Aggressive angiomyxoma of the vulva: a case report in a Brazilian patient

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Abstract

Aggressive angiomyxoma is a locally aggressive tumor of mesenchymal origin. The condition predominantly affects females, with a male/female ratio of 6:1. Most cases occur during the reproductive years, with a peak between the third and fourth decades of life. The symptoms are non-specific, and the principal differential diagnosis is with Bartholin’s cysts or abscesses. The treatment of choice is surgical excision of the lesion, including evaluation of the margins. This case report refers to a 41-year-old patient with an insidiously growing lesion on the right vestibular area measuring approximately 9 x 5 x 5 cm, associated with dyspareunia. Surgical excision was successful, and there have been no signs of tumor recurrence in the six months of follow-up. Differential diagnosis in cases of vulvar lesions is of the utmost importance. A detailed vulvar examination is essential to ensure early diagnosis and to reduce the rate of underdiagnosed cases of aggressive angiomyxoma.

Keywords: Aggressive angiomyxoma; Vulvar neoplasms; Diagnosis; treatment.

INTRODUCTION

Aggressive angiomyxoma is a locally aggressive, mesenchymal tumor. Pathogenesis has yet to be established and the incidence of the neoplasm peaks in the fourth decade of life.[1] The tumor occurs predominantly in the vulvovaginal, perineal and pelvic regions of females of reproductive age, with a female-to-male ratio of 6:1.[2]

The symptoms associated with this neoplasm are local pain and dyspareunia.[3] Clinically, differential diagnosis should be with Bartholin’s cysts, perineal hernias and vulvovaginal neoplasms.[1,4] The lesions are characterized by the appearance of an expansive, insidiously growing tumor that infiltrates the soft tissues of the pelvis and perineal regions, with a predominantly myxoid histological pattern and a high rate of local recurrence.[3] The recurrence rate of the lesion does not differ between patients submitted to resection with negative surgical margins and those with positive margins.[5] However, the occurrence of metastases is rare and underdiagnosis is very common.[4,5,7]

The present report describes the histopathological findings of a tumor compatible with an aggressive angiomyxoma of the vulva in a 41-year-old female patient receiving care at the Department of Obstetrics and Gynecology, Santa Casa de Misericórdia Hospital in Vitória, Espírito Santo, Brazil.

The internal review board of the School of Sciences, Santa Casa de Misericórdia de Vitoria (EMESCAM) approved the project under reference CAAE: 60116116.3.0000.5065. The patient gave her informed consent to the publication of this case report.

CASE REPORT

A 41-year old black woman (two pregnancies, two deliveries and no abortions) was admitted to the Department of Gynecology and Obstetrics, Santa Casa de Misericórdia Hospital in Vitória to undergo elective surgery to remove a lump in her vulva. At the time of admission to hospital, she reported that the lump had developed in her right vulvar region about a year previously, progressing with localized pain and dyspareunia. The patient reported no vaginal bleeding, fever or weight loss.
Physical examination showed the patient to be in a good general state of health. Cardiovascular, respiratory and urinary systems showed no abnormalities. Examination of the vulva revealed a nodular, largely immobile lesion with fibroelastic consistency, measuring approximately 9 x 5 x 5 cm, on the right vestibular area of the labium minus about 1 cm from the vaginal introitus and in contact with the posterior commissure of the labium majus (Figure 1).

Figure 1: Photograph of the lesion prior to surgical resection

Speculum examination showed an apparently normal cervical epithelium. The external cervical os was transverse, and there was no pathological discharge. Bimanual vaginal examination revealed a closed, moveable, painless fibroelastic cervix. The fundus of the uterus could not be palpated. Ultrasonography of the soft tissues showed a lobulated image measuring 6.8 x 7.5 x 5.1 cm with a volume of 101.6 ml on the right labium majus (Figure 2).

Figure 2: Ultrasound image of the lesion

Surgical excision of the lesion was conducted in an operating room, with the patient sedated and with the use of locoregional anesthesia. A vertical incision of about 4 cm in length was made in the lower part of the right labium minus. There was no fluid secretion. The lesion was poorly defined with a spongy consistency. Cold knife excision was performed, followed by hemostasis and wound closure. The surgical specimen, measuring approximately 9 x 7 cm and with a smooth surface, pinkish color and lobular appearance, was sent for anatomopathology (Figure 3). The patient progressed satisfactorily following surgery, with no complications. She was discharged with instructions to return for the histopathology results.

Figure 3: Macroscopic appearance of the lesion measuring 9 x 7 cm after the first surgical resection

At anatomopathology, macroscopic examination revealed a light brown, firm elastic nodular lesion measuring 9 x 7 cm (Figure 3). Microscopy of the histological sections revealed a stromal tumor with a predomination of lipoblasts, frequent mastocytes and other cells with an undulated spindle-shaped pattern. The lesion appeared well-vascularized and occupied the entire sample. The surgical margins were considered positive (Figure 4). Evaluation of the surgical specimen suggested a diagnosis of a stromal tumor (low-grade liposarcoma). Immunohistochemistry was performed to identify the phenotype.

Figure 4: Hematoxylin-eosin staining; magnification 400x. Mesenchymal tumor composed of myxoid stroma with spindle-shaped vessels; elongated, oval nuclei; cytoplasm with blurred borders and at times starry appearance. No evidence of mitotic figures.

The immunohistochemical profile identified was as follows: positive expression of CD34, negative staining of endothelial cells, protein S100-negative, alpha-smooth muscle actin-negative and desmin-positive, with 10% Ki-67. These findings are compatible with an aggressive angiomyxoma of the vulva.

Since diagnosis was of a malignant tumor, the patient in question was referred to the clinical oncology department for multidisciplinary follow-up. The oncology team recommended further surgery to increase the margins and evaluate them further, since they had not been evaluated at microscopy.

Inspection of the vulva nine months after the first surgery revealed a diffuse hardened area on the right side of the lower third of the vulva,
in the vestibular area, about 2 cm from the vaginal introitus and 1 cm from the posterior commissure of the right labium majus, at the site of the first surgery. Further cold knife excision was performed on the affected region. The material removed was again sent to anatomopathology. The patient progressed satisfactorily following surgery. There were no complications and she was discharged from hospital.

Macroscopic analysis of the surgical specimen identified two irregular, light-brown, firm, elastic tissue fragments measuring 3.0 x 2.0 cm. Microscopic analysis suggested a histologic diagnosis of aggressive angiomyoxa. The surgical margins were evaluated and found to be negative.

The patient continues to be followed up at the Department of Obstetrics and Gynecology of the Santa Casa de Misericórdia Hospital in Vitória and there has been no sign of any recurrence of the tumor six months after the second surgical procedure.

**DISCUSSION**

Aggressive angiomyoxa is a rare mesenchymal tumor that arises in the pelvic and perineal region of adult women, with its incidence peaking in the third to fourth decades of life.[1] The tumor growth is insidious, beginning with the appearance of a lesion on the vulva that may mimic other pathologies such as vulvar abscess, Bartholin's cyst or vaginal hernias.[2,5] Patients with an asymptomatic lesion may take two months to seventeen years to seek care at a medical facility.[4] In the case of the patient described here, clinical progression was similar to that of cases reported in the scientific literature, with diagnosis being made one year after the tumor first appeared in the genital area. Tumor diagnosis is reached by histological analysis of the lesion. Recurrence rates are high (30-72%); however, metastasis is rare.[4]

Little is yet known with respect to the pathogenesis of aggressive angiomyoxa. One of the hypotheses that have been suggested is that the tumor appears as a result of mutations in stromal cells in the lower genital tract. Immunohistochemical analyses of the tumors, which often contain cells in which vimentin is strongly expressed, desmin is poorly expressed and myosin is not expressed at all, support this hypothesis. These findings suggest, therefore, that an abnormal differentiation of fibroblasts may give rise to these tumors. Angiomyoxa is a tumor that responds to hormonal stimuli, as it expresses estrogen and progesterone receptors. Nevertheless, identification of these receptors does not help with the diagnosis of this tumor, since fibroblasts from the normal vulva may express these same receptors.[5,9-11]

At immunohistochemistry, findings of positivity for desmin, smooth muscle actin, vimentin, CD 34 and CD 44, and S100 protein negativity suggest a diagnosis of aggressive angiomyoxa. Cell mitosis is not usually found; however, mild atypia may be present.[4] In the case reported here, immunohistochemistry was required in order to reach diagnosis, with results showing an immune profile with abnormalities compatible with the tumor.

Wide surgical resection of the lesion, leaving free margins, is still considered the treatment of choice to avoid local recurrence of the disease and this was the approach used in the case reported here. Nevertheless, complete resection of an aggressive angiomyoxa is difficult, since the consistency of the tumor resembles that of the patient’s healthy connective tissue.[10,12] Neoadjuvant therapy with angiographic embolization and local radiotherapy is an acceptable means of reducing tumor size and the risk of recurrence; however, it is seldom used in clinical practice.[13]

Imaging methods such as computed tomography and magnetic resonance imaging (MRI) can be used to aid diagnosis and are important tools in the follow-up of the patient after surgical resection of the tumor in order to monitor the extent of the lesion.[14]

Pharmacological treatment with GnRH agonists has been proposed as an alternative and complementary treatment, since the majority of lesions are estrogen and progesterone receptor-positive. Nevertheless, the long-term use of this treatment is associated with various side effects such as menopausal-type symptoms and bone mass loss. Although add-back therapy can be used to minimize the side effects of hormonal treatments, there is concern with the use of estrogens/progesterone, since the tumor is receptor-positive for these hormones. Radiotherapy and chemotherapy are not recommended due to the reduced mitotic activity.[10,15]

Since recurrence rates are high, the patient should be followed up carefully over an extended period of time and submitted to physical examination and imaging tests, with MRI being the method of choice due to its greater sensitivity. This allows any recurrence to be identified early and treatment to be given, resulting in a lower risk of morbidity.[4]

The present case report serves as an alert to the medical community with respect to the importance of a differential diagnosis in cases of vulvar lesions, particularly the need to conduct a thorough and appropriate examination of the vulva during gynecological consultations. This should ensure a timely diagnosis and reduce the rate of underdiagnosed cases reported in the medical literature.

**Financial support:** None.

**Conflicts of interest:** The authors declare that there is no conflict of interest regarding the publication of this article.

**Authors’ Contribution:** ACF, ENVAA and FSFS contributed to the conception and design of the study; ENVAA and FSFS collected and assembled the data; ACF, ENVAA, FSFS and LLM were involved in the analysis and interpretation of data and in drafting the manuscript; ACF performed a critical revision. All authors read and approved the final manuscript.

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