Section: Pathology

Case Series

AGGRESSIVE ANGIOMYXOMA OF THE VULVA: CASE SERIES

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ABSTRACT

Aggressive angiomyxoma is a benign, soft tissue and locally aggressive tumour, predominantly occurring in women of reproductive age group and is rarely encountered. The term aggressive is used to indicate locally infiltrative and recurrent nature hence the need to differentiate it from the other mesenchymal tumours occurring in this region. They arise commonly from the vulvovaginal region, perineum or pelvis and are usually misdiagnosed. These cases are rare entities since a tumour of this size has not been reported in central India yet.

Keywords: Angiomyxoma, infiltrative tumor, vulvovaginal region.

INTRODUCTION

Aggressive angiomyxoma (AA) of the vulva is a rare, benign, and locally invasive mesenchymal tumour primariy originating from myxoid cells of connective tissue. The term deep angiomyxoma was coined by the World Health Organization in 2003.[2] AA occurs almost exclusively in women of reproductive age, with a most common incidence in the second and third decades of life,[3] but can rarely be seen in adolescents. It mostly presents as a painless mass in the perineal region. The word “aggressive” indicates its propensity to locally recur and also denotes its ability to locally invade and infiltrate the adjoining soft tissues. While it is mostly benign, the tumour shows multiple local recurrences with very high rates. However, the tendency of the tumour to metastasize is grim. Wide local excision with negative margins along with long-term follow-up is still the best course of action and management of the tumour. Adjuvant therapy in the form of gonadotropin-releasing hormone (GnRH) agonists,[4] were effective in reducing the chances of local reccurence. We discuss a case of AA of the left labia majora that was successfully managed by surgical excision and present a brief literature review.

Case report - 1

A 30-year-old pregnant female came with a complaint of mass in left labia majora since seven years. She presented to us due to rapid increase in size of the tumour since last 10 days which was initially a slow growing mass. On local examination showed a well circumscribed 25 x 19 x 6 cm pedunculated mass along with overlying ulcer measuring 6 x 4 cm in size. On palpation, the mass was non-tender, soft to touch and consistency. The adjacent lymph nodes were not enlarged. Her blood work-up showed mild anemia and otherwise unremarkable. On ultarsonography, the lesion showed heterogenic lesion with raised vascularity which was suggestive of benign/malignant neoplastic mass lesion. After examination and informed written consent provided to the patient, she underwent local excision of the mass along with reconstruction of the area. The specimen was received in the Department of Pathology, MGM Medical college Indore for histopathology examination. On histopathology, Haematoxylin and Eosin stained section studied shows hyperplastic stratified squamous epithelium. The sub-epithelium shows tumour composed of bland spindle to stellate cells having scanty cytoplasm in a myxoid stroma and scattered variable

sized haphazard dilated vessels seen. Few of the blood vessels were thick and hyalinised. Adjacent to blood vessels, loose clusters of fibrillar collagen and eosinophilic band of smooth muscles also appreciated. Adjoining tissue shows non-specific inflammation and extravasated red blood cells.

Features are suggestive of Deep Aggressive Angiomyxoma of vulva.

Case report 2

A 26-year-old female presented with complaint of bilateral labial swellings since 1 year.

On local examination, well circumscribed swellings of 1.5 x 0.8 cm on the left and 2.5 x 1.2 cm on the right, not associated with pain or rapid increase in size and soft to touch on palpation. The adjacent lymph nodes were not enlarged. After examination and informed written consent, she underwent local excision of the mass. The specimen was received in the Department of Pathology, MGM Medical college Indore for histopathology examination. On histopathology, Haematoxylin and Eosin stained section studied shows hyperplastic stratified squamous epithelium. The sub-epithelium shows tumour composed of bland spindle to stellate cells having scanty cytoplasm in a myxoid stroma and scattered variable sized haphazard dilated vessels seen. Few of the blood vessels were thick and hyalinised. Loose clusters of fibrillar collagen and eosinophilic band of smooth muscles also appreciated. Adjoining tissue shows non-specific inflammation.

Features are suggestive of Angiomyxoma of vulva.

Case report - 3

A 57-year-old female came with a complaint of mass coming out of vagina since 6 months. Local examination showed cervix with attached polyploidal mass 14 x 10 x 5 cm in size. On palpation, the mass was non-tender, soft to touch and in consistency. The adjacent lymph nodes were not enlarged. Her blood work-up showed mild anemia and otherwise unremarkable. On Ultrasonography, the lesion showed exophytic lesion arising from vagina with neoplastic etiology, nodular lesion in right perirectal region likely metastatic lesion.

The patient underwent local excision of the mass. The specimen was received in the Department of Pathology, MGM Medical college for histopathology examination. On histopathology, Haematoxylin and Eosin stained section studied shows hyperplastic stratified squamous epithelium exhibiting koilocytic changes at places. The sub-epithelium shows tumour composed of bland spindle to stellate cells having scanty cytoplasm in a myxoid stroma along with variable haphazard dilated blood vessels seen. Few of the blood vessels were thick and hyalinised. Adjoining tissue shows fibrocollagenous tissue along with non-specific inflammation and focal area of hemorrhage.

Features are suggestive of Angiomyxoma

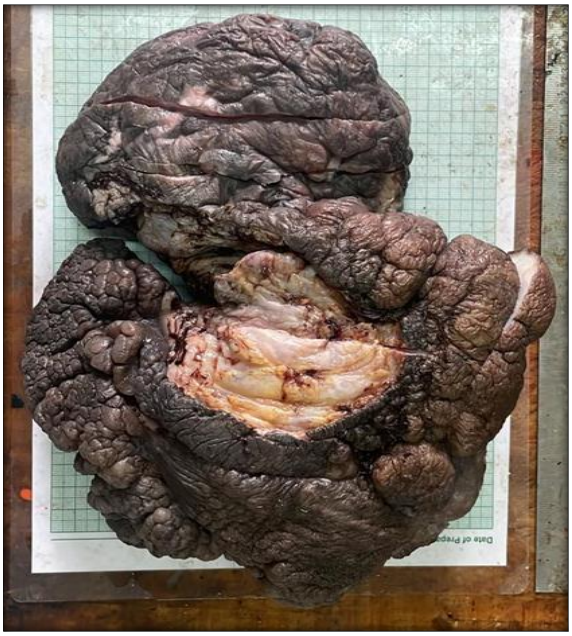

Figure 1: Gross image of Aggressive Angiomyxoma growth after excision and repair

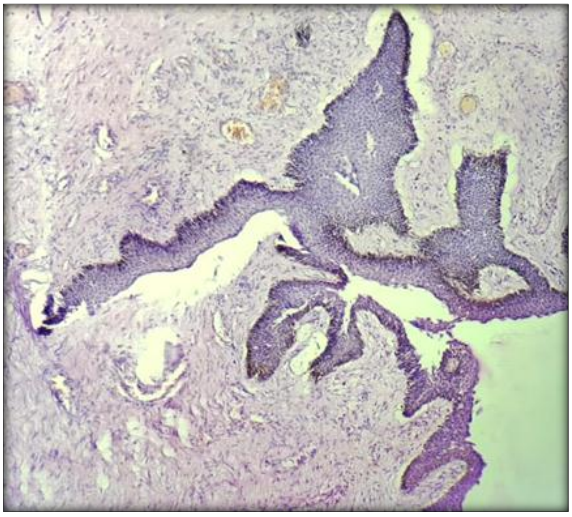

Figure 2: H and E stained section studied show stratified squamous epithelium (4x magnification)

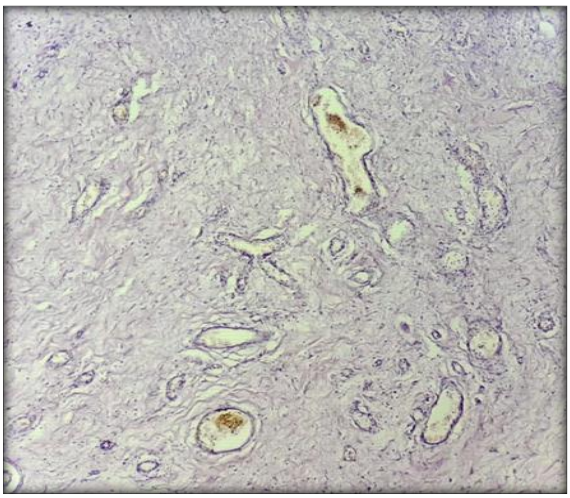

Figure 3: H and E stained section show dilated and congested vessels on low power

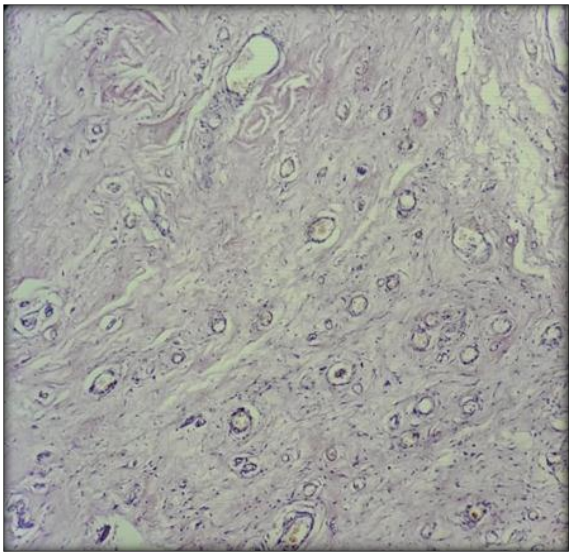

Figure 4: H and E stained section studied show stromal proliferation under low power

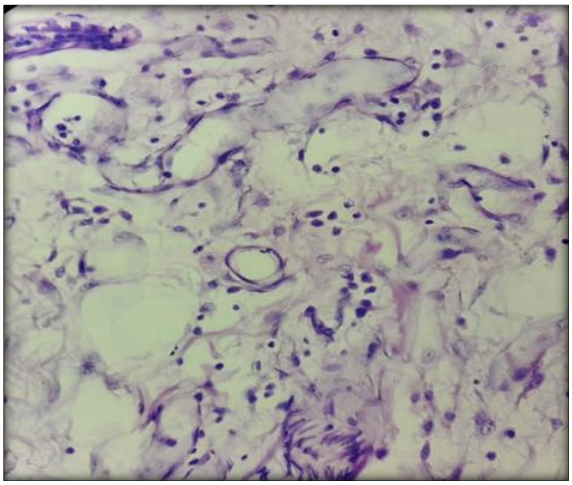

Figure 5: H and E stained section show stellate cells in the stroma under high power magnification

DISCUSSION

Angiomyxomas are classified either as superficial (also known as cutaneous myxoma) or AA. Superficial angiomyxomas usually present in middle-aged adults as a single polypoidal or nodular lesion in the head and neck region that may be clinically confused with other common benign lesions in this region. The stroma is mostly edematous with little myxoid material. On the other hand, AA occurs exclusively in the pelvic and perineal regions of women of reproductive age mainly in second to third decades of life and a few cases have been reported in perimenopausal females and children. This is to be attributed to the hormone-responsive nature of the tumor, as its growth is stimulated by progesterone and estrogen. This is backed by our case report of rapid enlargement of the tumor during pregnancy. Rarely, they are seen in male patients in sites like the scrotum and inguinal region. However, the ratio of occurrence in females to males is 6:1.[5] The term aggressive is used to indicate locally infiltrative and recurrent nature. Mostly, this tumor is non-metastasizing, but there are reports of multiple metastases in women treated initially by excision.[6,7] The tumor pathogenesis is still not very clear. This hormonally active tumor is believed to arise from mesenchymal cells of the pelvic–perineal region or from the multipotent perivascular progenitor cells, which often display variable myofibroblastic and fibroblastic features.[8] This hypothesis can be backed by the fact that the tumor cells express desmin and myofibroblastic component on histopathology in some cases. Immunohistochemically, there is positivity for desmin (less so in the male counterpart of this lesion), smooth muscle actin (about half of the cases), CD34 (about half) and estrogen and progesterone receptors (100%, irrespective of gender). A fourth of the cases also show keratin AE1/AE3 positivity. Some cases analyzed cytogenetically have shown a chromosomal translocation involving the region 12q14–15 where the high mobility group AT-hook 2 gene HMGA2 is located, resulting in overexpression of this molecule. Another case had a t(5;8) (p15;q22) translocation. This tumor is distinguished from the more common and innocuous fibroepithelial polyp because of its larger size, deeper location, and lack of bizarre stromal cells. The differential diagnosis also includes angiomyofibroblastoma, cellular angiofibroma, and massive vulvar edema. The ultrastructural and immunohistochemical features of aggressive angiomyxoma are those of primitive mesenchymal cells focally exhibiting myoid traits. Stains for acidic mucins are only weakly positive, suggesting that the stroma is more edematous than myxoid.[3] On computed tomography (CT) scan, it usually presents as a well-defined mass with attenuation less than or equal to that of adjacent skeletal muscle. It often has swirled enhancing tissue internally. On MRI, T1: tends to be iso to low signal. T2: predominantly high signal and typically has a swirled appearance. Due to the presence of collagen fibrils in the myxoid tissue, a laminated pattern may be seen on T2W images and post contrast T1 images, with alternating hyper- and hypointense linear areas. Rarely, cystic degeneration and intratumoural vessels may be seen.[9] The best treatment for AA remains unknown. Wide surgical excision is the main reported therapeutic approach. Achieving negative microscopic margins seems an obvious principle, but a literature search failed to prove that negative resection margins prevent recurrence. The extent of surgical excision has thus to be weighed against its risks, especially in young patients of childbearing age. Recurrences may occur from months to several years after excision (2 months to 15 years).[10] AA, despite the name, is not that aggressive, with only a 30% chance of recurrence. Radiation therapy and chemotherapy are available but not used frequently due to low mitotic activity. Hormonal therapy has been shown to reduce the tumor size and may help to make complete excision possible in feasible in large and widely infiltrated tumors and also in recurrence. As late recurrences are

known, all patients need to be counselled about the need for long-term follow-up. Magnetic resonance imaging is the preferred radiological investigation for detecting recurrences.

Table 1: Clinical and histopathological features of Angiomyxomas

	Superficial angiomyxoma	Aggressive angiomyxoma
Age	Ranges from 15-60 years(Mean: 23 years)	Most common: women of reproductive age. Ranges from 16–70 years
Incidence	~50–60 cases reported	~350–400 cases reported
Clinical presentation	Soft lobulated mass	Pedunculated mass, can be lobulated, soft to rubbery
Size	Usually small (ranges from 0.9 to 4 cm)	Usually larger (mostly> 10 cm), ranges from 3 to 60 cm),
Imaging	Preserved fat plane between the mass and levator muscles. MRI: Iso- to hypo-intense signal to muscle on T1WI, homogenous hyper-intense signal on T2WI with heterogeneous enhancement on postcontrast T1WI.	Tends to involve levator muscles and/or deep pelvic structures. MRI: Iso- to hypo-intense signal to muscle on T1WI, homogenous hyper-intense signal on T2WI with swirl/laminated appearance, and progressive avid enhancement on postcontrast T1WI.
Gross pathology	Variably circumscribed, unencapsulated, superficial dermal nodule with multinodular gelatinous cut surface with thin fibrous septa, may contain cysts with keratin debris	Variably circumscribed, unencapsulated, deep-seated lobulated or polypoid mass, myxoid, gelatinous, or rubbery cut surface
Cell origin	May arise from fibroblast-like mesenchymal cells	May arise from specialized mesenchymal cells and/or multipotent perivascular progenitor cells
Histology	Hypocellular dermal nodule of spindled to stellate cells in an abundant myxoid background (neutrophils present in a subset of cases). Numerous arborizing small thin-walled blood vessels. Entrapped benign epithelial elements may be present.	Hypocellular lesion of small spindled to stellate cells with an infiltrative growth pattern (entraps fat and nerves), abundant myxomatous stroma with collagen fibers, Numerous variably-sized blood vessels with occasional perivascular smooth muscle proliferation, stromal mast cells and extravasated red blood cells.
Nuclear atypia	Absent	Absent
Mitotic index	Low	Low
Immunohistochemistry	Vimentin + S100 –Mucin (via Alcian blue PAS) + Desmin – or focal ER/PR – SMA – or focal CD34 + HMGA2 –	Vimentin + S100 –Mucin (via Alcian blue PAS) + Desmin + ER/PR + Variable SMA CD34 – HMGA2 overexpressed
Genetic testing	If associated with Carney complex, may have autosomal dominant inactivating mutations in PRKAR1A (17q22-24)	Various rearrangements involving *HMGA2* (12q13-15) in approximately 1/3 of cases
Treatment	Simple excision	Wide local excision +/- Adjuvant hormonal therapy
Recurrence rate	30–40% (~with inadequate resection)	50–70% (~with inadequate resection)

CONCLUSION

Aggressive angiomyxoma is a rare, benign and locally aggressive neoplasm. It should be considered and sort out as a differential diagnosis whenever a patient presents with growth in the perineal region or pelvis. As the tumor is well known for local recurrences, timely diagnosis and management are of great importance.

Footnotes

Conflict of interest: None.

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