AGGRESSIVE ANGIOMYXOMA OF THE VULVA IN POST-MENOPAUSAL PERIOD: LITERATURE REVIEW AND CASE REPORT

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AGGRESSIVE ANGIOMYXOMA OF THE VULVA IN POSTMENOPAUSAL PERIOD: LITERATURE REVIEW AND CASE REPORT (Abstract): Aggressive angiomyxoma (AA) is a rare, benign and slowly growing mesenchymal tumor which affect women especially on the reproductive age. Because over 80% of cases are misdiagnosed and most of them are often confused with lipomas, the diagnosis is made by histological examination. We describe here a case of an 89-year-old female, at menopause, that presented with a large pedunculated angiomyxoma on the right upper of major labia. The vulvar AA diagnosed was made due to clinical-pathologic findings and histologic result after the local excision of the tumor. The patient was discharge 7 days after surgery and along of 7 months of follow-up no recurrence or metastasis were documented. In this case we showed the diagnosis, management and prediction for vulvar angiomyxoma in postmenopausal period, but further follow-up period is necessary for surveilling the recurrence, knowing that the tumor it may reappear in between 2 months and 12 years. Keywords: VULVAR AGGRESSIVE ANGIOMYXOMA, VULVAR BENIGN TUMOR, VULVAR LIPOMA.

Steeper and Rosai, firstly described an aggressive angiomyxoma (AA) in 1983 and, at the moment, there have been reported in the literature around 300 cases of this tumor type (1, 2). Aggressive angiomyxoma of the vulva is a benign, invasive myxoid tumor that primarily occurs in the pelvic, perineal and genital region. This tumor affects especially adult women in their reproductive age, having a women-men ratio of 6.6 : 1. When occurs in men, usually is being spread in different places like scrotum, perineum, spermatic cord, testicular/spermatic cord neoplasm, spermatocele and hydrocele (3, 4).

Its development is mainly from the connective tissue, having a fibroblastic or myofibroblast origin. Mostly, AA appears in premenopausal women, and resembles with another similar lesions from this areas like Gartner’s duct cyst, Bartholin’s gland cyst, inguinal hernia, lipoma and leiomyoma (2). Even if it is a benign tumor, in the literature has been reported an increased rate of local recurrences and invasion, around 30% to 72%; metastases cases and even death.
The pathophysiology of the tumor remains unclear and the diagnosis has to be certified by histological examination, due to its large number of misdiagnose, more than 80% (5).

After analyzing the tumor cell biology, the researchers had reached the conclusion that suppressive hormonal therapy with estrogen and progesterone plays a crucial role in the pathogenesis of AA, due to its favorable clinical response after treatment with GnRH analogues, estrogen/progesterone receptor blockers and aromatase inhibitors (6). In this pathology, another treatment possibilities with successful results are represented by radiotherapy and angiographic embolization (7).

**CASE REPORT**

We report the case of an 89-year-old female with vulvar aggressive angiomyxoma who entered on the menopause since she was 45 years old and had no significant pathological conditions at the moment of the examination. She presented in our department accusing the arising of a slow growing mass that started two years ago. The patient did not accuse any pain and had no other complains about it, except the unpleasant appearance. The clinical examination revealed a tumor mass that measured approximately 18 cm and developed from the 1/3 upper level of the right labia with a pedicle that has a length of 4 cm (fig. 1). The tumor was soft, had a gelatinous consistency and its pedicle root did not infiltrate the vaginal wall; on gynecological examination, the vaginal and cervical mucosae were normal. No associated lymphadenopathy were found. The patient’ laboratory investigations were found within normal limits including complete blood count (CBC), liver and renal function tests, serum ionogram test and Ca-125 marker (10.8U/mL).

During the vaginal ultrasound examination in the left parameter, on ovarian topography, a circle nonhomogeneous isoechogenic image was detected, with a hyperechogenic aria of 76/47 mm diameter; color Doppler imaging showed random and irregular dispersed blood vessels toward the center of ovarian tumor.

![Fig. 1. A - Gross vulvar mass which developed from the right labia. B - Image with the tumor after surgical resection. C - Image after surgical excision of the lesion in immediate postoperative period.](image-url)
The patient refused the surgical treatment for the ovarian tumor. She only consented the surgical treatment for labial tumor. This it was performed with section of the tumor pedicle (4 cm length) that was localized on the right major labia; the excision of the lesion was made with a clear resection margin. The tumor resected was sent for histological extemporaneous exploration (fig. 2). A fine local hemostasis was obtained and the lesion was closed performing an intradermal suture with Vicryl® suture (polyglactin 910). The results of extemporaneous examination of the tumor objectified a labial lipoma with the reserved result of paraffin processing of the tissue.

The patient postsurgical evolution was favorable under Ciprinol 200 mg, two tablets per day, and analgesia treatment. She left after 7 days of hospitalization. The histological examination of the tumor mass certified the vulvar angiomyxoma diagnose.

**Fig. 2.** Images of post operatory dissection of the labial tumor

Macroscopic histopathological examination revealed the presence of an 18/13 cm diameter tumor mass, covered by skin with ulcerated areas; the growth mass included a 3 cm thick pedicle without any visible tumor infiltration. The surface sections were gray-white with a gelatinous and glistening appearance and congestion areas.

Microscopy presented paucicellular proliferation of cells with oval or fusiform nuclei, a difficult visible cytoplasm and lack of nuclear pleomorphism or atypical mitoses. The tumor mass had relatively well delimited margins and contained abundant myxoid stroma, collagen bands and numerous blood vessels of different diameters with thin walls that were observed in hematoxylin and eosin (HE) staining (fig. 3). No hemorrhagic or necrotic areas were found. The pedicle and the excision margins found no signs of tumor infiltration.

The histopathological diagnose revealed an aggressive angiomyxoma of the major right labia. The patient had been followed during 7 months after the surgery and no recurrence or metastasis signs were remarked.
Fig. 3. The histologic aspects of aggressive angiomyxoma. A – Surface squamous epithelium (HE x4); B – Ulcerated surface epithelium (HEx4); C – Dilated blood vessels with different diameters and thick walls, myxoid stroma (HE x4); D - Myxoid stroma and fusiform cells without atypia (HEx10).

**DISCUSSION**

The vulvar aggressive angiomyxoma is threatening due to its characteristic of regional infiltration and recurrence (8). Nine cases were firstly reported in the literature by Stepeer and Rosai, who described different mesenchymal tumors located in the pelvis or perineum of youth females (9). Even if the number of cases increased over the years, and at this moment are counted approximately 300 cases, there are few cases reported in postmenopausal period (10, 11).

The pathogenesis of AAM is still unclear, it is believed that AAM develops from dysfunctional mesenchymal cells with genetic defects. There had been commonly found some chromosomal abnormalities that determine a translocation in the region of 12q 14-15 (12).

There are two clinico-histopathological entities: superficial angiomyxoma (SAM) and aggressive angiomyxoma (AAM). Both of them are diagnosed by the pathologist. The first category has a decreased rate of local recurrence compared with AAM, which can rise from 30% to 72%, causing the necessity of long-term monitoring (13, 14). Even if AAM has met also a favorable prognostic, two reported cases in the literature encountered a poor evolution which converted into cancer (15). The average of recurrence is one time for AAM (14).

In cases where AAM is suspected is necessary to perform preoperative imaging in order to establish the extension of the surgical excision. Computed tomography (CT) scan and Magnetic resonance imaging (MRI) offer a good predictability to what regard the tumor’s extent, both being superior to physical examination (12).
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Superficial angiomyxomas are normally negative for IHC markers, except for vimentin and CD34, whilst AAMs are estrogen receptor (ER) negative and/or progesterone receptor (PR)-positive. This situation explains why clinical response is that good after treatment with GnRH analogues, estrogen/progesterone receptor blockers and aromatase inhibitors.

The “gold” standard cure is represented by radical excision of the tumor with negative margins, offering the optimum outcomes and evolution of the treatment. Aggressive angiomyxoma had shown variable responses to several adjuvant therapies such as hormonal blockade, radiotherapy and angioembolization. Hormonal therapy with GnRH agonists (leuprolide acetate or goserelin) are valuable in decreasing the tumor size in situations where surgical excision is not manageable. Radiotherapy and chemotherapy do not provide any benefits due to the tumor’s decreased mitotic activity (16). Adjuvant therapy, using arterial embolization it may be needed in cases with partial excision of the tumor mass (17).

CONCLUSIONS
The outcomes of the vulvar aggressive angiomyxoma strategies have not been properly evaluated because of the limited amount of cases for study, and evidence relies on small series and case reports. In this situation, AAM is a topically benign but aggressive mesenchymal tumor in which the surgical excision is the optimal treatment with no recurrence sign during 7 months of follow-up.

REFERENCES

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**THE INTERPLAY BETWEEN VAGINAL MICROBIOTA AND INTRAUTERINE ADHESION USING NEXT GENERATION SEQUENCING METHODS**

Intrauterine adhesion represent a disease that is a very common cause for female infertility. Since it has an increased recurrence rate after surgical interventions, its pathogenesis and recurrence causes are important to understand better this condition. Liu et al. (2019) analysed, using high-throughput sequencing method, the vaginal microbiota of females diagnosed with intrauterine adhesion and healthy patients` vaginal secretion. The results shown that intrauterine adhesion does not bring any important changes for vaginal microbiota, having a slightly effect on the number of vaginal bacterial species. The patients with intrauterine adhesion presented at the phylum level a reduced percentage of Firmicutes and increased percentage of Actinobacteria whereas in the healthy females group the rate was more lower (P<0.05). Moreover, in about half of the intrauterine adhesion vaginal samples was identified at the genus level a remarkable decreased number of Lactobacillus and enhanced growth of Prevotella and Gardnerella (P<0.05). The interplay between synechiae and vaginal microflora can reveal remarkable changes in the vaginal microbiota diversity in patients with intrauterine adhesion. The increase of Lactobacillus population may bring interesting benefits in the endometrial regeneration process but also may help to decrease de recurrence rate of intrauterine adhesion (Liu Z, Kong Y, Gao Y, et al. Revealing the interaction between intrauterine adhesion and vaginal microbiota using high-throughput sequencing. *Mol Med Rep* 2019; 19(5): 4167-4174).