Aggressive Angiomyxoma of the Perineum in a 50-Year-Old Woman: Case Report and Current Level of Education

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Abstract

Background: Aggressive angiomyxoma is a rare soft tissue mesenchymal tumor, locally infiltrative with a tendency to repeated local recurrence. The first description was in 1983. Normally it occurs in the vulvovaginal region, perineum and pelvis of females in reproductive age. Local wide excision of the tumor is the primary management. The local recurrence rate is high. The expression of estrogen and progesterone receptors in aggressive angiomyxoma suggests a hormone dependency of the tumor.

Case report: A 50-year-old woman reported first in 2013 with a painless swelling at the perineum. She underwent surgical excision. Pathologic findings reported the tumor as an aggressive angiomyxoma. The patient did not appear to the follow-up examinations. In 2016 she reported again with a painless swelling at the perineum and underwent a local wide resection. The perineal body had to be reconstructed because of the deep infiltration of the tumor.

Conclusion: Aggressive angiomyxoma is a rare disease, but when treating women with a painless swelling in the vulvovaginal region, perineum or pelvis aggressive angiomyxoma should be considered as a differential diagnosis. There is no standardised therapy described, but complete resection seems to be important. Descriptions of pharmacologic treatment exist with gonadotropin-releasing hormone agonists.

Keywords: Aggressive angiomyxoma; Vulvovaginal region; Local recurrence rate

Introduction

Aggressive angiomyxoma is a very rare soft tissue mesenchymal neoplasm (only about 350 cases described in literature) [1], locally infiltrative with a tendency to repeated local recurrence. The first description was in 1983 [2]. It normally occurs in the vulvovaginal region, perineum and pelvis of females in reproductive age. It grows slowly as a painless solid mass with unclear boarders and the aggressive angiomyxoma often infiltrates the deep tissues. The growth can be expansive until the whole pelvic cavity is occupied [3]. Even if the tumor infiltrates the bladder, the rectum, the retroperitoneum, the pelvic bone or the levator ani muscle, the patients are often asymptomatic [4,5]. There are rare cases of aggressive angiomyxoma in the inguinoscrotal region of males and usually appear in older age [6]. This difference between males and females cannot be explained [7]. Other rare cases are described in children and perimenopausal women [5]. The female-to-male ratio is about 6:1 [8]. Metastases have been described in three cases. These distant metastases were all found in the mediastinum or lungs [9-11]. This suggests that aggressive angiomyxoma is not only a local disease. Wide local excision of the tumor is the primary management. The local recurrence rate is 25% to 47% after surgical excision [12]. The expression of estrogen and progesterone receptors in aggressive angiomyxoma and the growth of the tumor during pregnancy suggest a hormone dependency of the tumor [13]. Descriptions of drug treatment exist with gonadotropin-releasing hormone (GnRH) agonists in premenopausal women [14-17]. This locally aggressive tumor is a rare disease, therefore the state of knowledge how to treat patients with this soft tissue mesenchymal neoplasm is low.

Case Report

A 50-year-old woman reported first in 2013 with a painless swelling of 1.2 × 0.8 inches at the perineum. She underwent surgical excision. Pathologic findings reported the tumor as an aggressive angiomyxoma. The margins were not tumor-free. The patient did not appear to the follow-up examinations. In 2016 she reported again with a painless swelling of 0.8 × 0.8 inches at the perineum (Figure 1) and underwent a wide local excision. The tumor infiltrated the perineal tissue deeply and for the complete resection it was necessary to resect a part of the bulbocavernous muscle and the soft tissue of the perineum above the rectum. Then the perineal body had to be reconstructed by the urogynecologist. To stabilize the distal part of the rectum a plication of the rectovaginal fascia, after
preparing both sides, was necessary, followed by closing the posterior vaginal wall. The rebuilding of the perineal body consisted in mobilization of fatty tissue laterally from both sides. This tissue was used as an interposition layer to the perineal space. Finally, the perineal skin was closed.

There is no specific immunohistochemical marker for aggressive angiomyxoma and the most markers overlap with other mesenchymal lesions. Except for estrogen and progesterone receptors, there are other immunohistochemical markers, such as vimentin, desmin, SMA (smooth muscle actin), CD 34. But not all the cases are positive for these markers [7,19-21]. Genetic findings show a chromosomal abnormality involving chromosome 12, associated with rearrangement of the high mobility group A (HMGA2) gene. HMGA2 is an architectural transcription factor, which is important during embryogenesis. In adult tissues it is not usually detected. The pathogenesis of aggressive angiomyxoma is poorly understood [6,7,21-24]. Other benign mesenchymal lesions like uterine leiomyomas, endometrial polyps and other mesenchymal neoplasms have the same rearrangement of HMGA2 [19].

As diagnostics ultrasound and computerized tomography are nonspecific. In the ultrasound the neoplasm is usually a hypo echoic soft tissue mass and it could also appear as a cystic lesion [6]. In the computerized tomography the aggressive angiomyxoma appears variably as a homogenous hypo dense mass, cystic or even as a swirling solid mass. In magnetic resonance imaging the aggressive angiomyxoma is distinctive. On T1-weighted scans the mass is iso intense or hypo intense like muscle. On T2-weighted scans the tumors are characteristically hyper intense, except for their lower signal internal structure which looks swirled or layered. Magnetic resonance imaging is also helpful in planning the surgical excision with the aim of tumor-free margins [6,17,25,26].

All over the world the published number of cases is very small (about 350 cases) and so the interpretation of the data is often difficult. The first therapy is a wide local excision with the aim of tumor-free margins. But in the published data the influence of tumor-free margins is not clear. Complete resection is important, but when the operative morbidity is too high or the preservation of the fertility is necessary incomplete resection seems to be acceptable [8,18]. It is recommended to treat the tumor at an initial stage, when complete resection is possible. Wide surgical margins have the same influence on prognosis as narrow margins [8,17,27,28].

For a successful therapeutic concept, it is important to know if the tumor has positive estrogen and/or progesterone receptors. If both are negative, a hormonal treatment will not be successful and the surgical excision with, if necessary, pre-operative arterial embolization is the best option. The tumors often have multiple feeding vessels, so it is difficult to succeed in embolization alone [8,17,29].

When the receptors are positive and the tumor is limited, the best therapeutic option is the surgical excision. If there is a residual disease after surgery, a hormonal treatment can be recommended. If the morbidity of the tumor resection is not tolerable, a neoadjuvant hormonal therapy is a feasible alternative with following surgical excision [17]. Descriptions of only drug treatment without surgery and with complete radiologic remission exist [16].

Discussion

Aggressive angiomyxoma is a very rare disease, which occurs primarily in young women in reproductive age. The initial presentation is often a painless, asymptomatic perineal or vulval nodule. Therefore, a clinical misdiagnosis is not unusual. The nodule can be mistaken as a lipoma, Bartholin’s or Gartner’s duct cyst, abscess or even as a malignant pelvic floor tumor. Because of the rarity of the aggressive angiomyxoma pre-operative diagnosis is difficult and a lot of cases are diagnosed on histological findings after the surgical excision [6,18].

Macroscopically the surface of the tumor is smooth and partially or completely encapsulated [6].

Microscopically the aggressive angiomyxoma is composed of many thick-walled vessels of varying size in a loose collagenous and myxoid stroma with spindle and stellate like cells [15]. Generally, the lesions show no cytologic atypia, no cell necrosis and a low mitotic activity [6].

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In the literature gonadotropin-releasing hormone (GnRH) agonists is the recommended hormonal treatment in premenopausal women. The response to gonadotropin-releasing hormone (GnRH) agonists varies, because the estrogen and progesterone receptors are not always strongly positive in aggressive angiomyxoma [15-18]. There exist no data of the optimal duration of the therapy [27]. A long-term therapy is not recommended because of the adverse effects like menopausal symptoms and bone loss. Often there is a recurrence of the tumor after discontinuing therapy. [17]. But until now it has not been shown that a long-term adjuvant therapy prevents the recurrence of the tumor [1].

In postmenopausal women aromatase inhibitors are preferred in estrogen positive aggressive angiomyxoma [30]. Hormone replacement therapy should be stopped [17].

In the exceptional situation of non-operative tumor without response to embolization or hormonal treatment radiation therapy can be considered [27].

The low mitotic activity of the tumor is the reason why radiation therapy or chemotherapy are not really successful [19,23].

A deep infiltration of the perineal tissue requires a resection of a part of the bulbocavernosus muscle and the soft tissue of the perineum above the rectum to get a complete resection of the tumor, followed by reconstruction of the perineal body. To get an acceptable functional result the pelvic floor reconstructive surgery is to be done by a urogynecologist. Knowledge of gynaecologic oncology is also useful in the management of aggressive angiomyxoma. A multimodal, interdisciplinary approach is pivotal to minimize the recurrence rate in combination with a low morbidity. This concerns clinical examination, imaging, surgery, adjuvant treatment and follow-up.

**Conclusion**

Aggressive angiomyxoma is a rare disease, but when treating women with a painless swelling in the vulvovaginal region, perineum or pelvis aggressive angiomyxoma should be considered as a differential diagnosis. There is no standardised surgical or pharmacologic procedure described, but complete resection seems to be crucial. A multimodal approach is important. Even tumor-free margins do not prevent a recurrence [5,19,31]. There is no established relation between the size of the tumor, the patient’s age and the risk of recurrence [8].

Long-term follow-up is important because of repeated local recurrence. Clinical examination and radiological imaging, especially magnetic resonance imaging is recommended [13,25].

**Disclosure and Conflict of Interest**

- All authors of this paper have directly participated in the planning, execution analysis of the study. They have read and approved the final version submitted.
- The contents of the manuscript have not been copyrighted or published previously and are not now under consideration for publication elsewhere. There are no directly related manuscripts or abstracts, published or unpublished, by any author(s) of this paper.
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