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Soft Tissue Lesions of Vulva: Histomorphology Vs Immunohistochemistry of These Rare Entities

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Abstract
Soft tissue lesions of the vulvo-vaginal tract are uncommon entities and are likely to be confused clinically with more common lesions like Bartholin's cyst or fibro epithelial polyp. Due to a common cell of origin, both histomorphology and immunohistochemistry are essential for correct diagnosis. Due to the rarity of the lesions there is limited data on the biological behaviour of these lesions. However, correct diagnosis of these benign lesions from more aggressive ones prevents unnecessary follow-ups
Keywords: *Soft tissue lesion, Vulvovagina, Angiomyofibroblastoma, Angiomyoma, Angiomyxoma.*

Introduction

Soft tissue lesions of the vulvovaginal area are uncommon lesions with similar clinical features. Their histological characterization is equally troublesome due to overlapping morphology and immunohistochemical features. This is largely attributed to the common cell of origin ie the sub epithelial mesnchymal stromal cells. A large percentage of these tumors are initially treated as Bartholin's cyst or fibro epithelial polyp clinically till they are resected and histomorphology carried out [1-4].

Knowledge of the biological behaviour of these entities has been limited due to the rarity of the lesions. Nucci MR and Fletcher CD reviewed all the soft tissue lesions and updated the clinical aspects, biological behaviour and pathology in 2000 [1] followed by McCluggage in 2005 [2] and another one in 2009 [5]. However, since then there have been only case reports and few reviews or case series. Histologically the lesions are primarily composed of spindle cells in a loose fibromyxoid stroma and are intimately associated with blood vessels. The architecture, vascular morphorphology and immunohistochemical profile are keys to diagnosis [4]

One of the rarest lesions in this area, Angiomyo-fibroblastoma, arises predominantly from the vulva and tends to be well circumscribed. It was first described in 1992 by Fletcher CM as an entity distinct from aggressive angiomyxoma [6]. A thorough search of the databases indicates less than 100 cases have been reported in the last 25 years. The key histological feature of angiomyo-fibroblastoma is the alternating hypo and hyper cellular areas with blood vessels spread out randomly. The other benign, completely resectable tumors like superficial angiomyxoma, fibroepithelial stromal polyp and angiofibroma

needs to be kept as differential in a well circumscribed tumor [7-9].

Smooth muscle tumors of the lower genital tract are quite rare, however characteristic morpholo-gycal features and actin positivity usually points to the correct diagnosis. Aggressive angiomyxoma needs to excluded conclusively as they are prone to recurrence and have a more aggressive course [10].

Cases

Our first case was a 25 year old lady who presented with a gradually increasing swelling over the right labia for 5 months. With a clinical impression of Bartholin's cyst, she was placed on conservative management. The lesion was later resected and sent for histopathological examin-ation. The surgical specimen was grey white and measured 2.5 cm in diameter, had a firm consistency with no areas of hemorrhage or necrosis. Microscopically, the tumor was well circumscribed by a thin fibrous capsule and composed of plump spindled to epithelioid cells in an alternating hypo and hypercellular areas (Fig 1). These cells had ovoid nuclei, inconspicuous nucleoli and spindled eosinophilic cytoplasm. Numerous randomly interspersed thin walled small blood vessels were present with focal pallisading of the tumor cells around some of them (Fig 2). RBC extravasation was not seen. Multinucleated giant cells were absent. No pleomorphism, necrosis or mitosis were seen. On immunohistochemistry, the stromal cells were positive for desmin and vimentin. The tumor cells strongly expressed estrogen (ER) and progesterone receptors (PR) but did not express S100 and smooth muscle actin (Fig 3). A diagnosis of angiomyofibroblastoma was given based on the morphology and characteristic hormone receptor positivity.

Fig 1: Alternating hypo and hyercellular areas in angiomyofibroblastoma (H&E 10x) with interspersed thin walled blood vessels (block arrows) better appreciated at higher magnification (Inset : H&E 20x). Angiomyofibroblastoma

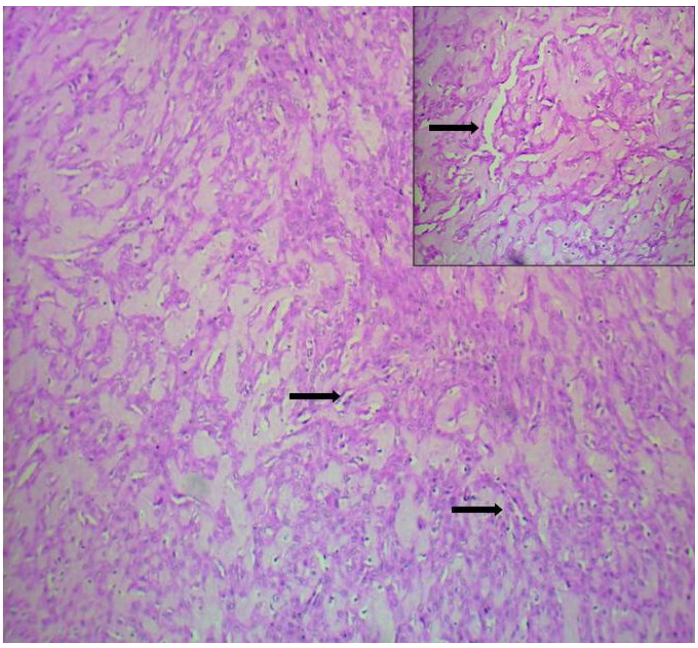


Fig 2: The cells are ovoid to spindled and are seen surrounding the blood vessels (H&E 40x). Angiomyofibroblastoma

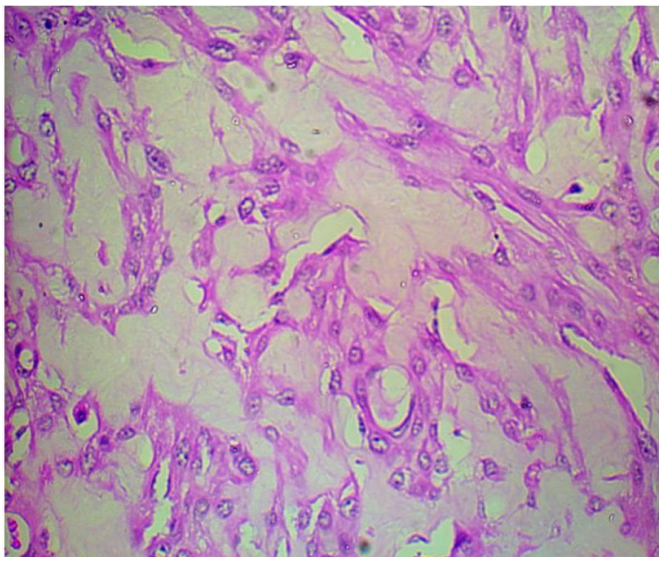
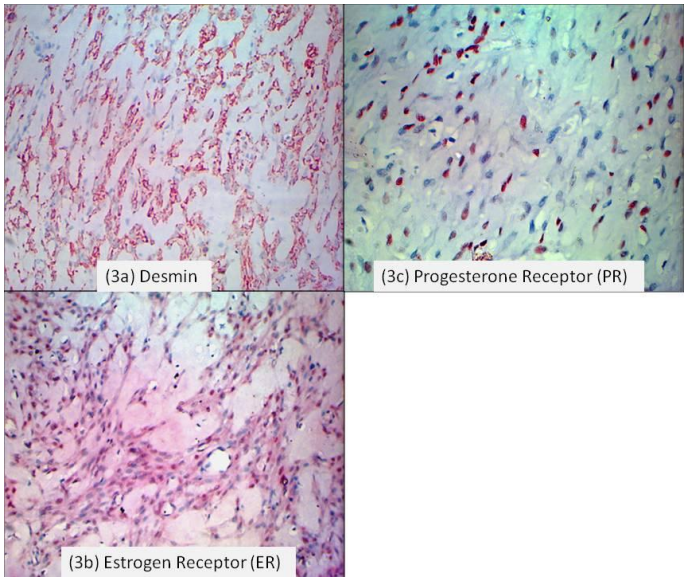


Fig 3: Immunohistochemical in Angiomyo-fibroblastoma panel showing Desmin (3a), ER (3b) and PR (3c) in tumor cells.



The second case was a 46 year old peri-menopausal lady who presented with a small but painful boss elated mass arising from the left vulva near the vestibule. The lesion was excised and sent for histopathology. The specimen was 1.5 cm in diameter with a greyish white surface. No areas of hemorrhage or necrosis were seen. Microscopically the lesion was predominantly composed of interlacing bundles of spindle cells in a loose fibromyxoid stroma and thick walled blood vessels which seem to be merging with the surrounding smooth muscle bundles (Fig 4). The cells were bland, showing minimal pleomorphism and no mitosis. Smooth muscle actin was consistently expressed in these spindle cells. CD 34 was highlighted in the blood vessels (Fig 5). It was negative for estrogen receptor and progestogen receptor. The lesion was diagnosed as Angiomyoma.

Fig 4 (a-c): Interlacing bundles of spindle cells in a loose fibromyxoid stroma and thick walled blood vessels which seem to be merging with the surrounding smooth muscle bundles in Angiomyoma.

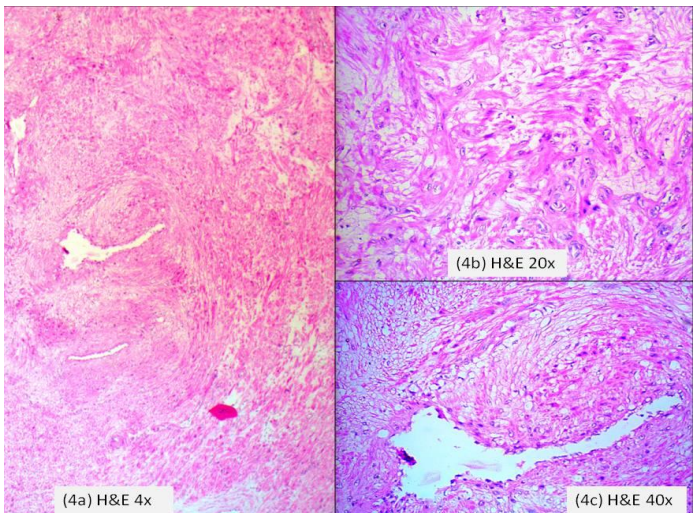
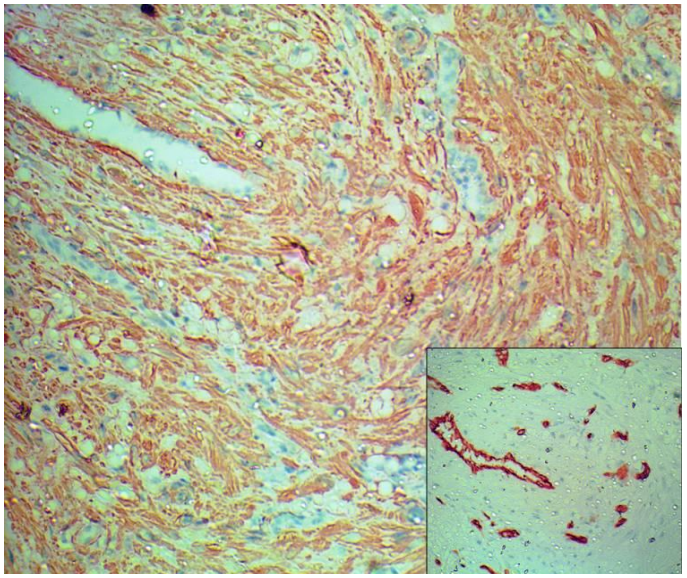


Fig 5 Immunohistochemistry: SMA is positive in the spindle cells while the blood vessels are highlighted by CD 34 (inset)



A 3 year old female presented as the third case with gradually increasing swelling over the right lateral aspect of labia majora extending to right groin. The mass was excised and sent for histopathology. The resected specimen was a tan grey soft globular mass which was well circumscribed grossly and measured 4.5x3.5 cm. No areas of hemorrhage or necrosis were seen. Microscopic examination showed a thin continuous fibrous capsule enclosing a hypocellular

tumor composed of benign fibroblasts. Capillary size blood vessels were seen scattered in a background rich in myxoid material, few of them showing thick walls. Few stellate cells were also seen. (Fig 6) Immunohistochemically the cells expressed vimentin (Fig 7) and was negative for either S100 or actin and therefore the tumor was diagnosed as Superficial Angiomyxoma

Fig 6 (a-b) Hypocellular tumor composed of benign fibroblasts with scattered capillary size blood vessels in a background rich in myxoid material. Few stellate cells were also seen (b) in Superficial Angiomyxoma

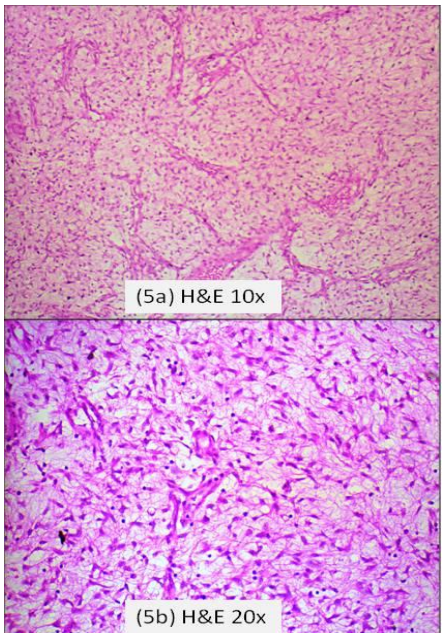
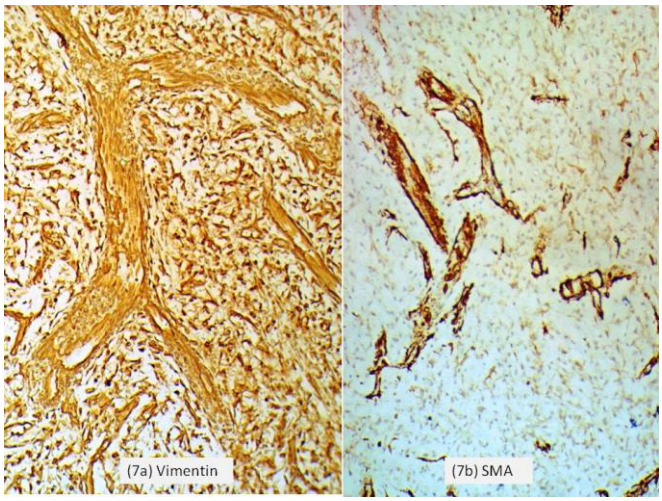


Fig 7 Immunohistochemistry: Vimentin positive cells (a) and Negative for SMA (b) in Superficial Angiomyxoma



Discussion

The overlapping clinical, morphological and immunehistochemical features of soft tissue lesions of the vulvovaginal area has been attributed to the common cell of origin – the mesenchymal stromal cells [5]. Table 1 shows the morphological and immunohistochemical profile in our cases.

Table 1 shows the overlap of morphological markers and the role immunohistochemistry played in diagnosis of these tumors

	Angiomyofibrblastoma	Angiomyoma	Superficial angiomyxoma
Gross features			
Size	2.5 cm	1.5 cm	4.5 cm
Consistency	Soft	Firm	Soft with myxoid areas
Surface	Smooth	Smooth	Bosselated and smooth
Microscopic features			
Circumscription	Well circumscribed	Well circumscribed	Well circumscribed
Architecture	Alternating hypo and hypercellular areas	Interlacing bundles of smooth muscle	Hypocellular tumor
Blood vessels	Thin walled and randomly distributed	Thick walled with merging of the vessel wall with surrounding smooth muscle	Thin walled capillary size vessels
Necrosis, mitoses	None	None	None
Immunohistochemistry			
Smooth muscle actin	Negative	Positive	Negative
Desmin	Positive	Positive	Negative
S100	Negative	Negative	Negative
ER & PR	Positive	Negative	Negative
CD 34	Highlights the blood vessels		

The problem in accurately diagnosing is compounded by the very low incidence of these tumors which have till date been published only as case reports and few update articles[5]. The incidence is maximally reported in reproductive age group with a mean in the fourth decade [1-3]. Angiomyofibroblastoma has been seen in the early reproductive age [8-11]. Very rarely have these tumors been seen in the young age in both sexes [12]. James White with Yuen Fu-Chan and has reported angiomyxoma in children similar to one of our cases, though the latter was the superficial variant [13, 14].

Although angiomyofibroblastoma have been seen to occur in the inguino-scrotal region of males [15],

retroperitoneum [16], but the commonest site is the vulvovaginal region. Our case also presented with a swelling from the vulvo-vaginal area and hence formed an important clue to the diagnosis. She had the classical presentation of a vulvovaginal swelling being treated for Bartholin's cyst which later was excised. The morphology of hypo and hyper cellular areas with interspersed thin walled blood vessels which was seen in our case alongwith the positivity for ER and PR was diagnostic of angiomyofibroblastoma and is presently being reported due to the rarity of the lesion in literature. Aggressive angiomyxoma was not considered due to the well circumscription and absence of thick walled blood vessels and mitosis.

Mesenchymal lesions of the vulvovaginal area are rare in the pre-pubertal age and only few cases of fibroma have been reported [17,18]. Our third case was a 3 year old child with a gradually progressive swelling which reached upto 4.5 cm and had a myxoid cut surface. Histologically the tumor showed features of angiomyxoma and had the charecteristic thin walled capillary sized blood vessels traversing a hypocellular fibromyxoid lesion. The differential of aggressive angiomyxoma was excluded based on the absence of infiltrating margins, thick walled blood vessels, atypia and mitoses. Immunohistochemically it was positive for desmin and negative for actin and S100. It was first described in 1988 and has been reported infrequently as a vulvovaginal lesion. Considered as a tumor of the superficial dermis, it has to be differentiated from the more aggressive counterpart [19]. A myxoid neurofibroma also needs exclusion in such cases, especially in the young. S100 negativity ruled out neural lesion in our case.

Angiomyoma also called as angioleiomyoma is common in females of 30-60 yr age group and is a soft tissue lesion predominantly affecting the lower limb, although it has been reported from various other sites including the nasal turbinate [20] and mediastinum [21]. They are generally less than 2 cm in diameter and simple excision is treatment of choice as they do not recur [22,23].

Morphologically they have been classified by Morimoto in 1973[24], albeit without any clinical significance into solid - having compact smooth muscle, venous - showing thick walled vessels which merge with the surrounding smooth muscle bundles and cavernous with dilated vessels [24]. Our case had morphology similar to the venous variant and was positive for smooth muscle actin, which excluded cellular angiofibroma, angiomyxomas and other mesenchymal stromal lesions.

Our cases represent the broad spectrum of histopathological entities that present as a vulvovaginal mass in all age groups. Considering the common cell of origin, there is considerable overlapping of morphological features. However, a combination of morphology and Immunohistochemistry is adequate to correctly diagnose the tumor. Recognition and exclusion of more aggressive lesions is mandatory to prevent unnecessary follow-up as most of these benign lesions are cured by complete excision.

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