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CASE REPORT

AGGRESSIVE ANGIOMYXOMA OF THE FEMALE EXTERNAL GENITALIA

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Abstract. *Aggressive angiomyxoma (AAM) is a rare and benign mesenchymal tumor that localizes predominantly in the female pelvis. Its invasive growth and local recurrence are challenging for professionals. Histologically, AAM is a tumor with a myxoid stroma that is highly vascular and hypocellular. The diagnosis is made relatively late due to nonspecific symptoms. Treatment of AAM is extensive local surgical excision with intact resection lines. Gonadotropin-releasing hormone agonists are added postoperatively. The prognosis is good and metastasis is rare. We present a case of an aggressive angiomyxoma located in the left greater labial area in a 50-year-old woman. After discussion and informed consent signed by the patient, on 27.01.2023 at the University Hospital "St. Marina" Pleven, the patient was admitted to the hospital. The tumor was extirpated under epidural anaesthesia on the date of the patient's informed consent. The patient was prescribed postoperative therapy with Zoladex 3,6 mg implant according to the schedule.The patient was subjected to monthly gynecological check-ups for one year after the surgical intervention. To date, no recurrence of the underlying disease has been detected. Long-term results show a good trend. In conclusion, we can say that the optimal treatment of AAM is wide local excision. It is not recommended to aim for radicality because of the risk of postoperative complications. Postoperative administration of GnRH-a is advisable to avoid recurrences. All patients undergo regular follow-up examinations for long-term follow-up.*

Key words: *aggressive angiomyxoma, soft tissue tumors*

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INTRODUCTION

Aggressive angiomyxoma (AAM) is a slow-growing mesenchymal tumor that is relatively rare. It localizes predominantly in the soft tissues in the small pelvic area of women (external genitalia, vagina and perineum). This tumor is benign. It is aggressive because of high incidence of local recurrence. AAM was first introduced in 1983 by Steeper and Rosai. To date, approximately 400 cases have been described in the world literature. It is mainly diagnosed in women of reproductive age, premenopausal and menopausal. The peak incidence has been shown to be around forty years of age. The female to male ratio is about 7:1. In males, aggressive angiomyxoma is localized in the inguinoscrotal region [1, 2]. The age distribution is as follows: the youngest patient diagnosed with AAM reported in the medical literature was a child at two years of age, and the oldest was 65 years of age [3, 4]. In WHO classification of soft tissue tumors (2003) AAM

was classified as a benign tumor with uncertain differentiation. It was then officially named "aggressive angiomyxoma". In 2020, following the update of this classification, aggressive angiomyxoma was classified in the same way. The pathogenesis of AAM remains unclear, but its specific invasive growth and local recurrence are a challenge for professionals [5]. Resection lines are often involved because the tumor is poorly circumscribed and infiltrates adjacent tissues. The recurrence rate is wide ranging, between 25% and 47% [6, 7]. In almost all cases reported in the literature, the provisional diagnosis differs from the final diagnosis made after histological examination. In most cases, patients are misdiagnosed with more common conditions such as inguinal or femoral hernia, Bartholin's cyst, perianal abscess, Gartner's cyst, fibroma or lipoma. In men, differential diagnosis should be made with tumors of the scrotum, spermatic cord, and perineum [8]. Most often, aggressive angiomyxoma has nonspecific symptoms. Patients report long-standing tumor formation, pelvic pain, local compression, dysmenorrhea, dyspareunia, and disturbances in micturition and intestinal peristalsis [9]. The most common localization of AAM is in the external genital area of the woman, especially the labia majora. In most cases, the lesions are unilateral. Other anatomical areas affected are: the lesser pelvis, perineum, vaginal introitus, vagina, cervix. Cases with multifocal localization have also been reported in the literature. In these patients, the external genital organs and the pelvic cavity, the vagina and perineum, the small intestine and lung, the pelvis and the heart are simultaneously affected [10, 11]. Under experimental conditions, a possible invasion of AAM into the colon of rats has also been found with neurotransmitter consequences in its longitudinal and circular muscles [11, 12, 13].

We present a clinical case of an AAM.

CASE PRESENTATION

The patient was referred to a surgeon due to a suspected left inguinal hernia. The patient was in her 50s and had no family history, with 2 children born by cesarean section and regular menstrual cycles. According to the patient, an extirpation of a left Bartholin's gland cyst was performed 12 years ago, but the medical records were lacking. Gynecologic examination showed a spherical, lobulated, mobile tumor, elastic consistency, located in the left labia majora area, measuring approximately 6/4 cm, without fluctuation. Vagina – compressed by the described formation. Ultrasonography of the lesser pelvis and the described tumor formation was performed: a superficial, spherical, lobulated and mobile tumor formation, with indistinct borders, with echo heterogeneous contents and measuring 62 x 40 mm in the left labia majora area (Fig. 1).

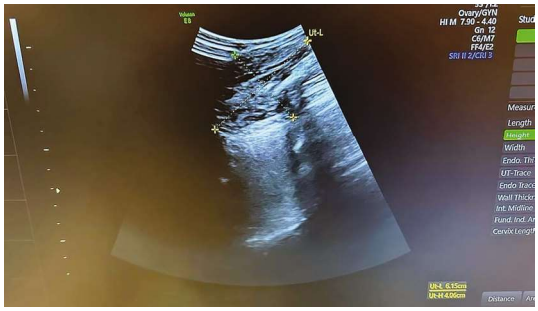

Fig. 1. Sonographic image of the tumor formation

The patient was consulted with a dermatologist, urologist and a gastroenterologist to rule out skin disease and gastrointestinal problems. After discussion and informed consent signed by the patient, antibiotic and anticoagulant prophylaxis was administered, and extirpation of the tumor formation was performed under epidural anesthesia in our hospital in January 2023. The stages of the operation are presented in figures 2, 3 and 4.

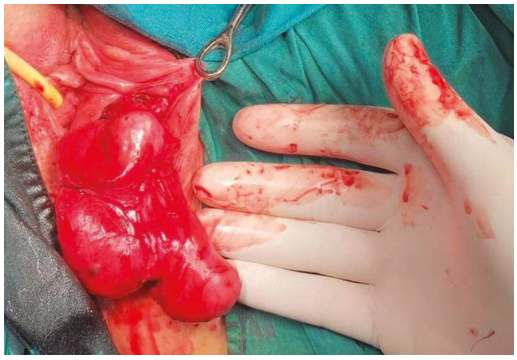

Fig. 2. Dissection of the tumor formation

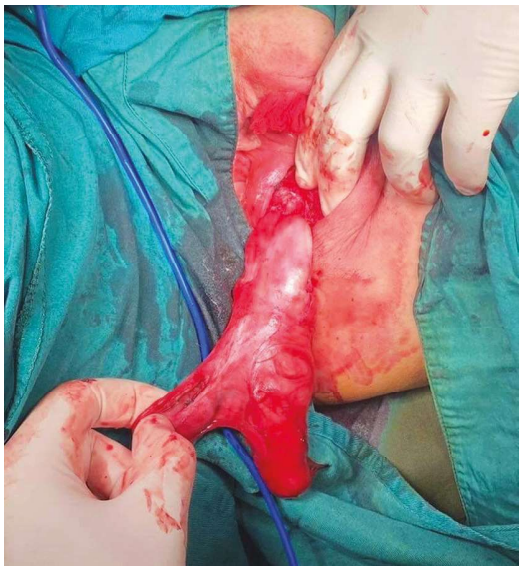

Fig. 3. The tumor formation before extirpation

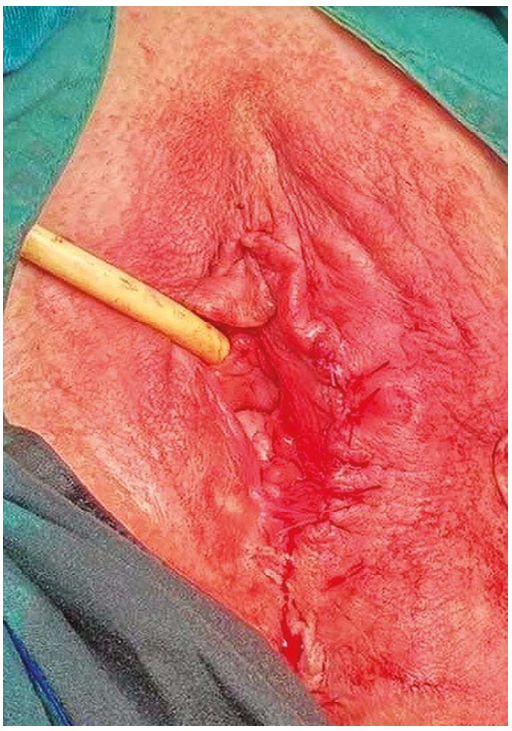

Fig. 4. Repair of the surgical wound with single sutures

In figure 5 we have demonstrated the macroscopic appearance of the lesion (Fig. 5).

The patient tolerated the manipulation well, without complications. We obtained the following result of histological examination: non-encapsulated and locally infiltrative tumor formation, represented by monomorphic, relatively small-sized spindle-shaped or stellate cells with delicate chromatin, mostly hypocellular, with focal increased cellularity; myxoid stroma with scattered delicate collagen fibers at periphery with accumulation of mature mast cells; focal erythrocyte extravasates; dilated capillaries and scattered large, thick-walled (with medial hypertrophy) or hyalinized vessels; clustering of stromal smooth muscle bundles around vessels; resection lines uninvolved. The result of immunohistochemical analysis showed: high expression of desmin and vimentin (100%); positive ER expression; lack of expression of the Ki-67 marker. Diagnosis of aggressive angiomyxoma of the external genitalia was made. The patient was assigned postoperative therapy with GnRH-agonists (Zoladex 3.6 mg implant) according to the following schedule: one subcutaneous application every 28 days for 6 months. Administration of the GnRH agonist ended in August 2023. In Figure 6, we demonstrate the esthetic outcome of the surgical intervention at the seventh postoperative month (Fig. 6).

The patient underwent monthly follow-up gynecological examinations for one year after the surgical intervention. To date, no recurrence of the underlying disease has been detected. Long-term results show a good trend.

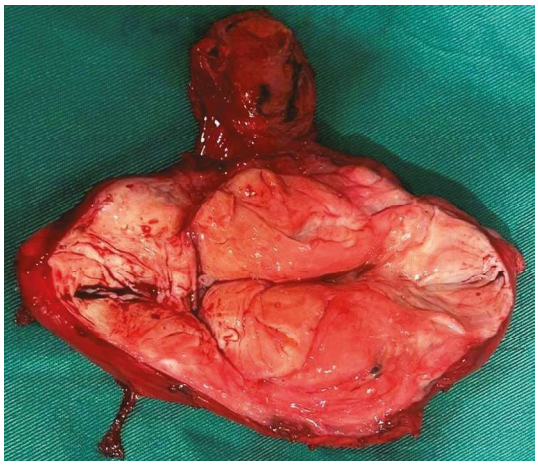

Fig. 5. Macroscopic appearance of the lesion

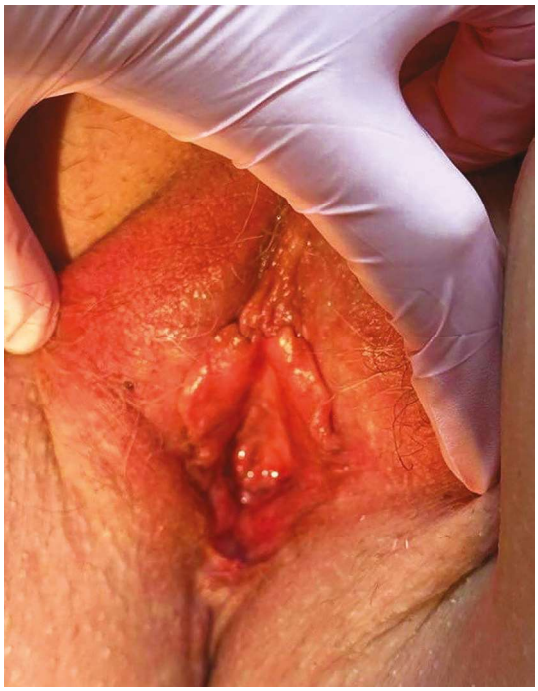

Fig. 6. Esthetic result of surgical intervention 7 months after tumor extirpation

DISCUSSION

Aggressive angiomyxoma is a benign mesenchymal tumor that is rare and of unknown etiology. It predominantly affects female patients. Approximately 400 cases have been described in the literature. It is most commonly located in the pelvic and perineal regions and is prone to local recurrence [14]. As early as 1996, the Kenny–Moynihan team described their study. They found that the likely pathogenesis of the disease was loss of the X chromosome (45, X) in about 40% of the cells of patients with AAM [15].

AAM occurs in patients of various ages (from 2 to 80 years of age), with a peak incidence between 30 and 40 years of age. In 2022, Muskan et al. presented a case of aggressive angiomyxoma diagnosed in a 19-year-old female patient located in the external genital area [16]. In 2020, Xu and his team from Fujian University Hospital, China, described a case of vulvar AAM detected during the first pregnancy of a 25-year-old female patient. After pregnancy, partial resection of the formation was performed due to increasing size. During the second pregnancy of the same patient, a recurrence was diagnosed, which was removed after delivery. Current studies have shown that AAM is a hormone-dependent tumor as it affects one third of reproductive age women. The diagnosis is made late due to the lack of symptoms in the early stages. Orfanelli and his co-authors present a case demonstrating the hormonal sensitivity of AAM. They observed rapidly increasing AAM during pregnancy and described its spontaneous regression in the postpartum period [17]. The imaging diagnosis of AAM helps to establish the diagnosis and is determinant for the extent of surgical treatment. According to Tariq's team, the ultrasonographic image of the lesion is hypoechogenic, but preferably a nuclear magnetic resonance imaging is performed. Fine-needle aspiration biopsy under ultrasonographic guidance helps to clarify the diagnosis [18]. The only possible treatment of AAM is surgical. According to Chan and his associates, the optimal extent of surgery is wide local excision. However, they demonstrate that the width of the resection lines do not have much significance for the long-term prognosis. The authors followed 106 patients operated on for AAM for 10 years after surgical treatment. They demonstrated that there was no statistically significant difference in recurrence rates between patients with intact and involved resection lines. However, this is associated with a high incidence of surgical trauma and perioperative complications. The Espejo-Reina team described the management of AAM diagnosed during pregnancy. They characterized the rapid growth due to hormonal stimulation of the tumor's estrogen receptors. Due to the risk of significant bleeding, it is not advisable to remove the formation during cesarean section. In patients who refuse surgical treatment, the alternative is conservative therapy with GnRH-a. This will help to reduce symptoms and tumor volume [19, 20]. In 2009, Aye and colleagues described for the first time the follow-up of AAM in a woman before, during and after pregnancy. Before becoming pregnant, they removed an AAM located in the right labia majora area. At the 20th gestational week, the authors reported a significant growth formation located at the site of the primary tumor. Six weeks after cesarean section, they described spontaneous regression of size [21]. In patients of reproductive age, due to positive ER, a reduction in the recurrence rate is targeted. In these cases, postoperative treatment with GnRH-a is recommended.

CONCLUSION

Aggressive angiomyxoma is a benign mesenchymal tumor, but its clinical symptoms cause discomfort and reduce patients' quality of life. The optimal treatment of AAM is wide local excision. It is not recommended to aim for radicality because of the risk of postoperative complications and the lack of a statistically significant difference in recurrence rates between patients with intact and involved resection lines. Postoperative administration of GnRH-a is recommended to avoid recurrences. All patients should undergo regular follow-up examinations for long-term follow-up.

Disclosure summary: *The authors have nothing to dislose.*

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