Indian Journal of Pathology and Oncology 2023;10(1):76–79

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Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Report

Cytodiagnosis of multilobulated aggressive angiomyxoma clinically mimicking sarcoma – A case report

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ARTICLE INFO

Article history:
Received 04-02-2023
Accepted 14-02-2023
Available online 16-03-2023

Keywords:
Angiomyxoma
Cytology
Histopathology

ABSTRACT

Introduction: Aggressive angiomyxoma is a rare but locally aggressive infiltrative mesenchymal tumour arising in the soft tissues of the lower genital tract. Incidence is very less (only about 350 cases have been recorded in the literature) with female to male ratio of 6:1. Average age at presentation is around 40 years.
Case Report: A 32 years old female presented with multiple swelling in the vulval region for 1 and a half years associated with mild pain. The patient complains of dysmenorrhoea, pressure sensation, pelvic fullness, dyspepsia, weight loss and generalised weakness. She is married and has a 3-year old male child. Her menstrual cycle is regular with normal menses. FNAC of the vulval swelling was suggestive of angiomyxoma. The swelling was excised in the Gynaecological Operation Theatre and the specimen was sent to the Department of Pathology for Histopathological examination where it was diagnosed as aggressive angiomyxoma. On follow up, the patient was healthy with no complains of recurrence so far.
Conclusion: Aggressive angiomyxoma is an aggressive tumour because it has a high risk of infiltration and local recurrence. Therefore, it should be distinguished from other myxoid tumours. Preoperative cytological diagnosis helps in surgical management with appropriate wide local excision with clear margins.

1. Introduction

Aggressive angiomyxoma is a rare but locally aggressive infiltrative mesenchymal tumour arising in the soft tissues of the lower genital tract. Incidence is very less (only about 350 cases have been recorded in the literature) with female to male ratio of 6:1. Average age at presentation is around 40 years. In 1983, Steeper and Rosai first described aggressive angiomyxoma as a mesenchymal neoplasm.[1–5] Although non metastasizing, it is locally aggressive and has a high risk of local recurrence. Only 3 cases of metastatic aggressive angiomyxoma have been reported till date.[6–8]

2. Case Report

A 32 years old female presented with multiple swelling in the vulval region for 1 and a half years associated with mild pain. The patient complains of dysmenorrhoea, pressure sensation, pelvic fullness, dyspepsia, weight loss and generalised weakness. She is married and has a 3 year old male child. Her menstrual cycle is regular with normal menses.Her bladder and bowel habits are normal. On local examination, multiple pedunculated globular masses were seen originating from the right labia majora lateral to introitus at 6 o'clock, 7 o'clock and 11 o'clock positions. The largest lump measured (16x15x6) cubic cm. All the lumps were non tender, well-defined with a smooth surface and soft to firm in consistency. Overlying skin was normal and no ulcer or dilated vein was present over the surface. Temperature was normal. Per speculum and per vaginum

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https://doi.org/10.18231/j.ijpo.2023.015

examination were unremarkable. With an informed consent Fine needle aspiration of the lumps was done. After the cytological diagnosis of Angiomyxoma, the patient was counselled and prepared for the excision of lumps in Gynaecological operation theatre under general anaesthesia. The lumps were excised and sent in formalin to the department of pathology for Histopathological examination.

2.1. *Cytological findings*

Smears from FNAC of the multiple vulval swelling show scattered oval to spindle shaped cells with abundant intact blood vessels in a myxoid background. (Figure 1 C & D)

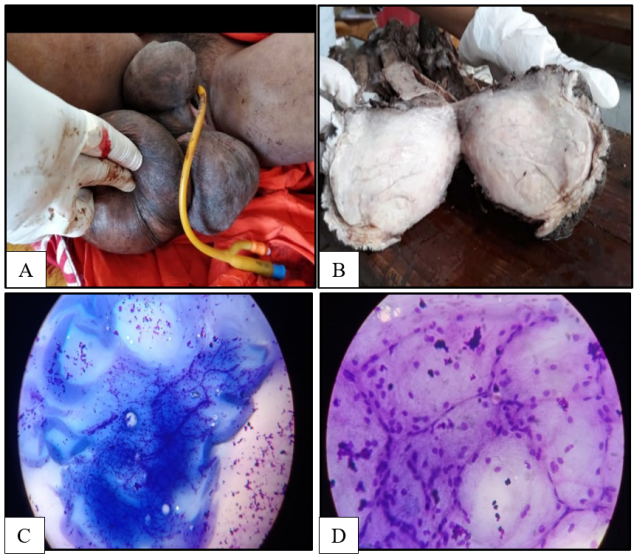

Fig. 1: A): Gross image of the vulval mass on OT Table. Multiple pedunculated masses can be seen at 6, 7 and 11 O' clock positions; **B**): Cut section of the vulval mass shows an unencapsulated, well circumscribed solid, whitish mass with a glistening and gelatinous appearance. We can also appreciate a rim of tissue surrounding the mass highlighting the wonderful intervention of FNAC in guiding the surgeon for an adequate wide local excision; **C**): MGG stained smear (100X) of the vulval mass shows myxoid matrix and capillary strands with scattered oval to plump spindle shaped cells; **D**): MGG stained smear (400X) of the vulval mass shows oval to plump spindle shaped cells with bland nuclear chromatin lining the vascular strands and also scattered in a myxoid background

2.2. *Histopathology*

2.2.1. *Macroscopic findings*

Grossly, we received 6 irregular pieces of tissue, largest measuring (17x16x7) cubic cm with attached skin measuring (14x11) square cm. On cut section, it is solid and whitish. No areas of necrosis and haemorrhage noted. (Figure 1 A & B)

2.2.2. *Microscopic findings*

Multiple random sections from the tumour masses show poorly circumscribed tumour composed of bland spindle and stellate cells together with non- arborizing bland vessels of varied calibre, embedded in a hypocellular myxoid stroma. Occasional thickened or hyalinised vessels are also noted. Few thin bundles of smooth muscle fibres are also present in the stroma and around some vessels. No evidence of cellular atypia, necrosis or mitosis noted. Hence, the histopathological features are consistent with the Cytodiagnosis of Aggressive angiomyxoma. (Figure 2 A & B)

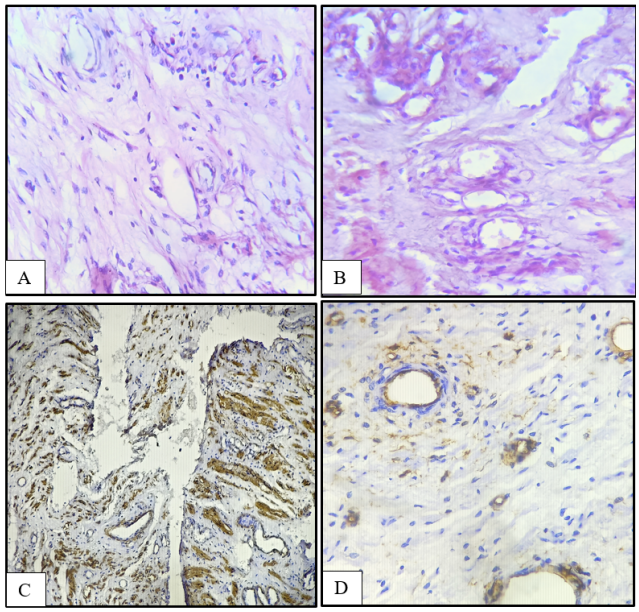

Fig. 2: A, B): H&E (400X) stained section of the vulval mass showing bland spindle and stellate cells together with non- arborizing bland vessels of varied calibre, embedded in a hypocellular myxoid stroma. Few thin bundles of smooth muscle fibres are also present in the stroma and around some vessels; **C**): IHC for SMA (100X) showing strong cytoplasmic positivity. **D**): IHC for CD34 (400X) showing strong membranous positivity around the blood vessels

2.2.3. *Immunohistochemistry*

IHC for SMA and CD34 shows cytoplasmic and membranous positivity respectively. (Figure 2 C & D)

3. Discussion

Aggressive angiomyxoma is a rare aggressive neoplasm occurring in more than 90% cases due to the fusion gene HMGA2 located in the chromosome 12q15 leading to proliferation of stromal cells, fibroblasts and myofibroblasts.[9–12] It is more common in women of reproductive age than in men.[13] It has been reported to occur in the vulva, vagina, inguinoscrotal region, perineum

etc. Mostly, patients are asymptomatic with a visible mass on local examination. In few cases, patients may complain of pelvic fullness, dysmenorrhoea, dyspareunia, vulvovaginal pain.[14,15] On gross examination, it can have a wide range of dimensions and on cut section appear glistening, gelatinous unencapsulated and solid whitish in colour. On microscopy, it is a hypocellular tumour consisting of bland spindle to stellate shaped cells with delicate cytoplasmic processes admixed with abundant blood vessels of various calibre in a myxoid stroma of collagen fibres. On immunohistochemistry, the tumour shows membranous positivity for CD34 in the cells lining the blood vessels, cytoplasmic positivity for SMA, desmin in the myofibroblasts and nuclear positivity for ER and/or PR.

The differential diagnosis of Aggressive angiomyxoma includes Superficial angiomyxoma, Angiomyofibroblastoma, Cellular Angiofibroma, Fibroepithelial stromal polyps, Myxolipoma, Angiomyxolipoma, Myxoid Liposarcoma, Myxoid Leiomyoma, Myxoid Neurofibroma, Low grade Myxofibrosarcoma and Low grade Fibromyxoid sarcoma.[16]

Superficial angiomyxoma (Cutaneous angiomyxoma) is a mesenchymal neoplasm that is more common in extragenital areas and not as large as aggressive angiomyxoma. It is generally well circumscribed and has a lobular or nodular architecture with both myxoid and vascular components but the vessels are not of very large calibre as that of Aggressive angiomyxoma. Immunohistochemically, it is generally ER and PR, HMGA2 negative.[16]

Angiomyofibroblastoma is a well circumscribed and non infiltrative mesenchymal neoplasm which is smaller in size compared to aggressive angiomyxoma. Microscopically, it contains both hypocellular and hypercellular areas consisting of bland epithelioid to plasmacytoid cells that cluster around small to medium sized blood vessels. Immunohistochemically, it is HMGA2 negative.[16,17]

Fibroepithelial tumor is a polypoidal neoplasm with hyperplastic or unremarkable squamous epithelium and a myxoid or oedematous stroma which contains variably sized vessels and multinucleated stromal cells with a wreathlike appearance. Occasionally, it may show increased cellularity, cytologic atypia, increased mitotic rate and atypical mitoses and are termed pseudosarcomatous fibroepithelial stromal polyps. Local excision is curative, even if pseudosarcomatous features are present.

Myxolipoma and Angiomyxolipoma are benign neoplasms that contain both mature adipose tissue and myxoid stroma consisting of bland spindle and stellate shaped cells. Angiomyxolipoma, as the name implies also contains prominent blood vessels. However, the abundant adipose tissue and the even greater hypocellularity of the neoplasm comes to the rescue in diagnosis.[18]

Myxoid Liposarcoma is a cellular neoplasm consisting of lipoblasts, spindle to stellate shaped cells and the characteristic arborizing capillary network.Immunohistochemically, it is ER and PR negative and characteristically contains the DDIT3-FUS fusion gene, t(12;16).[16]

Myxoid leiomyoma consists of spindle shaped cells with cigar shaped nuclei and eosinophilic cytoplasm admixed with large, thick walled blood vessels. Immunohistochemically, it is SMA, desmin and caldesmon positive.[16]

Myxoid neurofibroma consists of spindle shaped cells with buckled nuclei and less prominent vasculature. Immunohistochemically, it is S100 positive.

Low grade myxofibrosarcoma consists of spindle cells with mild nuclear atypia admixed with non dilated curvilinear blood vessels. Immunohistochemically, it is ER, PR and desmin negative.

Low grade fibromyxoid sarcoma consists of bland spindle cells with whorled architecture and less prominent vasculature in a collagenous to myxoid stroma. Immunohistochemically, it is MUC4 positive and desmin, ER and PR negative.

Aggressive angiomyxoma has a high risk of local infiltration. The goal of treatment in aggressive angiomyxoma is to achieve a negative margin so as to reduce the chances of recurrence. As a result, the first line of treatment in aggressive angiomyxoma is surgery with wide local excision. In cases of extensive infiltration into the nearby structures, radical operation needs to be performed if there are no morbidities associated with the extensive surgery. Patients with positive margins are as likely to have recurrence as those with negative margins.[19,20] Gonadotropin releasing hormone agonist has been used both preoperatively and postoperatively in recurrent cases with positive outcome in some patients with aggressive angiomyxoma.[21–24] Even though chemotherapy and radiotherapy are considered to have no role in the management of aggressive angiomyxoma, radiotherapy can be a good alternative treatment in patients resistant to antihormonal therapy, with recurrence or in inoperable cases.[25,26]

4. Conclusion

Aggressive angiomyxoma is an aggressive tumour because it has a high risk of infiltration and local recurrence. Therefore, it should be distinguished from other myxoid tumours. Preoperative cytological diagnosis helps in surgical management with appropriate wide local excision with clear margins.

5. Source of Funding

None.

6. Conflicts of Interest

None.

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Cite this article: Devi J, Phukan N. Cytodiagnosis of multilobulated aggressive angiomyxoma clinically mimicking sarcoma – A case report. *Indian J Pathol Oncol* 2023;10(1):76-79.