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Histomorphological and Immunohistochemical Spectrum of Mesenchymal Tumours of Vulva

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ABSTRACT

Background

The vulvar neoplasms are relatively less common female genital tract tumours. Most women present with vulval symptoms such as painless lump, ulcer, and itching, while others may be asymptomatic. The vulval neoplasms range from epithelial in origin being most common followed by adnexal, melanocytic and rarely mesenchymal tumors. The current study has highlighted the morphological spectrum of vulval tumours with emphasis on the varied spectrum of mesenchymal vulval neoplasms.

Material and Methods

This is a five-year prospective study of vulval tumours especially highlighting mesenchymal tumours encountered on vulval biopsies/specimens.

Results

Out of the 100 cases, 79 cases were reported as squamous tumors followed by 6 as Glandular neoplasms, 5 cases of melanocytic origin and the remaining 10 cases as mesenchymal tumours. The various subtypes of mesenchymal neoplasms were as follows Leiomyoma 2 cases, Angiomyoma 3 cases, Spindle cell lipoma 1 case, Neurofibroma 1case, Rhabdomyoma 1case, Granular cell tumor 1 case and Leiomyosarcoma 1case.

Conclusion The surgical pathologist should be aware of the varied spectrum of vulval tumours, especially overlapping morphological features of vulval mesenchymal tumours for accurate diagnosis which helps clinicians to decide an exact course of treatment.

Keywords: Mesenchymal neoplasm, vulva, histomorphology, immunohistochemistry

Introduction

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Anatomically vulva consists of labia majora and minora, clitoris, vulvovaginal glands, vestibular bulbs and urethral meatus. The majority of the vulva is lined by keratinized skin except at the introitus. The labia majora has numerous sebaceous, eccrine and apocrine glands. Vulvar and vaginal neoplasms make up a small percentage (3%) of female genital cancers, the majority being epithelium, adnexal and melanocytic in origin (1). They can be benign or malignant. However mesenchymal tumors of the vulva are rare. A variety of mesenchymal tumours can arise in the vulvovaginal region including lipomatous neoplasms, peripheral nerve sheath tumors and sarcomas. The aim of the current study was to highlight the varied spectrum of vulval neoplasms with an emphasis on the histomorphological and immunohistochemical spectrum of mesenchymal tumours of the vulva.

Material and Methods

This is a five-year prospective study from April 2018 to April 2023 during which 100 vulvar biopsies/specimens were submitted to the Department of Pathology. All the specimens and biopsies were grossed and processed according to standard procedures. The slides were stained with Hematoxylin and eosin-stained in the histopathology laboratory of our institution. The clinical and vulvar examination details were obtained from patient files and histopathology requisition forms. All the slides were examined independently by two pathologists. IHC markers were used wherever necessary and applicable. The ethical approval was obtained for this study.

Results

The present study is a five-year prospective study of 100 cases. The patient's age ranged from 25 years to 70 years, and the mean age was 42.1 years. Out of the total cases 79 were reported as Squamous neoplasia followed by 6 as Glanular neoplasms, 5 cases of melanocytic origin and the remaining 10 cases as mesenchymal tumors. The tumours of squamous neoplasia included squamous intraepithelial neoplasia in 20 cases and the remaining 59 cases were reported as squamous cell carcinoma. Among Glandular neoplasia, 2 cases were reported as carcinoma in situ and 4 cases as adenocarcinoma .5 cases were reported as melanoma. The various mesenchymal tumours included in our work were leiomyoma (2 cases), angiomyxoma (3 cases), spindle cell lipoma (1 case), neurofibroma (1 case), rhabdomyoma (1 case), Granular cell tumour (1 case) and leiomyosarcoma (1case).

The details of these mesenchymal tumors including clinical presentation, histopathology and percentage are tabulated in Table 1.

TABLE No. 1

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Age and gender	Clinical presentation	Histological diagnosis
48 years female	Bartholin cyst	Leiomyoma with cystic degeneration
42 years female	Polypoidal mass	Leiomyoma
25 years female	Pedunculated non-tender mass	Angiomyxoma
30 year female	Sessile polyp	Angiomyxoma
38 year female	Labial cyst	Angiomyxoma
34 years female	Painless lump	Spindle cell lipoma
44 years female	Nodular mass	Neurofibroma
40years female	polyp	Rhabdomyoma
50 years female	Non-tender circumscribed lump	Granular cell tumour
70 years female	Ulcerated irregular mass	Leiomyosarcoma

We have discussed the gross description and histomorphological features of various mesenchymal neoplasms in detail in the following paragraph.

Leiomyoma

During the present study, we encountered two cases of leiomyoma both of which were seen in females who were in their fourth decade. On gross both comprised a partially encapsulated well-defined nodular mass Fig 1a. The cut surface was grey-white with slit-like areas as shown in Fig 1b. Microscopy shows a benign tumour composed of sheets and fascicles of oval to spindle-shaped cells with abundant dense cytoplasm and areas of hyalinization Fig 1c and Fig 1d. Necrosis, nuclear pleomorphism and brisk mitosis were absent. On IHC cells exhibited positivity for desmin and SMA. The final diagnosis of benign vulvar leiomyoma was made.

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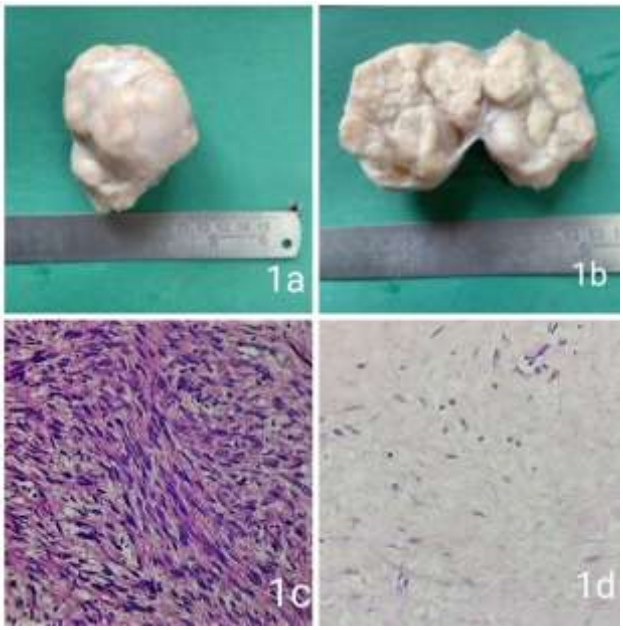

Fig 1 Leiomyoma a) &b) photomicrograph showing gross appearance c) H& E stained sections show fascicles of spindle cells d) H& E sections show hyalinization

Angiomyxoma

In our study, three female patients aged 25,30 and 38 years presented to gynecology OPD with a slow-growing mass on labia major for six months, one year and one and half years respectively. In the latter lump was deep-seated. The mass was excised and sent to the pathology department. Grossly it had a gelatinous homogenous appearance Fig 2a. On microscopy, it comprised of spindle and stellate-shaped cells embedded in myxoid stroma along with interspersed thin-walled blood vessels Fig 2b. On IHC spindle and stellate cells exhibited immunoreactivity for desmin fig 2c and actin however it was negative for S100. Therefore distinguishing from angiofibroma. The diagnosis of Aggressive Angiomyoma was made. This tumor has the tendency to reoccur therefore our patients were kept on close follow-up by the gynecologist.

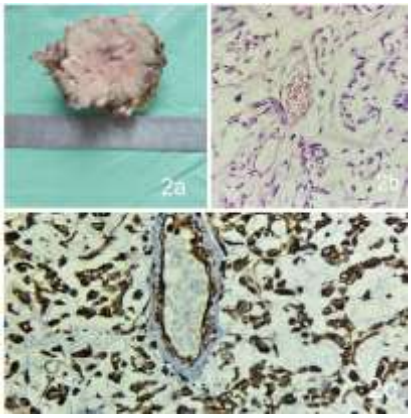

Fig 2 Angiomyxoma a)Cut section gelatinous b) H& E section (x40) c) Desmin strongly positive (x40)

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Spindle cell lipoma

A 34 year-old married woman presented with 3 year history of large painless progressively increasing vulvar mass. There was no history of trauma, vaginal discharge, urinary symptoms or similar swelling in any other part of the body. Surgical excision of the mass was done and sent for histopathological examination. Gross examination revealed a partially encapsulated grey-white soft tissue mass measuring 5x4×3cm. The cut surface was lobulated, yellow fig 3a. Microscopic examination showed an admixture of mature adipocytes and spindle cells separated by fibrovascular septa Fig 3b and 3c. The spindle cells showed bland oval nuclei with moderate eosinophilic cytoplasm. Areas of atypia, necrosis, and abnormal mitosis were absent. On IHC spindle cells were strongly positive for CD34 Fig 3d, however, lacked reactivity for S-100. Diagnosis of spindle cell lipoma was made.

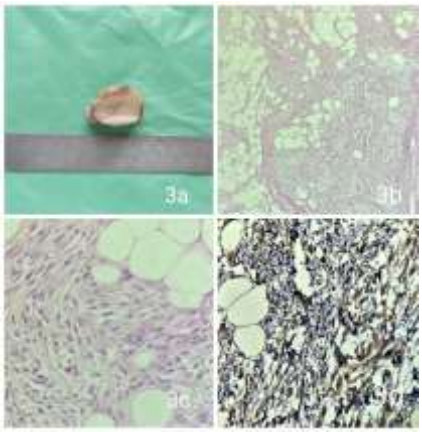

Fig 3 Spindle cell lipoma a) Gross appearance b) and c) H and E sections (x10,x40) d) CD 34 positive spindle cells (x40)

Neurofibroma

A 44-year-old woman presented with a 5 -month history of painless progressive vulvar mass. On examination, there was a nodular, soft, non-tender, mobile mass on the right labium majus. Excision biopsy was done and sent for histopathological examination. Grossly it was 4x4x3 cm well circumscribed solid gray-white. On histological examination, there were bundles and fascicles of elongated spindle-shaped cells with bland, wavy spindle nuclei, separated by loose stroma. There was a sprinkling of mast cells along with numerous small nerve fibres Fig 4a. On IHC cells were positive for NFP fig 4b and non-reactive for S-100 fig 4c. Therefore distinguishing it from schwanoma.

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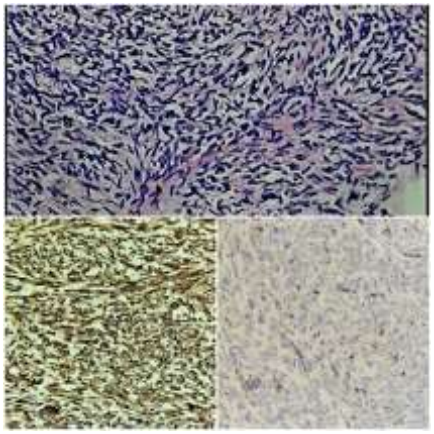

Fig 4 Neurofibroma a) Photomicrograph shows wavy tumor cells H& E (x40) b) NFP postive (x40) c) S-100 negative

Rhabdomyoma

We received a received right labial biopsy of a 32-year-old female. The cut section was solid. On microscopy, there were fascicles of elongated strap-shaped rhabdomyoblasts with elongated nuclei and eosinophilic cytoplasm. No nuclear atypia and mitosis were noted. Fig 5a.On IHC cells were positive for myoglobin and desmin

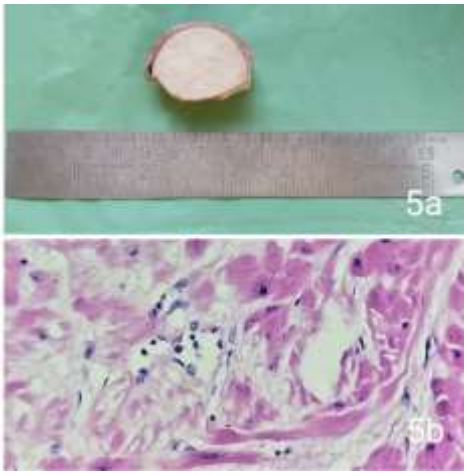

Fig 5 Rhabdomyoma a) circumscribed gross appearance b) Hand E stained section shows rhabdomyoblasts (x40)

Granular cell tumour

A 50-year-old female presented to the gynecology outpatient department with a nodule in vulvar region with complaints of pruritus and pain. A wide excision of nodules was done and sent to the department of pathology. Grossly it was circumscribed 3x3 cm grey white mass fig 6a. On microscopic examination showed tumour cells arranged in nests and trabeculae. Individual tumour cells were polygonal with small centrally located nuclei and an abundant amount of granular cytoplasm Fig 6b. On IHC cells exhibited positivity for S100 and NSE

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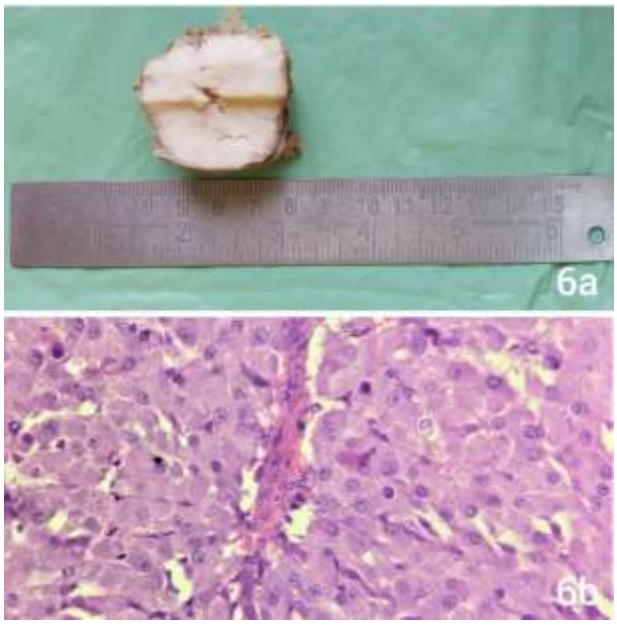

Fig 6 Granular cell tumor a) well circumscribed gross appearance b) Sections shows tumor cells having abundant granular eosinophilic cytolplasm

Leiomyosarcoma

Maligmant mesenchymal tumours are a rare malignancy of the vulva. We encountered 70-year-old female patient who presently with 6 cm mass on the vulva fig 7a. On light microscopy sections comprised of spindle-shaped cells exhibiting a moderate degree of nuclear aypia Mitotic count was 12/10hpf with areas of necrosis Fig 7b. On IHC exhibited positivity for SMA and desmin. The deep resected margins were positive, therefore patient underwent radical hemivulvectomy with ipsilateral inguinal lymphadenopathy along with adjuvant chemotherapy.

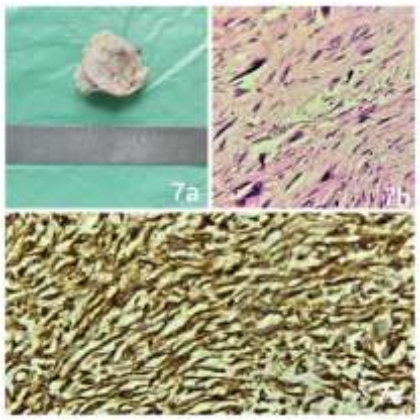

Fig 7 Leiomyosarcoma a) photomicrograph showing gross appearance b) H and E stained sections show pleomorphic spindle cells x40 c) SMA strongly positive x40

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Discussion

The vulva is lined by skin and is rich in apocrine glands, sebaceous glands and eccrine glands resulting in numerous epithelial and adnexal tumors. The most frequently encountered tumours in the vulva are squamous cell carcinoma. Mesenchymal neoplasms are less encountered in this region. Our study has highlighted the varied spectrum of vulval tumours with emphasis on the morphological and immunohistochemical spectrum of mesenchymal tumours in the vulva.

Leiomyomas are benign tumours arising from smooth muscle cells in any anatomical site within the body (2). Vulvar leiomyoma is a rare type about 160 cases have been reported in the literature so far (3-4). It has a number of histological origins including smooth muscle cells, spindle cells, and epithelioid cancer cells of eosinophilic cytoplasm. When immunohistochemical stains were done, vulvar leiomyomas stained positive for estrogen receptors or progesterone receptors and sometimes both. Leiomyoma of the vulva is rare and usually misdiagnosed as a Bartholin cyst as in our case too.

Angiomyxoma was first described by Steeper and Rosai in 1983 (5). The peak incidence is during the third decade of life, suggesting that estrogen may stimulate its growth (6). It generally involves the genital, perineal and pelvic regions, with the vulvar region being the most common site of involvement (7). Tumours occurring during pregnancy have rapid growth as there is a state of increased estrogen and progesterone production during this period (8). Tumor needs to be differentiated from angiofibroma.

Aggressive angiomyxomas are slowly growing and are locally invasive. They exhibit positivity for desmin and actin. The excision of these tumors is difficult as they have the same consistency as that of normal connective tissue and therefore have a propensity for local recurrence.

Spindle cell lipoma was first described by Enzinger and Harvey in 1975 as a distinct histopathological entity of conventional lipoma which is composed of spindle-shaped cells with mature adipose tissue in a fibro cellular stroma made up of bundles of ropey collagen fibers (9). Histopathological differential diagnoses of SCL include solitary fibrous tumour (SFT), neurofibroma, schwannoma, and leiomyoma (10). In the present case, antibodies to CD34 were used which exhibited positivity leading to the diagnosis of SCL.

Vulvar involvement by neurofibroma is found in about 18% of women with NF 1 while approximately half of all vulval neurofibromas are found in women with NF 1 (11). Although these tumors are usually small in size (<3 cm in diameter) and slow-growing, giant rapidly growing solitary ones have been reported in the literature (12). Solitary, genital neurofibromas have been described by Gordon et al which presented with intractable chronic pelvic pain and dyspareunia respectively (13). In their study, Kane et al reported an isolated vulval neurofibroma in an 18-month-old female child (14). Amita et al have reported cases of giant neurofibroma in young females (15).

Adult Rhabdomyomas are rare with the majority occurring in the head and neck region with predilection in men. Genital rhabdomyoma arises as a solitary, polypoid lesion in the vagina,

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vulva or cervix (16). We encountered a single case of vulvar rhabdomyoma in 40 years 40-year-old female.

GCT was described by Abrikossoff as granular cell myoblastoma in 1926 (17). GCTs are generally small, firm, solitary nodules that are whitish in colour, lack encapsulation and are located in the subcutaneous layer. The most common location of GCT in the female genital tract is on the labium major (18). They are typically slow-growing and usually asymptomatic and are sometimes confused with sebaceous cysts. However, there have been reports of GCTs of the vulva, which are aggressive with multicentric or metastatic disease and can have fatal outcomes. The incidence of multicentric lesions ranges from 3% to 20% and this raises the suspicion of malignancy (19).

Sarcomas are rare tumors of mesenchymal origin that may develop in soft tissues and viscera. Primary soft-tissue sarcomas account for less than 2% to 3% of all malignant tumours occurring in the female genital tract (20). The most common gynecological sarcoma is uterine sarcoma. Other gynecological sarcomas include vulva, vagina, ovary, fallopian tubes, and uterine ligaments sarcomas (10%) (21). Invasive vulvar carcinoma accounts for about 5% of gynecologic cancers and sarcoma of vulvar are extremely rare (22). Leiomyosarcoma constitutes 1% of all vulvar malignancies (23). The criteria for predicting malignancy in vulvar smooth muscle tumours include the presence of at least three of the following: infiltrating margin, size of 5 cm or greater, moderate to severe cytological atypia, and presence of five or more mitotic figures per 10 high power field. Radiation does not appear to affect survival but it has a tumor-reducing effect. Chemotherapy occasionally provides significant improvement in survival and quality of life in patients with leiomyosarcoma of soft tissue.

Conclusion

The most common tumour of the vulva encountered in our study is squamous cell carcinoma. Mesenchymal tumours of the vulva are rare. The current study has focused on the varied morphological spectrum of neoplasms of the vulva with emphasis on mesenchymal tumours and it has further highlighted the role of adjuvant immunohistochemistry. Accurate diagnosis helps clinicians decide the exact course of treatment, especially the role of adjuvant therapy in the treatment of malignant tumors.

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