Aggressive angiomyxoma of the vaginal wall at the initial stage: a case report

G. Carta[1], V. Parisse[1], V. Accurti[1], L. Sollima[2], L. Di Stefano[1], A. D'Alfonso[1], F. Patacchiola[1]

[1]Department of Surgical Sciences, [2]Department of Health Sciences, University of L'Aquila (Italy)

Summary

Aggressive angiomyxoma (AA) is a rare mesenchimal tumor usually located in the pelvic and perineal region. Less than 30 cases of aggressive angiomyxoma with vaginal location have been reported in the literature up to this date. The authors report the case of a 50-year-old female patient diagnosed with vaginal AA whose characteristics at its initial stage were macroscopically indistinguishable from those of a polypoid lesion. Therefore this case suggests that this type of tumor should be considered as part of the differential diagnosis of vaginal polypoid lesions.

Key words: Aggressive angiomyxoma; Polyp; Vagina.

Introduction

Aggressive angiomyxoma (AA) is an uncommon, benign, and mesenchymal tumor of unknown etiology with a high-isk of infiltrative growth and local recurrence, occurring in the vulvo-vaginal region, pelvis, and perineum of women during their reproductive years. AA was first described in 1983 by Steeper and Rosai [1] and around 250 cases have been reported in world medical literature since then [2]. Ninety percent of women presenting this tumor are in their reproductive years with a peak incidence in the fourth decade of life [3]. Similar lesions have been described in men, postmenopausal women, and in children. AA typically displays slow growth and has a gelatinous appearance; it is not encapsulated and has the same consistency as the surrounding connective tissue. Due to these characteristics, as well as its anatomical position, surgical excision is difficult and the tumor recurs following incomplete excision. Two cases of systemic metastasis have been reported [4, 5].

Materials and Methods

A 50-year-old woman with endometrial hyperplasia was admitted to San Salvatore Hospital in L'Aquila for a hysteroscopy and an endometrial biopsy. The patient was a smoker with a family history of breast cancer and a light, regular menstrual cycle. The patient had suffered a miscarriage and delivered two children, one by natural delivery and the other by Caesarean. She had been suffering from sideropenic anaemia in the months prior to her admission and was followed regularly by a gynaecologist: a pap test carried out in 2009 was negative while a scan performed in September 2009, revealed endometrial thickening (12 mm) that was not associated with her menstrual cycle. On examination, a polypoid mass was found in the right lateral wall of the vagina. This mass was one cm in diameter and soft in consistency. Routine blood tests were normal: haemoglobin of 12.9 g/dl and a white blood cell count of 5.47 mm^3: neutrophils (64.8%), lymphocytes (24.9%), eosinophils (1.7%), monocytes (6.1%), and basophils (0.3%). Liver and renal function tests were normal. The preoperative clinical diagnosis was vaginal polyp. A hysteroscopy and endometrial biopsy were performed under general anaesthetic; the lesion was excised with a sufficient margin at the site of the stalk and was reconstructed with a flap.

Results

The pathological diagnosis was "endometrial simple hyperplasia without atypia and aggressive angiomyxoma of the vagina". The surgical borders of the specimen were negative for tumor. Microscopically, the neoplasm was paucicellular and contained stellate and spindle cells embedded in an abundant myxoid stroma with some collagen formation and numerous blood vessels of varying calibre, open, thick-walled, and often hyalinized. Smooth muscle cells were observed in loose clusters or around blood vessels (Figure 1). Tumor cells had ovoid nuclei with dispersed chromatin and eosinophilic cytoplasm. Mitotic activity and nuclear atypia were absent. Immunohistochemically the cells showed positive reactivity for desmin, vimentin, CD34, and estrogen and progesterone receptors (Figure 2 and Figure 3). The patient was advised to return for a follow-up in two years, in view of the high rate of recurrence.

Discussion

The term 'aggressive angiomyxoma' was adopted by Steeper to underline the neoplastic nature of the blood vessels and its locally infiltrative and recurrent nature [1]. The World Health Organizaton describes AA as a "soft tissue neoplasm of uncertain differentiation" [6]. The tumor has been found in the pelvis and perineum, the vulvar region being the most common site [7]. Vaginal location has only been described in approximately 30 cases in literature. AA has been associated with a clonal chromosomal translocation in chromosome 12 (T(8,12), (p12;q15)) [8], that results in an aberrant expression of the HMGA2 protein (previously known as HMGIC), a

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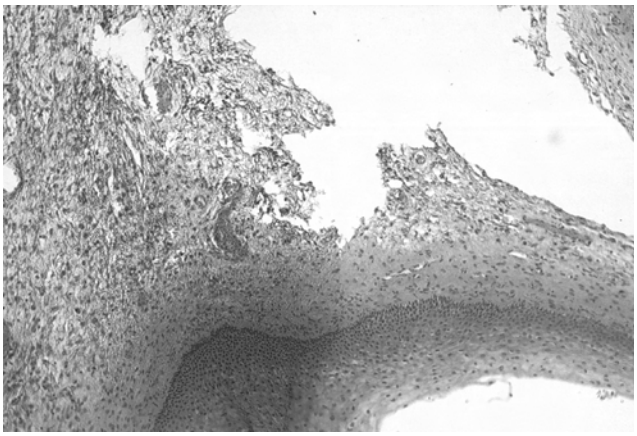
Fig. 1



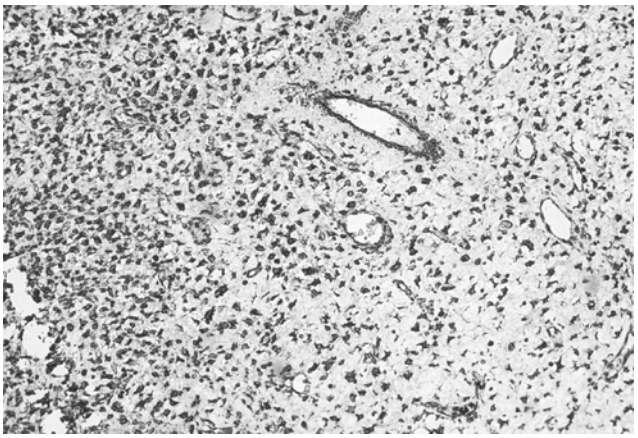


Fig. 2

Fig. 3

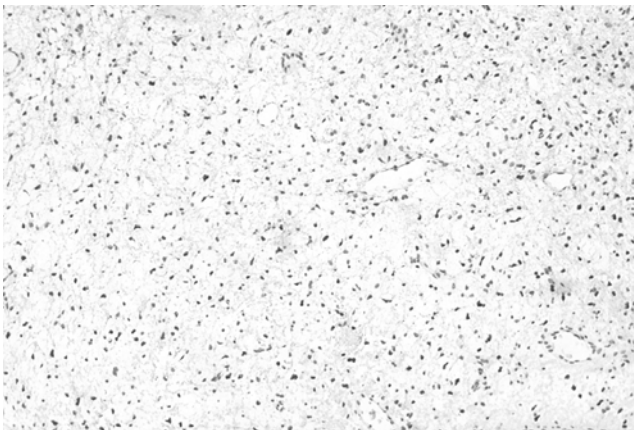


Figure 1. — Aggressive angiomyxoma: the typical morphology with spindle and stellate cells in a hypocellular myxoid stroma containing large thick open-walled blood vessels.

Figure 2. — Vimentin positive cells: tumor cells are typically immunoreactive to vimentin.

Figure 3. — Immunohistochemical staining: positive staining of stromal cells for the estrogen receptor.

DNA architectural factor which plays an important role in transcriptional regulation. The over-expression of HMGA2 may be useful as a marker when used in the immunoperoxidase technique. A recent study has shown that the HMGA2 protein can be used after the initial diagnosis to evaluate margins and for identifying foci of residual or recurrent tumor [9]. However the pathogenetic mechanism involved is still the subject of study. Macroscopically, AA is typically deep, poorly-circumscribed, of a gelatinous, myxoid or occasionally fibrous consistency, and larger than ten cm in diameter. On slicing, the tumor often sticks tenaciously to the knife. Clinically it may be mistaken for Bartolini's cyst, Gartner's duct cyst, vaginal prolapsed, a vulvar abscess, a vaginal mass, a polyp, hernia or lipoma. The tumor appears as a hypoecogenic mass similar to a cyst in an ultrasound scan, however, magnetic resonance imaging (MRI) is the gold standard for diagnosis: the tumor appears hypo-isointense with the muscle on T1-weighted images and hyperintense on T2-weighted sequences and shows a characteristic swirled intense pattern in gadolinium-enhanced T1-weighted sequences [10].

No radiological investigations were carried out as the clinical appearance of the tumor was that of a benign polyp. The differential diagnosis of this unusual tumor takes into account angiomyofibroblastoma, intramuscular myxoma, myxoid liposarcoma, myxoid neurofibroma, and sarcoma botryoides, a myxoid variant of malignant fibrous hystiocytoma. Distinguishing this disease from angiomyofibroblastoma (AMF) is very important. Both are rare mesenchymal tumors which were first compared by Fletcher [11]. AMF is characteristically a well-circumscribed and superficial lesion and is typically less than five cm in diameter; histologically it is composed of alternating hypocellular and hypercellular areas with plumper and round-shaped cells in clusters or in a linear array around small capillary-sized vessels. Tumor cells are typically immunoreactive to vimentin and often to desmin and α-SMA; there is also immunoreactivity to estrogen and progesterone receptors. AMF demonstrates hypointense and hyperintense signals on T1-weighted and T2-weighted sequences respectively, and has a strong and homogeneous uptake in gadolinium-enhanced T1-weighted sequences [10]. AMF is a benign and non-recurring tumor and local surgical excision with clear margins is adequate treatment. AA, on the other hand, is a low-cellularity neoplasm containing small bland ovoid, spindled or occasionally stellate-shaped cells embedded in an abundant myxoid matrix. Mitotic activity and nuclear atypia are absent. Blood vessels are medium to large sized with thick, muscularized, and hyalinized walls [1]. Immunohistochemical stains show cells positive for vimentina, desmin, smooth muscle-actin (SMA), CD34, estrogen and progesterone receptors, and negative for S-

100 [12]; androgen receptor positivity has been described in cases in men. The preoperative diagnosis is challenging because patients are asymptomatic. A correct differential diagnosis is necessary for appropriate treatment and when AA is suspected, peripheral tissue should be resected to prevent recurrence. However only a microscopic examination, with immunohistochemical staining can confirm the diagnosis. Treatment usually consists in local surgical excision; however hormone-receptive patients have been treated with SERM (tamoxifen and raloxifen), aromatase inhibitors and GnRH analogues. Embolization and chemoembolization have also been used as treatment [13] while prophylactic ovariectomy is still the subject of study. Chemotherapy and radiotherapy are not used because the tumor has low mitotic activity. The local recurrence rate of AA is 9-72% [12] in the five years after surgical excision: approximately 70% of these within the first three years but late recurrences of up to 14 years have been reported [2]. Recurrence frequently occurs at the resection margins and is usually the result of insufficient primary excision, due to the fact that the tumor is non-encapsulated and has the same consistency as that of the surrounding connective tissue. The ischiorectal fossa, perineum, pelvis, and retroperitoneum are the most common sites of recurrence documented in literature. In these cases surgical excision, radiotherapy and/or chemotherapy have been performed with some success. Follow-up should be clinical and radiological using MRI.

In the literature, angiomyxomas are consistently described as sizeable masses usually located elsewhere; however this presented case highlights the incidental finding of a neoplasia at an initial stage. This report details the initial growth phase of the neoplasia, before it acquires the characteristic features and dimensions that would lead a gynecologist to diagnose an angiomyxoma.

Indeed, pre-excision examination revealed a diameter of a few millimeters, a pink color that exactly matches the color of the vaginal mucosa, and the absence of abrased, bruised, or necrotic areas on the surface or the narrow base of implantation. These characteristics favored a preoperatory diagnosis of pedunculated polypoid lesion of the lateral vaginal wall, and thus photographic evidence of the lesion, which was under hysteroscopic monitoring for a different clinical indication, was not taken. Postoperative histological examinations, however, identified the lesion as an angiomyxoma. In addition to the rarity of the neoplasia and its unusual location, this angiomyxoma is notable for the early stage at which it was diagnosed.

The authors conclude, therefore, that angiomyxomas, at least those originating in the vagina, may derive from a polypoid lesion of small dimensions. Finally, since an angiomyxoma at its initial stage is indistinguishable from a vaginal polyp, it would be advisable to consider such an aggressive neoplasia in a differential diagnosis within clinical practice.

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Address reprint requests to:
G. CARTA, M.D.
Department of Surgical Sciences
University of L'Aquila
Viale San Salvatore Edificio 6 ingresso A
67100 Coppito, L'Aquila (AQ) Italy
e-mail: gasparecarta@libero.it
clinicaostgin@libero.it