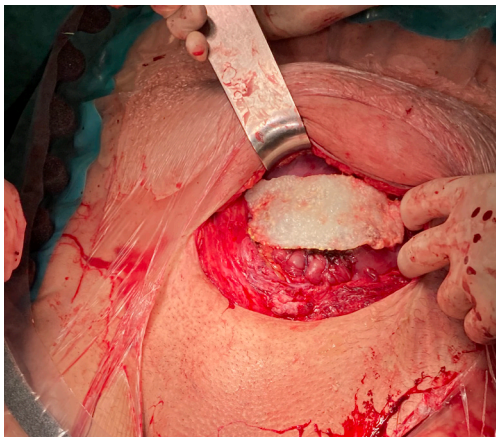

Image 2: TachoSil® on the surgical bed

Introduction

Postpartum hemorrhage is a leading cause of maternal mortality. It has been defined as the loss of at least 500 ml after vaginal delivery, or at least 1,000 ml after caesarean delivery in the first 24 hours[1].

Uterine bleeding is one of the main complications of caesarean sections. In relation to the clinical case to be developed, the importance of minor but significant microbleeds or sheet bleeding should be emphasized, which do not pose an immediate life-threatening risk to women but do increase the risk of postpartum anemia and surgical reintervention. Therefore, many devices with a local hemostatic effect have been developed, among them TachoSil®.

According to the technical specifications, TachoSil® is a drug matrix with local hemostatic function containing human fibrinogen and thrombin. Fibrinogen and thrombin are proteins that participate in the physiological process of coagulation, playing a crucial role in hemostasis. Upon contact with body fluids such as blood or lymph, a reaction occurs between fibrinogen and thrombin that triggers the final stage of coagulation, forming fibrin clots that adhere the TachoSil® collagen sponge to the wound surface and seal it[2].

The following is a description of a clinical case seen in our center, a woman who underwent a fourth caesarean section, requiring the use of hemostatic drugs due to difficult control of local hemostasis during the intervention.

Clinical case

Pregnant woman of 36 years of age, intervened in three cesareans in the years 2010, 2012 and 2015, for unknown reasons, without other medical or surgical history of interest. No transfusions or regular medications. No toxic habits. No known drug allergies. Blood group and Blood group A (Rh-)negative.

Partial and interrupted control of the pregnancy from 15 weeks. The ultrasound at 20 weeks shows normal fetal growth and morphology. The patient was diagnosed with gestational diabetes at 31 weeks gestation, after an O'Sullivan test showing 190 and an oral glucose overload of 100, 210, 201, 190. Doubtful adherence to diet after diagnosis. Blood tests, including a third trimester blood test showing hemoglobin of 10.2 g/dl, platelets 176,000 and coagulation within normal limits. No anti-D gamma globulin or pertussis vaccine administered.

Subsequently, the 39+1-week ultrasound scan showed a cephalic presentation, a positive fetal heartbeat, a normally inserted fundal placenta and normal amniotic fluid. Estimated fetal weight 3.515 g (AC at 2 weeks older), 74th percentile for gestational age and male sex. UA-PI 0.66 (normal).

Caesarian delivery at 13:05 on 08/02/2021 at 39+4-weeks of amenorrhea planned for a fourth iterative caesarean section. Spinal analgesia. Caesarian delivery. Manual delivery. Prevention of uterine atony with carbetocin. Administration of 750 mg amchafibrin during the procedure. It should be noted that a bilateral salpingectomy was not performed at the patient's request, despite prior consent. A 3.920 g male was born, with Apgar 9—10 and umbilical artery pH 7.33, umbilical vein pH 7.34. The surgical protocol reads as follows:

Supine decubitus, asepsis and field. Pfannenstiel incision, with opening of the abdominal wall planes, showing extensive fascial fibrosis and abdominal muscles. Firm adhesion of the parietal to the uterine visceral peritoneum is identified and ligated. Omentum adhesions to the anterior wall of the uterus were observed, which was ligated without incident, as well as an ascended bladder, with no clear view of the vesicouterine plica. The peritoneum is passed and the uterine cavity is accessed.

A transverse incision is performed with extraction of live foetus in cephalic position crying in a resuscitation cot. Manual delivery and cavity check without incident. A hysteroscopy is performed in monolayers with vicryl 1.

After the procedure, a large continuity defect was observed on the anterior wall (where there were previously described adhesions), which required electrocoagulation and multiple hemostatic stitches with vicryl, without local bleeding control, with generalized sheet bleeding on the previous resection bed highly adherent and persistent small active bleeding episodes *(→ Image 1)*.

Local hemostatic material was used, choosing two TachoSil® sponges, placing one on the anterior wall of the uterus *(→ Image 2)* and the second on the area corresponding to the vesicouterine plica. In addition, 750 mg of amchafibrin i.v. is administered.

The macroscopic examination of the uterus and adnexa is normal. No subsequent bleeding was observed. An intra-abdominal Blake 15 drain is placed exiting through the left iliac fossa. Closure of the wall in planes according to standard technique with monofilament suture. Closure of the incision with staples. Clear urine.

During the immediate postpartum period, patient in good general condition, with normal blood counts and pain well controlled with analgesics. On physical examination, uterus well contracted 0—1, serohematic lochia in normal quantity, and clean surgical wound dressing. At 24 hours, drainage with 300 cc of serohematic content was observed, so it was maintained for a further 24 hours, and 20 cc of serohematic content was observed 48 hours after the caesarean section, and the drainage was removed without incident.
The patient was discharged after 72 hours with oral iron supplement. Hemoglobin at discharge 9.6 g/dl. Administration of anti-D gamma globulin.

Discussion

A caesarean section is the major surgery most frequently performed by obstetric surgeons. The main recognised indications are suspected loss of foetal well-being, normally inserted placenta abruptio prematureis, cephalopelvic disproportion, non-progression of labour and dystocia, among others.

Thanks to improved surgical techniques, reduced anaesthetic risk, prophylactic administration of antibiotics and better control of bleeding, the caesarean section is increasingly becoming an accessible and relatively simple option for pregnancy delivery. This has led to its more frequent use, often elective and unjustified, turning it into a global public health problem[1].

There is a clear increase in the number of women who have undergone first caesarean sections[3], thus increasing the rate of iterative caesarean sections, as in the case of the patient presented in the clinical case.

The main complications of this surgery are haemorrhage, infection, thromboembolic phenomena and injury to other pelvic and abdominal organs, such as the bladder or bowels.

In relation to the clinical case described, it is important to note the high number of previous caesarean sections the patient had, this being her fourth. This background complicated the entry into the abdominopelvic cavity due to the large number of adhesions and fibrosis that the patient presented, as well as structural vulnerability and fragility.

During the operation, the adhesions were ligated and sealed using an electric scalpel and ligatures. However, after completion of the hysteroscopy, multiple sites of bleeding were observed on two main sites of adhesiolysis: the anterior wall of the uterus and the uterine segment close to the bladder. Due to the fact that complete hemostasis was not achieved using these techniques, the fragility of the tissues, and the proximity to delicate structures such as the bladder, the use of two TachoSil® matrices was decided, and bleeding ceased after compression for approximately 3 minutes[4,5].

Finally, it is very important to be aware of the existence and the possibility of using hemostatic materials such as TachoSil®, especially in interventions with fragile tissues where electrocoagulation and hemostatic stitches can cause damage to these tissues, or can even be ineffective as hemostatic techniques[6,7].

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TachoSil® — four versions, three sizes*

Illustrated in original size

TachoSil SEALANT MATRIX

*Not all versions are available in all countries

TachoSil Sealant Matrix
(5.5 mg per cm² of human fibrinogen, 2.0 IU per cm² of human thrombin)

Statement: Before prescribing, consult/refer to the full prescribing information. **Presentation:** An off-white sealant matrix. The active side of the matrix is coated with fibrinogen and thrombin, is marked by a yellow colour. Supplied, ready to use, in sterile packaging. **Legal Classification:** Restricted prescription only medicine. **Indications:** In adults and children from 1 month old, for supportive treatment in surgery for improvement of haemostasis, to promote tissue sealing, and for suture support in vascular surgery where standard techniques are insufficient; also, in adults for supportive sealing of the dura mater to prevent postoperative cerebrospinal leakage following neurosurgical procedures. **Dosage & Administration:** For epilesional use only. Use is restricted to experienced surgeons. The quantity to be applied is governed by the size of wound area, and the underlying clinical need for the patient. In clinical studies, the individual dosages have typically ranged from 1-3 units (9.5 cm x 4.8 cm); application of up to 10 units has been reported. For smaller wounds, the smaller size matrices (4.8 cm x 4.8 cm or 3.0 cm x 2.5 cm) or the pre-rolled matrix (based on a matrix of 4.8 cm x 4.8 cm) is recommended. TachoSil should be used under sterile conditions and immediately after opening the inner sterile cover. Prior to application, the wound area should be cleansed, e.g. from blood, disinfectants and other fluids. For Flat TachoSil, the sterile package should be pre-moistened in saline solution and applied immediately. The yellow, active side of the matrix is applied to the bleeding/leaking surface and held against it with a gentle pressure for 3-5 minutes. For pre-rolled TachoSil, after removing from the sterile package, it should be applied immediately through the trocar without pre-moistening. The yellow, active side of the matrix is applied to the bleeding/leaking surface using e.g., a pair of cleansed forceps and held against it with a moist pad under gentle pressure for 3-5 minutes. Pressure is applied with moistened gloves or a moist pad. Avoid TachoSil sticking to surgical instruments, gloves or adjacent tissues covered with blood by cleansing them before application. After pressing TachoSil to the wound, the glove or the pad must be removed carefully. To avoid TachoSil from being pulled loose it may be held in place at one end, e.g. with a pair of forceps. In the case of stronger bleeding, it may be applied without pre-moistening, while also pressing gently to the wound for 3-5 minutes. The active side of TachoSil should be applied so that it extends 1-2 cm beyond the margins of the wound. If more than one matrix is used, they should overlap. TachoSil can be cut to the correct size and shaped if too large. In neurosurgery, TachoSil should be applied on top of the primary dura closure. **Contraindications:** Intravascular use; hypersensitivity to the active substances or to any of the excipients. **Warnings & Precautions:** No specific data available on the use of this product in gastrointestinal anastomoses surgery. Life threatening thromboembolic complications may occur if the preparation is applied intravascularly. Allergic type hypersensitivity reactions are possible, as with any protein product. If hypersensitivity reactions occur, the administration must be discontinued immediately. To prevent the development of tissue adhesions at undesired sites, ensure tissue areas outside the desired application area are adequately cleansed before administration. In the case of shock, the current medical standards for shock treatment should be followed. Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV and for the non-enveloped virus HAV. Measures may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (foetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g., haemolytic anaemia). It is recommended to record the name and the batch number of the product administered to the patient. Some cases of product non-adhesion issues have been reported in the form of lack of product adhesion / lack of efficacy. Correct product handling and application is required **Interactions:** No interaction studies have been performed. Similar to comparable products or thrombin solutions, the sealant may be denatured after exposure to solutions containing alcohol, iodine, or heavy metals. Such substances should be removed to the greatest possible extent before applying the sealant. **Fertility, Pregnancy & Lactation:** Safety for use in human pregnancy or breastfeeding has not been established in the clinical studies. Only administer to pregnant and breastfeeding women if clearly needed. **Effects on Ability to Drive and Use Machines:** Not relevant. **Undesirable Effects:** Hypersensitivity or allergic reactions (in isolated cases these reactions may progress to severe anaphylaxis; some cases of product residue causing granuloma), thromboembolic complications may occur if used intravascularly, and adhesions and intestinal obstruction when used in abdominal surgery. Refer to the SmPC for details on full side effect profile and interactions. **Overdose information:** No case of overdose has been reported. **Interactions with Other Medicinal Products:** No interaction studies have been performed. Similar to comparable products or thrombin solutions, the sealant may be denatured after exposure to solutions containing alcohol, iodine or heavy metals (e.g., antiseptic solutions). Such substances should be removed to the greatest possible extent before applying the sealant. **Use in Special Populations:** Limited data are available to support efficacy and safety of TachoSil in the paediatric population. In clinical studies, a total of 36 paediatric patients aged 0-13 years were treated with TachoSil in hepatic surgery. **Pack Sizes:** Package with 1 matrix of 9.5 cm x 4.8 cm, Package with 2 matrices of 4.8 cm x 4.8 cm, Package with 1 matrix of 3.0 cm x 2.5 cm, Package with 5 matrices of 3.0 cm x 2.5 cm, Package with 1 pre-rolled matrix of 4.8 cm x 4.8 cm. Not all pack sizes may be marketed.

Marketing Authorisation Holder: Corza Medical GmbH,
Speditionstraße 21, 40221 Düsseldorf, Germany
The full SmPC can be obtained from Corza Medical GmbH.
Marketing Authorisation Numbers: EU/1/04/277/001-005

Date of Revision of the Text: 8 May 2025
Link to Full SmPC or Prescribing information

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