Case Reports

Aggressive angiomyxoma: case report and review of the literature

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Summary

Aggressive angiomyxoma is a rare benign mesenchymal neoplasm, found mainly in the female pelvis and perineum. Approximately 160 cases have been reported in the literature to date. The tumor is usually misdiagnosed at presentation. Surgical and margin-free excision is considered the treatment of choice. Other treatment options include use of hormone antagonists, such as tamoxifen, or GnRH analogs, and selective angiographic embolism. High recurrence rate of the tumor, up to 70% within a 2-year period, makes long-term imaging follow-up of the patient necessary.

Key words: Aggressive angiomyxoma; Vulva; Perimenopausal.

Introduction

Aggressive angiomyxoma is a rare soft tissue neoplasm, of mesodermal origin, that arises mainly in the female vulva, perineum and pelvis, most commonly among young patients. Approximately 160 cases have been reported in the literature to date. Clinical presentation resembles other benign lesions of the region, such as bartholinitis, and so diagnosis is not established in most cases pre-operatively. Imaging modalities can be used for both preoperative localization of the lesion and postoperative detection of recurrences. We report a case of aggressive angiomyxoma in a perimenopausal patient.

Case Report

A 45-year old woman, gravida 1, para 1, presented in 2004 with swelling of the left labium associated with superficial dyspareunia. The swelling was non tender and of soft consistency, and it first appeared six months earlier and gradually increased in size. The primary impression was that of a chronic bartholinitis. Because of this subjective impression no further preoperative imaging was undertaken. Excision of the mass was performed via an incision on the labia under general anesthesia. The surgery resulted in the excision of a soft, solid multilobulated tumor with finger-like projections. The size of the mass was approximately 10 x 5 x 3.5 cm and since it was ascending into the perineum infiltrating the adjacent soft tissues, we were not sure if the lesion was completely excised. Histologic examination revealed aggressive angiomyxoma. It was a solid lesion composed of stellate and spindle shaped cells in a collagen and hyaluronic acid containing stroma without evidence of nuclear atypia and infrequent mitosis. On cut section, vessels of various size and smooth muscle bundles were identified. Immunohistochemistry revealed positive reaction for desmin (50%), progesterone receptors (70%) and estrogen receptors (30%). The patient did not receive further treatment, such as tamoxifen or GnRH analogs. Magnetic resonance (MR) imaging scans performed at six months, one year and two years after the excision revealed no signs of recurrence.

Discussion

Aggressive angiomyxoma was first reported in 1983 as a clinicopathologic entity by Steeper and Rosai [1]. It is a rare benign mesenchymal tumor with predilection for involving the female pelvis and perineum. Only few cases of aggressive angiomyxoma have been reported in male patients; the female to male presentation ratio is estimated to be 6.6:1 [2]. The reported age range is 11 to 77 years [3], with more than 90% of the cases occurring in the second to fourth decade.

The size of the lesion at presentation varies considerably, however the tumor may often reach large dimensions before becoming symptomatic. Lesions as large as 60 cm have been reported [4], with the majority being approximately 10-20 cm in greatest diameter. However the true extent and size of the lesion is usually underestimated on the initial physical examination.

Aggressive angiomyxomas are frequently mistaken for Bartholin gland cysts, vaginal cysts, lipomas, abscess, Gardner's duct cyst, perineal hernia, sciatic hernia, obturator hernia and the rarely seen lymphangioma circumscriptum of the vulva [5]. Differential diagnosis should also include other benign lesions, such as angiomyofibroblastoma, fibroepithelial stromal polyps, cellular angiofibroma and superficial angiomyxoma [6].

Macroscopically, aggressive angiomyxomas present as large, soft homogeneous, non encapsulated, fleshy in consistency, easily compressible lesions. They are locally infiltrative with finger-like projections into the surrounding tissues without necessarily infiltrating the

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adjacent organs. Aggressive angiomyxomas may occasionally present as a pedunculated mass in the area of the vulva and introitus [3, 7-9]. They generally displace rather than invade the adjacent organs in the paravaginal and parametrial spaces, such as the rectum and the urinary bladder, and are rarely destructive [10]. Although aggressive angiomyxoma is a non-metastasizing tumor, it has the notorious tendency for local recurrence in approximately 70% of the cases within a two-year period [1, 4, 11]. Hence, the adjective "aggressive" is used to emphasize the potential for recurrence rather than the tendency to "attack" distant organs. Only two reports presenting a metastasizing aggressive angiomyxoma are available [12, 13]. One of those reports was later dismissed as a misdiagnosed sarcoma [14].

Microscopically, the tumor is composed of stellate and spindle-shaped cells in a collagen and hyaluronic acid containing stroma [1, 3, 4]. The stromal cells express fibroblastic or myofibroblastic features. Aggressive angiomyxoma may have a limited potential to full myogenic differentiation, with smooth muscle bundles seen in the stroma [10]. The lesions are paucicellular with minimal nuclear atypia and infrequent mitotic figures. On cut section, small to middle size vessels are recognized (Figure 1) [3].

Stromal cells uniformly express vimentin. Desmin, muscle-specific actin and α-smooth muscle actin are found in the majority of the lesions, although some have reported complete absence of the last in their studies [3, 4, 15]. CD44 is also expressed in most cases. Evidence suggests that CD44 has a significant role in the infiltrative growth behavior of the tumor. The strong prevalence of this marker in aggressive angiomyxoma, seen in many studies, alludes to its possible use as a diagnostic aid [3, 16]. Aggressive angiomyxoma has no immunohistochemical reactivity for myoglobin, cytokeratin, type IV collagen, CD68 or S-100. Finally, almost all cases reported showed presence of estrogen and progesterone receptors [3, 4, 17], suggesting that circulating hormones may influence the tumor. Immunocytochemistry is of little help when it comes to differentiating aggressive angiomyxoma from other mesenchymal benign lesions of the perineum. Perhaps, CD44 could be used for differential diagnosis among those tumors, but more studies are required in this direction [3, 15, 16].

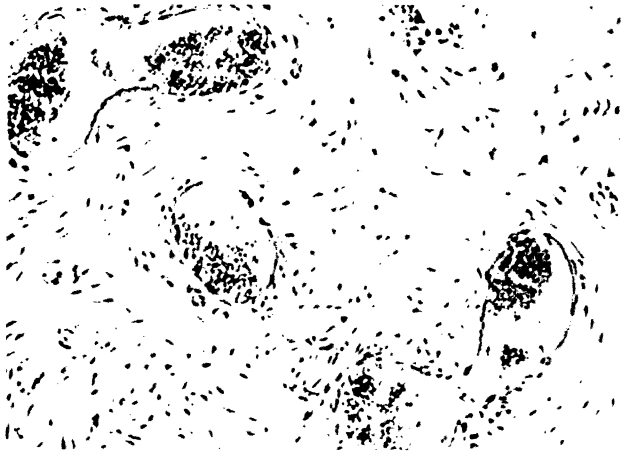

Figure 1. – Histological section (x100) of aggressive angiomyxoma showing small & middle-size vessels, stellate & spindle shaped cells in collagen-rich stroma.

Pretreatment imaging evaluation of the size and the lesion's relation to the pelvic floor and adjacent organs is significant to the surgeon, in order to plan a surgical resection and achieve complete margin-free excision. Ultrasonography demonstrates a polypoid hypoechoeic soft tissue mass, which may appear cystic, and it does not add any useful additional information [10]. Computerized tomography (CT) images are variable. The lesion will appear well defined, homogeneous and hypodense relative to muscle. An important diagnostic feature present in more than 83% of the patients is the characteristic swirling internal architecture [18, 19]. MR features are characteristic and typically demonstrate an isointense tumor relative to muscle on T1-weighted and hyperintense on T2-weighted imaging, due to the loose myxoid matrix and high water content. The avidity of the mass is enhanced when intravenous contrast medium is used, and may show a swirled component of lower intensity within the higher intensity lesion. MR imaging also has a place in the postoperative follow-up of the patient for early detection of possible recurrences. Intravenous pyelography, barium enema, pelvic angiography, and bone scan may add some information to the study of the extent of the tumor [18, 19].

Surgery is considered to be the primary treatment modality by most reports. The need for complete and margin-free removal of the tumor to minimize the risk of recurrence may result in a wide excision. Keeping in mind the proximity of the adjacent organs, such as the urethra, urinary bladder, vagina, rectum and anal sphincter and the fact that the lack of a capsule results in ill-defined borders of the lesion, suboptimal resection of the tumor may always be considered [10, 20, 21]. Chan *et al.* suggested that patients with clear resection margins have a risk of recurrence similar to that of patients with positive margins and that risk of recurrence is irrelevant to the size of the lesion [2].

Because of the low mitotic activity of the tumor, it is doubtful that systemic chemotherapy and radiotherapy are thought to be of limited therapeutic use [5]. On the other hand, the demonstration of estrogen and progesterone receptors in some cases lead us to believe that there is a place for hormone antagonists, such as tamoxifen, raloxifene and GnRH analogs, as a treatment option, especially in premenopausal patients [21]. Hormonal manipulation could also be used preoperatively in order to decrease the size of the lesion, and therefore reduce the extent of excision. Postoperatively administration of hormone antagonists could be indicated either in case of suboptimal resection or for recurrences of the disease. Selective angiographic embolization of the feeding vessel has been suggested as an alternative approach. Some studies confirmed that the tumor could be supplied by multiple vessels

[22]. Thus, embolization can only be applied, probably preoperatively, to reduce the tumor size [20].

In conclusion, although rare, aggressive angiomyxoma must at least be considered in the differential diagnosis of any woman presenting with a large asymptomatic perineal mass. If the diagnosis is confirmed preoperatively, then an MR imaging study should be performed to evaluate the size and location of the tumor in relation to the adjacent organs. Wide and margin free excision of the mass should be performed, followed by long-term imaging follow-up, so as to detect as early as possible any recurrence of the tumor.

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