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Case Report

Oncology Section

A Case Report of Aggressive Angiomyxoma of Vulva: An Often Misdiagnosed Neoplasm

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ABSTRACT

Aggressive angiomyxoma of vulva (AAM) is a very rare, slow growing, locally aggressive, and rarely metastasizing soft tissue neoplasm. Its preoperative diagnosis is often difficult. It has a high recurrence rate and requires prolonged follow-up. We report a case of a 36 years old female, who presented with a swelling on her left labium majus. Imaging studies could not confirm the diagnosis. She underwent wide local excision of the lesion and her final histopathology report was aggressive angiomyxoma of vulva. Patient has been in follow-up for the past four years with serial MRI without any recurrence.

Keywords: HMGA2 Protein, Recurrence, Soft Tissue Neoplasm, Vulvar Neoplasm

CASE REPORT

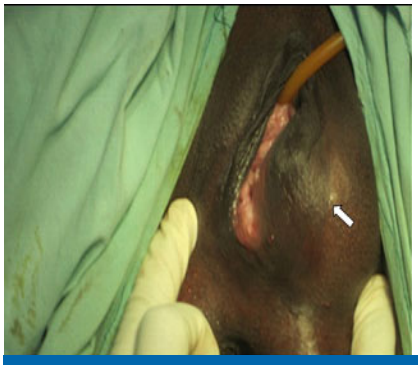
A 36-year-old female presented with a slow growing painless swelling on her left labium majus of two years duration. Other tumour related history and obstetric, menstrual, social and family histories were unremarkable. On examination, a 6 cm x 5 cm soft compressible globular swelling was observed. Regional lymph nodes were clinically negative [Table/Fig-1].

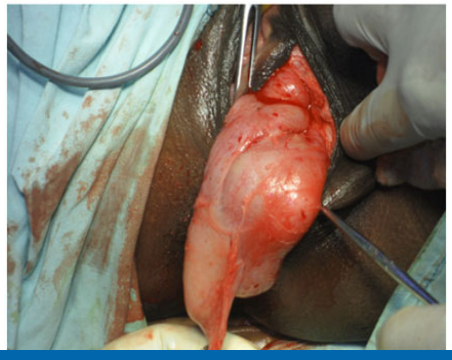
Ultrasound of the genital region detected a hypoechoic lesion with ill-defined margins and without intraperitoneal communication. Doppler imaging showed randomly dispersed blood vessels. MRI detected a hyperintense lesion on T2 weighted MRI extending into the ischiorectal fossa. FNAC was deferred as haemangioma was an imminent possibility. The differential diagnoses at this juncture were Bartholin's cyst, lipoma of the labia, and haemangioma.

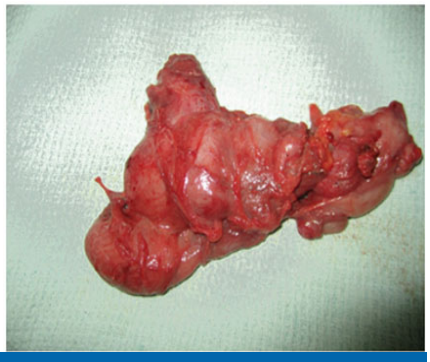
The tumour was excised with adequate margins. A solid, fleshy mass 8 cm x 4 cm x 10cm in dimensions extending into the ischiorectal fossa was removed [Table/Fig-2,3]. Histopathological examination was suggestive of aggressive angiomyxoma, showing hypocellular population of spindle shaped cells in a loose myxoid matrix with no cellular atypia. Thick walled vessels of varying calibre were noted. The cells stained positive for Oestrogen Receptor (ER) and vimentin. Since all margins were negative, no further treatment was given. She is under active surveillance with serial MRI for the past four years with no recurrence.

DISCUSSION

AAM is a very rare benign myxoid tumour. The challenge of diagnosing AAM, even histopathologically, cannot be emphasised enough. A wide range of other mesenchymal







[Table/Fig-1]: Preoperative picture of left labial aggressive angiomyxoma (arrow indicates the tumour) **[Table/Fig-2]:** Intraoperative picture of aggressive angiomyxoma of vulva **[Table/Fig-3]:** Postoperative specimen picture; bulky non-encapsulated mass (Images from left to right)

	Clinical features	Macroscopic appearance	Microscopy	Other	Malignant potential
Aggressive angiomyxoma	Most common in 3rd decade of life;	Soft, bulky masses with smooth surface	Spindle or stellate shaped fibroblasts or myofibroblasts in a myxoid stroma	High recurrence rate; CD34, ER, PR, vimentin positive; S100 negative	Benign, Locally aggressive, Rarely metastatic
Bartholin's cyst	All age groups; painful if large; Swelling adjacent to opening of Bartholin's duct	Retained cyst material	Cysts lined by squamous or urothelium with inflammatory infiltrates; Residual mucinous glands seen	Treated by marsupialisation	Benign
Lipoma	More common in adults; rare in children	Bright yellow homogenous appearance; greasy cut surface	Well encapsulated adipose tissue without atypia	1-4% recur	Benign
Superficial angiomyxoma	More common in males than females; 4th decade of life	Greyish white, sometimes haemorrhagic appearance	Thin walled vessels; non-infiltrative margins; Otherwise similar to AAM	Associated with Carney's syndrome; rarely recurrent	Benign
Angiomyofibroblastoma	Females, 4th & 5th decade	Pedunculated mass with pink grey cut surface; no necrosis	Well encapsulated, numerous hylanized vessels with plump stromal cells around vessels	Vimentin, desmin , ER & PR positive; Very weak CD34 positive	Benign
Myxoid liposarcoma	3rd or 4th decade	Fleshy opaque white nodules	Stellate, fusiform, round or spindle shaped cells depending on differentiation	S100 positive; Either well or poorly differentiated; High Ki-67 indicates poor prognosis	Malignant
Myxofibrosarcoma	Elderly females	Multiple nodules sometimes with necrosis	Multinodular, with pleomorphic spindle cells	Grade doesn't predict behaviour	Malignant; good prognosis when low grade

[Table/Fig-4]: Differential diagnoses of aggressive angiomyxoma of vulva

lesions occur commonly in this region and mimic AAM to a variable extent. The term "Aggressive Angiomyxoma" is of recent coinage, first reported in 1983 by Steeper and Rosai [1]. "Aggressive" denotes the local aggressiveness of the tumour. It has been classified by WHO as deep angiomyxoma and is considered a tumour of uncertain origin. Around 250 cases have been reported to date [2].

They have an indolent course occurring commonly in women of reproductive age during the 3rd decade of life, although rare cases have been reported in perimenopausal women, children and men [3,4]. A few cases have been reported during pregnancy with the tumour growing rapidly thus indicating their hormone dependency [5]. They commonly occur in the perineum and pelvis; in perineum they present as a soft painless mass. The other symptoms are dull aching pain, paraesthesia of the overlying skin, urinary retention and dyspareunia.

Preoperatively, they are misdiagnosed in > 80% of patients. Extensive imaging is necessary prior to surgery not only to aid in diagnosis, but also to find the extent of disease. On ultrasound, these lesions appear as hypoechoic cystic or solid masses. Plain CT shows a low density mass with attenuation less than surrounding muscle. Contrast enhanced CT shows a mildly enhancing mass with an internal swirling pattern [6]. MRI can delineate the perineal and pelvic extent of the tumour. Diffusion weighted MRI is both diagnostic and prognostic. In T2 weighted imaging, the tumour shows a swirled architecture and high signal intensity; the loose myxoid stroma with high water content is responsible for this appearance [7]. MRI is even more useful during follow-up for detecting early recurrence.

On gross examination, they appear as soft bulky masses with smooth external surface. Histological examination shows monotonous, sparsely arranged spindle or stellate shaped fibroblasts or myofibroblasts [8] in a background of myxoid stroma containing collagen fibres and dilated thick walled vessels of varying calibre. Mitotic figures are rare, indicating low proliferation activity. The margins can be infiltrative extending into adjacent muscles, adipose tissue, and rarely vessels. Vessel infiltration explains the isolated cases of metastasis.

The line of differentiation is not clear. But the cells are mesenchymal in origin. Some suggest they arise from multipotent perivascular progenitor cells. AAM stains positive for CD34 and vimentin and varyingly positive for ER, PR [5], desmin and smooth muscle actin (SMA). They are uniformly negative for factor VIII and S-100.

HMGA2 protein (encoded by HMGA2 gene at 12q15) has recently been implicated in the pathogenesis of AAM. HMGA2 is a transcription activating factor and rearrangements in its genes is responsible for some tumours of mesenchymal origin including AAM. McCluggage et al., described it to be positive in 10 of 12 patients with AAM [9]. It is a sensitive marker but not specific, as other tumours like uterine fibroids are also positive. The implication of this finding is that HMGA2 can be used as a potential marker for post-op evaluation of residual tumour and for detecting recurrences.

The differential diagnoses, both clinically and histopathologically are vast. The more common ones are listed in [Table/Fig-4].

Management of primary AAM has uniformly been surgery. Though it is well circumscribed, the challenge lies in achieving adequate margins as they are non-encapsulated and finger like extensions are almost always to be found beyond the assumed margins. The second reason is that they sometimes occur in close proximity to vital structures like urethra, vagina or anal sphincter. Translevator extension and encasement of the pelvic organs can also occur. Radical surgery will increase the morbidity in these settings. Moreover, even a wide local excision cannot absolutely prevent recurrence as they are sometimes multifocal in nature.

Recurrence is very common and varies from 30% to as high as 72% [10]. Most of them occur in the first three years, but late recurrences, some more than 20 years, have also been reported [11]. Complete resection nevertheless provides the lowest recurrence rate.

Two other modalities of treatment have been tried with variable success. Hormonal manipulation with SERMs like tamoxifen and GnRH analogues has been met with some success [12]. The reasoning is that these tumours usually occur in premenopausal women and are ER/PR positive. Arterial embolization has been tried for preoperatively shrinking the tumour and for recurrences [13]. But the results are inconsistent as there are multiple feeding vessels to the tumour. Radiotherapy and Chemotherapy are not viable options in AAM as these are tumours with low mitotic activity.

Only two cases of distant metastases have been reported to date [14]. But for the high recurrence rate, prognosis is very good.

CONCLUSION

Just a few hundred cases of AAM of vulva have been reported worldwide. This, coupled with the vast differentials, makes preoperative diagnosis very difficult with a misdiagnosis in > 80%. Excision with adequate margins is the treatment of choice. Hormonal manipulation and arterial embolization have been tried with varying results. The prognosis is good, but the major issue to be considered is recurrence; they require long term follow-up with serial MRI. Rearrangements in HMGA2 gene is a sensitive marker which can be used in the post-op period for detecting residual and early recurrent lesions.

Compliance with Ethical Standards

Informed consent: Informed consent was obtained from the patient included in the report.

Ethical Approval: For this type of study formal ethical clearance is not required.

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