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Case Report

Aggressive angiomyxoma

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ABSTRACT

Angiomyxoma is a rare slow-growing, benign low-grade tumor occurring in women of reproductive age group which is known for its recurrence. The symptoms are variable. Mrs. K. aged 33 years, reached our outpatient department (OPD) with complaints of painless swelling on the right labial region which she was feeling uncomfortable while sitting. Mass was found to be mobile with no evidence of inflammatory change. The location of the mass made us think about, Bartholin's cyst and hence surgical excision of the mass was done. The whole mass was found to be lying below the fat in the right labial region and wide excision was completed. The histopathology of the mass was reported as angiomyxoma. Angiomyxoma arises from the mesenchymal tissue and it is locally invasive with high recurrence rate. It is more common in females. Mostly seen in the vulvovaginal, pelvic cavity and perineum. The lesion can reach huge size. It has to be differentiated from gynecologic malignancies, cyst, abscess and hernia. Histology along with immune-histochemistry can confirm the lesion. Wide excision is the mode of treatment. Incomplete excision can lead to relapse. Relapse can happen in 35-72% of the cases. Local recurrence may occur between 2 months to 15 years following initial diagnosis. Hence, follow up is essential. Angiomyxoma is a very rare condition and only around 250 cases have been reported in the world literature. It has to be differentiated from other benign conditions. Diagnosed by non-invasive techniques like ultrasound sonography (USG), magnetic resonance imaging (MRI) and computed tomography (CT). Wide excision is the treatment of choice. Long term follow up is needed as recurrences are high.

Keywords: Angiomyxoma, Bartholin's cyst, Reproductive age, Wide excision, Follow-up for recurrence

INTRODUCTION

Angiomyxoma is a rare benign mesenchymal tumour which is slow-growing, low-grade neoplasm mostly occurring in the vulvovaginal (perineal) region which has a tendency for recurrence and infiltrates into the surrounding skeletal muscle and fat.[1,2] Presenting complaints include dull aching pain, urinary and gastrointestinal symptoms such as dysuria, urinary retention and dyspareunia. Most commonly occurs in the women of reproductive age group and was first described by Steeper and Rosai in 1983. They reported a case series of 9 female patients, who presented with benign-appearing myxoid and vascular tumour that was infiltrative and had a tendency for local recurrence and hence the term aggressive.[3]

Recurrence often occurs after many years.[4] Incidence of angiomyxoma based on gender is seen in the ratio of female:male-6.6:1. Fibroblastic or myo-fibroblastic origin seems most likely.[5] WHO classifies aggressive angiomyxoma as a 'Tumour of uncertain differentiation'.[6] Initially, angiomyxoma was thought to be a tumour with no metastatic potential, but this is no more acceptable, as few case reports of metastasis has been reported.[7] Liver, lungs, larynx, orbit and supraclavicular fossa are other rare sites for angiomyxoma.[8] The reported age of presentation ranges from 1 to 82 years, with a median age of 33 years.[9,10] Literature evidence are quite sparse, almost limited to 250 cases. There is lack of consensus on the clinical presentation, treatment protocols and follow up pattern because of its rarity. We are presenting our case as

initially we thought it was Bartholin's cyst and the diagnosis was made after excisional surgery.

CASE REPORT

The 33 years old female came to the OPD with chief complaint of right side swelling over the labia majora for 2 months, which was sudden in onset and gradually progressed to attain the present size of 10×2.5 cm in longitudinal direction. There was no pain, fever, redness, blood vessels over the swelling and discharge from the swelling. She had only discomfort and gritty sensation while sitting. She had a family history of such mass over the labia for her elder sister for which she was operated 3 years ago and there was no recurrence.

On examination in the OPD, swelling was mobile, non-tender, without discharge or ulceration. Speculum examination showed a healthy cervix. Uterus was normal in size. As we thought of Bartholin's cyst, we did not do any imaging study and surgical excision was planned under spinal anaesthesia. A linear incision was made over the mass on right labia majora. The mass was below the labial fat with measurements of 10×2.5 cm and was removed in toto. Deeper structures were not involved. There was not much of bleeding and primary wound closure was done. Wound healed very well and delayed suture removal was done. Cyst was sent for histopathological examination (HPE).

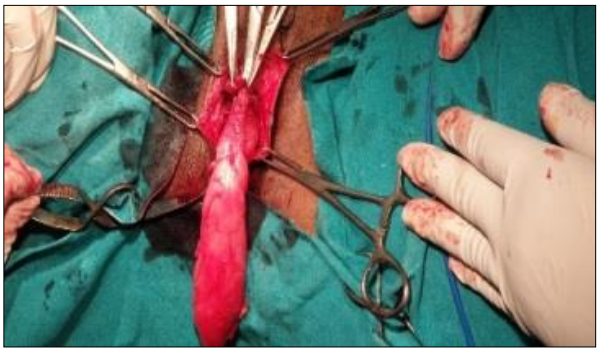

Figure 1: Intra operative of angiomyxoma.

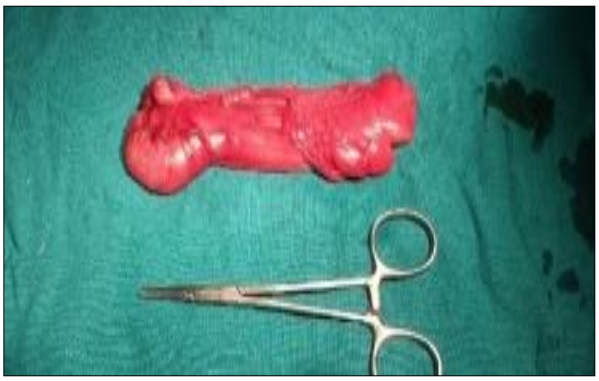

Figure 2: Specimen of angiomyxoma.

Histopathological report

Gross pathology

Specimen consists of a single grey-black to grey-white soft tissue mass with rubbery consistency measuring 9×4×3 cm. Cut-section appears solid, fibrous and glistening.

Microscopy

Sections showed a tumour composed of spindle to stellate shaped cells with scanty cytoplasm. Background showed myxoid stroma with collagen fibres. Many dilated capillaries and thick-walled blood vessels were also seen. No mitosis or atypia was seen in sections studied. HPE was consistent with angiomyxoma. No immune-histochemical studies were done.

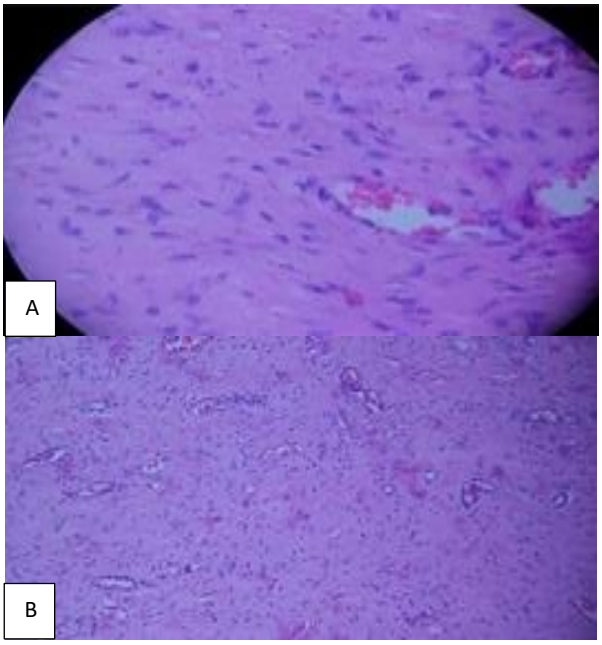

Figure 3 (A and B): Histopathological report of angiomyxoma.

DISCUSSION

Angiomyxoma is a benign neoplastic disease that originates from mesenchymal tissues with extensive local invasiveness and a high recurrence rate.[11] Angiomyxoma are classified into superficial or aggressive angiomyxoma. Superficial angiomyxoma occurs in adult males over the trunk, head, neck and lower extremities and are usually slow growing. The rate of relapse varies from 35% to 72%.[12] It mainly occurs on the vagina, vulva, pelvic cavity and perineum in women of reproductive age group.

However, there were also cases occurring in the scrotum or spermatic cord of males.[13,14] Tumour size is highly variable and ranges from 1 to 60 cm. In a case study by Sozutek et al a tumour measuring 24×12×6 cm with a weight of 4.2 kg was reported.

Angiomyxoma has to be differentiated from angio-fibroblastoma which is usually small in size, and involves only the superficial portion of vulva and vagina whereas angiomyxoma is usually a large mass involving deeper planes. Angiomyxoma is usually pink in colour and has a rubbery consistency and glistening surface. Owing to its localization, it is often misdiagnosed as Bartholin's gland cyst, labial cyst, Gartner duct cyst, vaginal cyst, abscess, leiomyoma, fibroepithelial polyp, sarcoma, lipoma or inguinal /femoral hernia, vaginal prolapse and gynaecological malignancy.[15] Histologically it has to be differentiated from myxoma, fibrous histiocytoma, angiofibroma, liposarcoma, nerve sheath tumour, mixed mesodermal tumour, and angio-myofibroblastoma (AMF).[16,17] Misdiagnosis rates have been reported as high as 82%.[18]

USG, CT and MRI can diagnose angiomyxoma. MRI shows high signal intensity on T2-weighted images and typically gives the same as in CT, swirling appearance related to its high-water content and myxoid composition.[19] On CT, it may be hypodense or equal in attenuation to adjacent skeletal muscle, or have both cystic and solid components. A combination of trans-abdominal, trans-perineal and trans-vaginal ultrasound examination could be helpful for the proper assessment that describes the lesion as a hypoechoic and heterogeneous mass.

Primitive multipotent mesenchymal cells of lower genito-urinary tract give rise to this angiomyxoma which is supported by the immune-histochemical expression of desmin.[20] Macroscopically, angiomyxoma has a gelatinous appearance, and it is microscopically characterized by a myxoid stroma and abundant thin to thick-walled vascular channels.[9,16]

Histologically tumour is sparsely cellular, contains spindle and stellate shaped cells. Internal blood vessels have thick and muscular walls. Immuno-histochemistry shows vimentin, desmin, and moderate positivity for CD34, CD3 and Ki-67 activity and positivity for hormone receptors for oestrogen and progesterone and negative for SMA, S100, H Cal Desmon, ALK, beta catenin and CK.[21] The Ki 67 proliferation index was 2% to 3%.

These findings usually help us to distinguish from other mesodermal origin tumours. Cytogenetic studies of aggressive angiomyxoma are sparse. Nucci and Fletcher suggested a translocation at the level of chromosome 12, where the high mobility group protein HMGA2 (a transcription factor expressed during embryogenesis) is located.[22] It has been shown that aberrant HMGA2 protein expression is present in angiomyxoma.[23]

HMGA2 are not a specific marker of aggressive angiomyxoma as it can be found in other vulvovaginal mesenchymal lesions (for example leiomyomata's neoplasm). It could help in the detection of small foci of residual or recurrent tumour in re-excision specimens.[24] Besides, a novel translocation HMGA2-YAP fusion was described in a woman diagnosed as aggressive angiomyxoma, who was responsive to oestrogen antagonism which can help in the development of new target therapies.[25]

First line treatment is always wide excision of the lesion. Radiation therapy and chemotherapy have no practical implications due to low mitotic activity.

Medical treatment with GnRh agonists shrinks the tumour size before excision and can also treat the recurrence as they have oestrogen receptors.[26] Raloxifen, tamoxifen can be used as neo-adjuvant therapy in residual or recurrent tumour growth.[18] Recurrence can be reduced by pre-operative embolization or external beam irradiation. Close follow-up is recommended at least for 2 years to detect local recurrence and invasion which are the principal causes of morbidity.[27] In a retrospective review by Chan et al and Han-Geurts et al it has been suggested that patients having positive margins were as likely to have recurrence as those with negative margins.[28,29] Also, the tumour size is not correlated with recurrence. Long-term follow-up includes MRI for detecting recurrences as it is the most effective imaging modality.[30]

Local recurrence may occur between 2 months to 15 years following the initial diagnosis and the recurrence rates vary from 9% to 72%.[31] Extension of the tumour to urethra, vagina, rectum and anal sphincter as well as extension through pelvic diaphragm is associated with incomplete resection and thus high risk of local recurrence.

CONCLUSION

Angiomyxoma is a very rare condition and often it is called as "aggressive angiomyxoma" because of its tendency for rapid growth and recurrence. Worldwide only around 250 cases have been reported in the literature. It has to be differentiated from other benign conditions like vaginal cyst, Bartholin's cyst, Gartner's cyst, abscess and other gynecological conditions. It is diagnosed by non-invasive techniques like USG, MRI and CT. Wide excision is the treatment of choice. Histopathological examination and immune-histochemistry can diagnose this aggressive angiomyxoma. The tumor is also receptor positive for estrogen and progesterone and hence, GnRH agonists, selective progesterone receptor modulators can be used for medical management. Long term follow up is needed as recurrences are high. Recurrence can be reduced by pre-operative embolization or external beam irradiation.

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