Case Report

Aggressive angiomyxoma presenting as a vulval polyp

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Abstract

Aggressive angiomyxoma is a rare, locally invasive mesenchymal tumor, occurring predominantly in the pelvic-perineal region of adults and carries a high risk for local relapse and hence the need to differentiate it from the other mesenchymal tumors occurring in this region. Presentation as a pedunculated polyp, like in our case, is unusual for this rare tumor. Except for positive surgical margins, there are no clinical or histological means for predicting the tumor recurrence. A diligent long-term follow-up is mandatory. Though rare, this tumor needs to be considered in the differential diagnosis of vulval polyps.

Key words: Aggressive angiomyxoma, polyp, vulva

Introduction

Aggressive angiomyxoma is an uncommon, locally aggressive, slow growing mesenchymal neoplasm, notorious for recurrences after surgical excision.[1,2] The reported local recurrences varied from 9% to 72% during long-term follow-up.[1] So far two cases have been documented in the literature where the recurrent tumor metastasized to the lungs, resulting in death of the patient in one case.[3] They often present as an infiltrative mass in the pelvic-perineal region of adults, more common in women.[1,2,4] Clinical presentation as a polyp is rare, with only six such cases being documented in the world literature so far.[5] The pathologist should closely scrutinize the resected margins for any evidence of tumor extension, which is the most significant predictor for tumor recurrence.[4] A careful histological examination helps to differentiate this neoplasm from the other mesenchymal tumors in this region.[4] A close and a diligent long-term follow-up is necessary.[1-6]

Case Report

A 34-year-old lady, presented with a polypoidal, slowly enlarging, painless mass of two years duration, arising from the right vulva. The lady was on antidepressant medication for the past three years. On clinical examination, a large skin covered nontender, polypoid mass was found to arise from the right labia majora. The skin over the mass was intact. She had no similar mass elsewhere in the body. Clinically a diagnosis of leiomyomatous polyp was made and polypectomy was done.

Grossly, the skin covered pedunculated polyp measured $10 \times 8 \times 6$ cm in size, with the pedicle measuring two centimeter in length. Cut surface was solid, glistening white and myxoid with no areas of hemorrhage or necrosis [Figure 1].

Microscopy showed a polypoid, infiltrative, paucicellular, mesenchymal neoplasm composed of widely dispersed, uniform population of spindle to stellate cells. The cells had round to oval bland nuclei containing delicate chromatin, with bi to multipolar cell processes. They were present in abundant myxoid matrix containing loosely arranged wavy bundles of collagen. Variably sized blood vessels were seen throughout the tumor, with some of the medium sized vessels showing thickening and hyalinization of the media [Figure 2]. Extravasation of red cells was observed. No cellular pleomorphism, mitotic figures or necrosis was seen. The tumor with its infiltrative margins involved the pedicle base, due to which the surgeon had to resort to further exploration, to secure tumor-free resected margins.

Figure 1: Pedunculated vulval mass showing solid, glistening white and myxiod cut surface. In the inset is the skin-covered mass with a short pedicle

The myxoid stroma was weakly positive with alcian blue at pH 2.5. On immunohistochemistry, the neoplastic spindle cells were strongly positive for vimentin and progesterone receptors [Figure 3], weakly positive for desmin and estrogen receptors and were negative for cytokeratin, CD34 and S-100. The patient is on a regular follow up for the past 42 months and has no recurrence of the disease.

Discussion

Steeper and Rosai first reported an aggressive angiomyxoma in the female pelvis in 1983.[2] This tumor is common in the pelvic perineal region of the adults.[1,2,5,6] Its occurrence in retroperitoneum, urinary bladder, vagina and vulva in women and in scrotum, epididymis, testis, inguinal region and bladder in males, has also been documented in the literature.[6] The reported female to male ratio is approximately 6:1.[6] The tumor commonly occurs in the reproductive age group,[4] but can be seen over a wide age range from 16 to 70 years.[6]

Clinically the tumor presents as a locally infiltrative mass with potential for recurrence, many years after the primary excision.[1,2,5,6] In all the seven cases including the present one, where the presentation was that of a pedunculated mass, the diagnosis was unsuspected preoperatively[5] and in these cases, local excision around the pedicle base can effect a cure, provided the pedicle base is free of tumor. Except for positive surgical margins there are no clinical or histological predictors for tumor recurrence and hence the effort should be towards obtaining adequate clearance with tumor-free resected margins.[2] This is achieved by wide local excision, which could cause significant morbidity due to the large tumor size and its proximity to the genitourinary and anorectal structures. Fine *et al* claimed to have achieved complete remission by the use of gonadotropin- releasing hormone (GnRH) agonist for three months, in a case of recurrent angiomyxoma, which showed strong expression of estrogen receptor (ER) and progesterone receptors (PR) by the tumor cells.[6-8] However, this treatment modality needs further evaluation.

There is no complete consensus regarding the tumor pathogenesis. This hormonally responsive tumor which express ER and PR, is believed to arise from specialized mesenchymal cells of the pelvic-perineal region or from the multipotent perivascular progenitor cells, which often display variable myofibroblastic and fibroblastic features.[9] This hypothesis is supported by the fact, that the tumor cells express desmin and in some cases α- smooth muscle actin along with desmin.[1,2,4,5] Ultrastructural evidence for smooth muscle

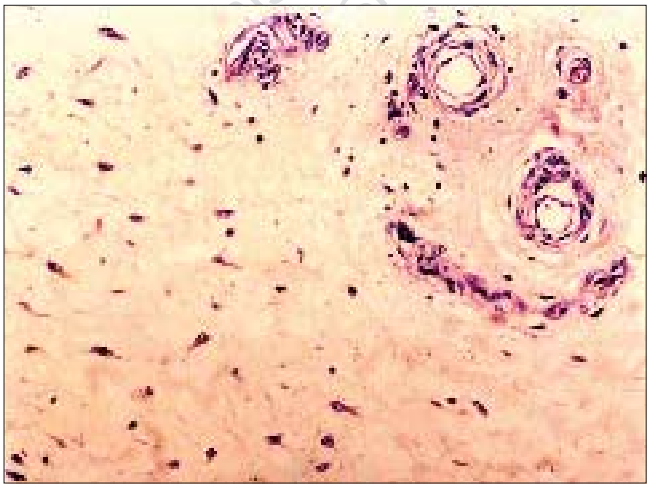

Figure 2: Paucicellular mesenchymal tumor showing variably sized blood vessels surrounded by widely dispersed bland stellate to spindle cells in a myxoid background. (H and E, X200)

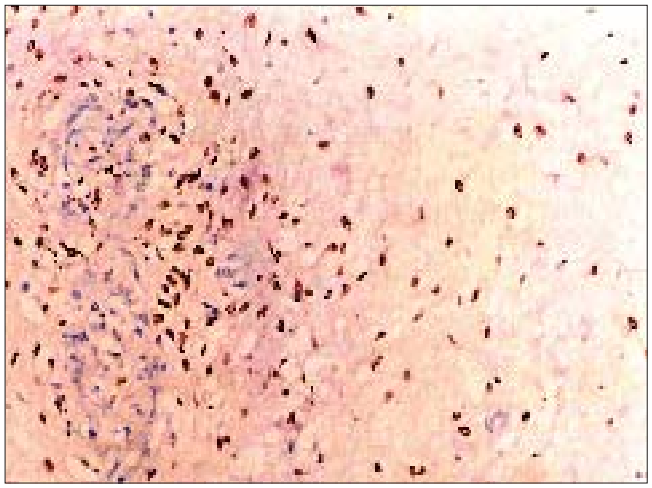

Figure 3: Immunostaining for progesterone receptor demonstrating nuclear positivity within the tumor cells (H and E, X200)

differentiation has also been described.[8]

Recent cytogenetic and molecular studies have identified a variety of genetic alterations, involving the chromosome 12, in the region 12q13-15.[1,4] HMGI-C, a gene in this region, which encodes proteins, involved in the transcriptional regulation, appears to have a role in the pathogenesis of this tumor.[1,4] *CDK4* (encoding a cyclin dependent kinase) and *MDM2* ("murine double minute", encoding a zinc finger protein that contains a TP53 binding site) are also found to be amplified in many cases.[1] Type - D cyclins bind to and activate cyclin dependent kinases such as CDK4, the amplification of which promotes cell-cycle progression. *MDM2* inhibit wild type TP53 activity, potentially promoting further amplification of *MDM2* and stimulating uncontrolled cell proliferation.[1] Detection of inappropriate HMGI-C expression using immunoperoxidase technique with anti HMGI-C antibody may potentially be a useful marker for microscopic residual disease.[4]

Fibro-epithelial stromal polyp, superficial angiomyxoma, angiomyofibroblastoma, aggressive angiomyxoma, cellular angiofibroma and smooth muscle tumors need to be considered in the differential diagnoses of a polypoid mass in the perineum.[4] A careful histomorphological analysis helps in differentiating this tumor from the other mesenchymal neoplasms occurring in this region.[4,5]

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