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Benign Vulvar Lesions: A Clinico-Pathological Review

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Abstract: The commonest growth pattern seen in the vulva are benign cystic lesions. However other important tumours, most of which are rare, are the hidradenomas, the condylomas and leiomyomas. Vulvar lesions require histopathological evaluation to rule out malignant growth and commence early treatment. The literature on benign vulvar masses, especially vulvar cysts, is scanty. This may be due to the painless character of the lesions and the location of the organ, which may create anxiety over the invasion of privacy during a clinical examination, resulting in reduced willingness to seek medical consultations. A review here of vulvar lesions is to improve awareness, especially for the premalignant lesions.

Keywords: *Vulva, Lesions, Benign.*

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I. INTRODUCTION

The vulva is the female external genital organ and it is composed of the Mons pubis, the labia majora and labia minora, the vestibule, the bulb of the vestibule, vaginal introitus, urethral meatus, the Bartholin's gland and the skene glands.(1)

Apart from such congenital anomalies like ambiguous genitalia manifesting as clitoromegaly, bifid clitoris or fusion of the labio-scrotal fold, benign lesions of the vulva include tumors and cystic lesions like Bartholin's cyst, epidermal inclusion cyst, Skene duct cyst, hydradenoma, endometriosis, vulvar leiomyoma and lipoma which has been reported to be the second most common solid tumor of the vulva.(2,3,4) The minor vestibular gland or the remnants of the mesonephric ducts may be the site of a mucous cyst of the vulva as typified by the cyst of the canal of Nuck from the procesus vaginalis, the content of which is peritoneal fluid.(5) Often times, benign vulvar growth can be the consequence of infection of the genital tract such as the warty growth of human papillomaviral infection (condylomata accuminata).(6) It may also be appropriate to add such vulvar dermatoses like lichen planus and lichen sclerosus which are chronic inflammatory vulvar lesions resulting from the itch-scratch cycle of vulvo-vaginal candidiasis.(7,8) These varieties of benign lesions seen in the vulva is a reflection of the embryonic origins of the organ; being a union of the endodermal cloacal membrane, the paramesonephric mesoderm and the ectoderm of the urogenital membrane.(9)

The general incidence of vulvar lesions is not known except for the individual lesions as they may occur. The lesions are often considered rare, but this may be due to underreporting rather than their non-existence (10,11). The vulva is seen as "sacred" to the owner; the female folk and thus it is accorded the utmost privacy with the result that the affected female may not report the presence of any lesion even to her spouse. She will be reluctant to present the problem to the doctor because of anxiety over the likelihood of invasion of her privacy in the course of examination and treatment. Consequently, vulvar lesions are often ignored, and late presentation is usually the case, except for those manifesting with pruritus right from its onset.(12)

The commonest presentation of most vulvar lesions is pruritus with or without a visible growth. There is the tendency for them to remain asymptomatic for long periods, with continuing growth until pressure symptoms, ulceration or some other discomfort ensues.(11,13)

Additionally, vulvar lesions can sometimes present a diagnostic challenge to the clinician, and the final diagnosis is often made by the histopathologist. For instance, these authors once treated a patient who had a right vulvar swelling that progressively increased in size over a period of more than

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five years' duration prior to presentation. A clinical diagnosis of Bartholin's gland cyst was made. The "cyst" was excised in whole at surgery and sent for histology wherein a vulvar leiomyoma was reported.[14] Similarly, James D Perkins et al reported a case of "Traumatic Vulvar Haematoma Masquerading as a Bartholin's duct Cyst in a Post-menopausal woman". [15] In this case report, the haematoma was evacuated in the 66 years old woman and their fear of malignancy was allayed when their subsequent biopsy was negative for such morbidity.

Often, the patient with benign vulvar growth may present in the primary health care clinic or to the dermatologist where valuable time may be expended on diagnostic work-up and with heightened anxiety on the part of the patient and sometimes the physician too. This review aims to identify characteristics and clinical presentations of common benign vulvar lesions, the awareness of which will reduce diagnostic delays and patient anxiety.

II. CLASSIFICATION

Vulvar lesions reflect the multiplicity of tissues present in the organ and their varying degrees of susceptibility to changes induced by various agents, including hormones, allergens and irritants. Classifying vulvar lesions solely on the basis of the tissues present or these agents will not be totally inclusive. There is no clearly demonstrable cause and effect relationship in all of them that have a defined clinical presentation.[15] Thus, there is as yet no universally agreed method of classifying vulvar lesions, as noted in our literature search.

A simplistic approach is employed here by grouping vulvar lesions into those arising from tissues of ectodermal derivatives (the epidermis and its appendages) and those arising from the mesoderm (the dermis). The various lesions are briefly discussed in turn with their clinical presentations, histopathological features and treatments for those requiring treatment.

- *Epidermal Lesions*

These include inflammatory lesions, inclusion cysts, fibro-epithelial growths, infective lesions, and pigmented lesions.

The inflammatory vulvar lesions include lichen sclerosus, lichen planus and vulvar vestibulitis. They all manifest with vulvar itching, causing vulvar bruising and dyspareunia.

In lichen sclerosus, the role of estrogen deprivation in its aetiology may require investigating, as the condition is reported to be commoner in pre-menarchial girls and postmenopausal women.[16]

Fig 1a Lichen Sclerosus.

Gross image [17] Bilateral and symmetrical disease and loss of labia minora.

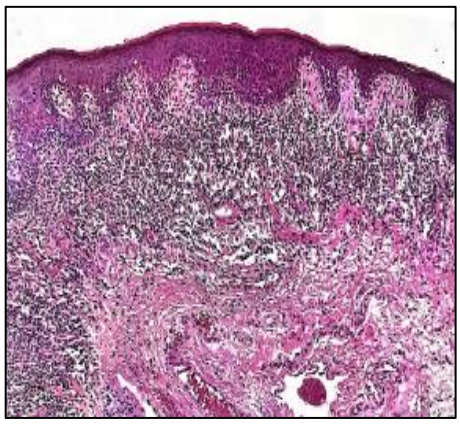

Fig 1b Lichen Sclerosus.

Microscopy. Psoriasiform dermal hyperplasia, dense band-like lymphocytic infiltrates, papillary dermal fibrosis, and hyperkeratosis.

The trauma induced by the itch-scratch cycle of vulvovaginal candidiasis, immune deprivation and genetic factors have all been suggested in the aetiology of lichen sclerosus but together with the other two non-neoplastic vulvar lesions listed above, their causes remain unknown.

Fig 2a Lichen Planus.

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Gross image [19] Linear hyperpigmented lesions.

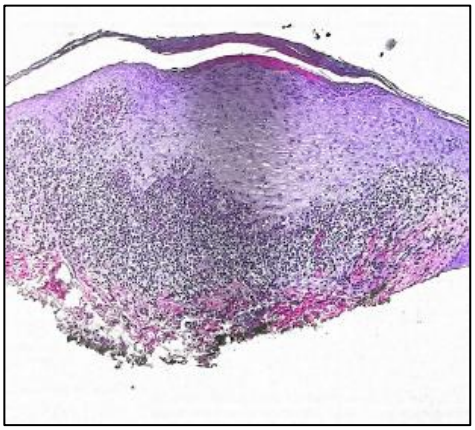

Fig 2b Lichen Planus.

Microscopy[20] Bandlike infiltrate at the dermoepidermal junction. Dyskeratosis and squamatization of the basal keratinocytes. Acanthotic epidermis with hyperkeratosis and hypergranulosis.

Lichen planus and lichen sclerosus are treated with topical steroids. Although lichen planus can resolve on its own, persistent cases may require a biopsy and histopathological evaluation to rule out malignancy.[21]

➢ *Vestibulitis*

Vulvar vestibulitis manifests with pain and erythema of the vestibule especially on contact. Initially thought to be an inflammatory dermatosis, it is now regarded as a chronic pain disorder. The inflammatory changes seen on microscopy are non-specific and seen in normal vaginal epithelium.[22]

It may be primary or secondary depending on whether it is a first occurrence or a relapse after experiencing a period of remission from a previous episode. It is reported to be a leading cause of dyspareunia. The treatments include the application of soothing creams or lotions to the vulva, tricyclic antidepressants and surgery in extreme cases (vulvar vestibuloplasty).[23]

➢ *Cysts*

In simple terms, a cyst is an enclosed sac that has an epithelial lining. The sac is called pseudocyst if it is not lined by an epithelium. Contents of a cyst range from fluid to semi-solid to outright solid debris. Vulvar cysts mostly arise from the blockage of gland ducts.

Common cysts of the vulva include epidermal inclusion cyst, Bartholin duct cyst, mucinous cyst, mesothelial cyst, and mesonephric-like cyst.[1] The cysts are usually incidental findings due to their being mostly asymptomatic. Cysts that are painful and bleeding, and those seen in women of 40 years and above require special attention.[2]

➢ *Epidermoid Cyst*

Epidermoid cyst or epidermal inclusion cyst is a benign lesion. It appears as a semi-solid cystic enclosure within the dermis, with average diameter of 2cm, lined by regular stratified squamous cornified epithelium. The contents are mostly creamy keratin debris.

The plugging of follicular orifice with bacteria and keratin, leads to cyst formation and accumulation of keratin debris. It may complicate penetrating trauma to skin, such as a sewing needle, with resultant implantation of squamous epithelium into the dermis.[2] Wondimu Gudu presented a case of epidermal cyst containing stones, resulting from female genital circumcision.[24] Awareness of such complications will prevent misdiagnosis.

Grossly it appears as a soft round to oval skin mass. Microscopically, the cyst epithelium is stratified squamous. Adnexal structures are absent. The cyst contains keratin and has a prominent granular layer. Treatment is by surgical excision.

Fig 3a Epidermoid Cyst. [25]

Gross appearance with a clearly visible punctum

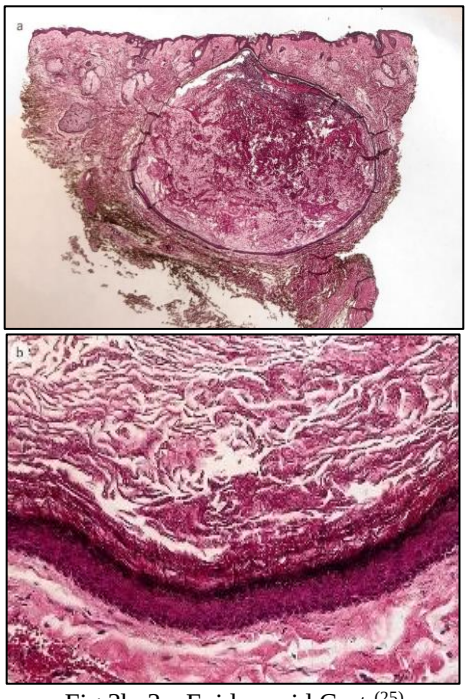

Fig 3b, 3c. Epidermoid Cyst.[25]

Microscopy. Cyst wall is of squamous epithelium with a granular layer, enclosing laminated keratin

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➢ *Bartholin's Duct Cyst*

Bartholin's glands are a pair of oval glands of average diameter of 0.5cm, each with a secretory duct of 2cm that leads to the posterior-lateral aspect of the vaginal orifice, between the hymen and the labia minora. They are situated in clock positions 4 and 8 (or 5 and 7) in the vaginal vestibule, and secrete mucus that lubricates the majora, the minora, and the vagina.

At the Federal Teaching Hospital Abakaliki (FETHA) Ebonyi State , Nigeria, researchers studied cases of Bartholin's cysts/abscesses over a 4-year period. Out of the 1015 gynaecological surgical cases seen during the period, 18 were Bartholin's gland cysts or abscesses, giving an incidence of 1.78%.[(26)] They concluded that symptomatic Bartholin's gland cyst and abscess cause significant morbidity for the sufferers and decreased quality of life.

In another study, spanning a period of ten years, out of 3,924 gynaecological surgical cases managed at Usman Dan Fodio University Teaching Hospital, Sokoto, 81 were Bartholin's gland cysts and abscess (19 were cysts and 62 were abscesses) giving prevalence of 2.02%.[(27)] They concluded that Bartholin's cysts are asymptomatic and usually ignored by patients until they become infected and produce symptoms.

Microscopically the gland consists of numerous alveoli, lined by cuboidal cells with intraluminal mucinous secretions. The duct is lined by cuboidal to transitional epithelia.

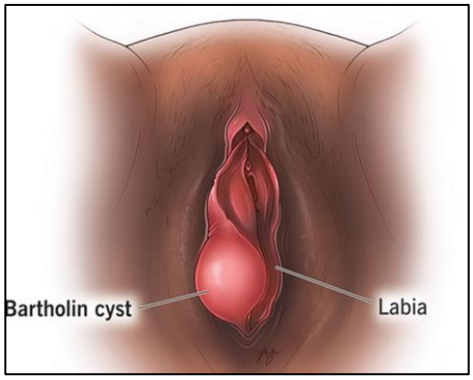

Fig 4a Bartholin's Duct Cyst. [(28)]

Gross appearance. Right labia minora mass

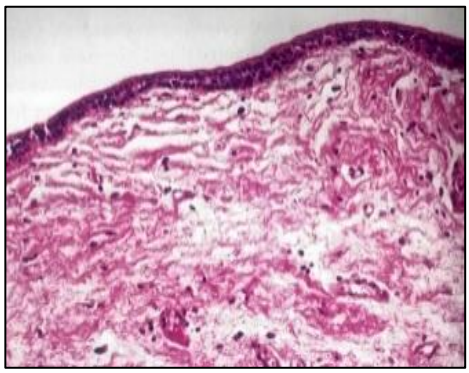

Fig 4b Bartolin's Duct Cyst [(29)]

Microscopy showing cyst lined by transitional-type epithelium

➢ *Mucinous Cyst*

Mucinous cysts are rare and benign, found more often in the elderly. They easily mimic other cysts macroscopically. However, microscopic ally, they have a single layer of simple mucinous epithelium.

Fig 5a. Mucinous Cyst [(30)]

Gross image of left labia majora with a non-reducible cystic mass

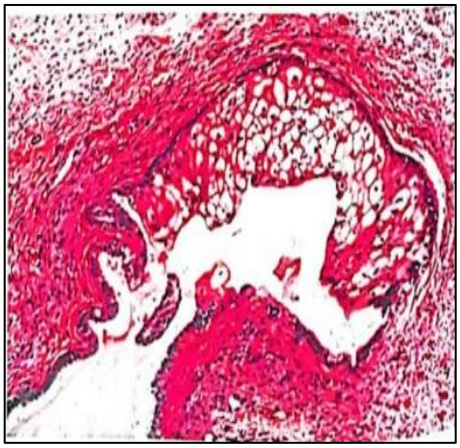

Fig 5b Mucinous Cyst [(31)]

Microscopy showing cystic space lined by simple mucus secreting cells

K Campbell et al had a 39-year-old lady with a massive mucinous vulvar cyst.[(11)] The indication for surgical incision was the large size, causing pressure symptoms. Although mucinous cysts are mostly asymptomatic, early diagnosis and surgical removal will prevent progression into a symptomatic lesion.

➢ *Hidradenoma*

Vulvar hidradenomas emanate from the sweat glands commonly of the apocrine variety, but occasionally grow from the eccrine glands. Clinically, they present as small

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sessile masses of not more than a centimeter in diameter and often found located in the medial wall of the labia majora. They are generally not symptomatic but may become painful following ulceration. The treatment is by surgical excision.[31]

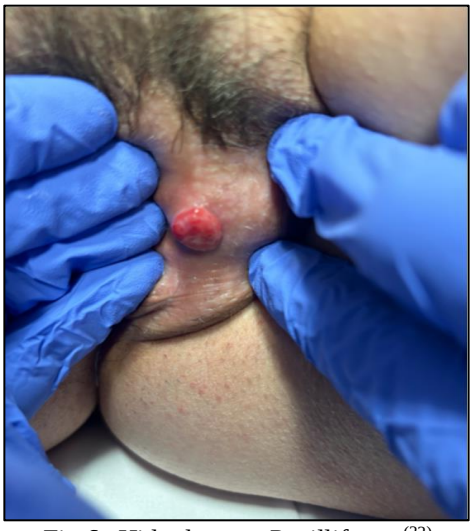

Fig 6a Hidradenoma Papilliferum[32]

Gross image. Lesion on the right labia majora

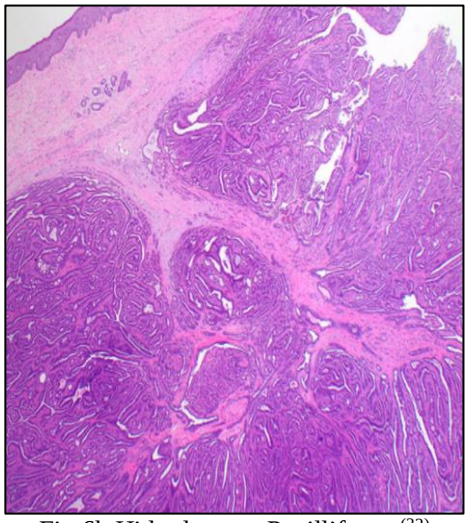

Fig 6b Hidradenoma Papilliferum[32]

Microscopy showing lesion with papillary epithelial proliferation.

➢ *Syringoma*

Vulvar syringomas grow from the sweat gland of the eccrine variety. They may present in multiple locations including other areas of the body. Typically, they are asymptomatic except for an occasional association with pruritus requiring treatment with steroids. George RT et al, reported a case of syringoma in a 45year old woman with severe pruritus vulvae causing sufficient distress to seek medical care.[34] Asha GS et al reported a case of syringoma in a 32-year-old female. The lesion was over her genitalia and below both lower eye lids, and of 2 years duration. Patient declined surgical excision, electrodessication, cryotherapy and CO_2 laser because it was asymptomatic. [35]

Fig 7a Syringoma [35]

Gross image. Multiple dome-shape papules over the labia majora.

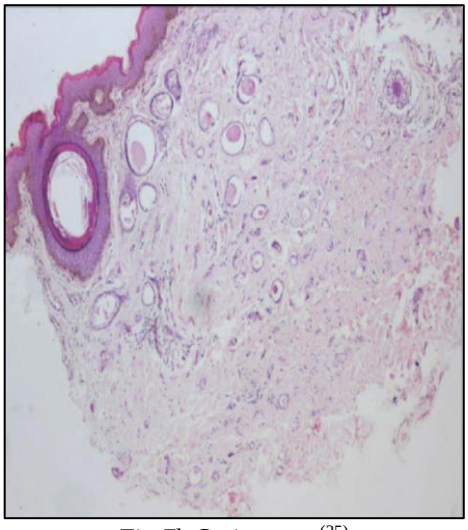

Fig 7b Syringoma [35]

Microscopy showing epidermis with hyperkeratosis.

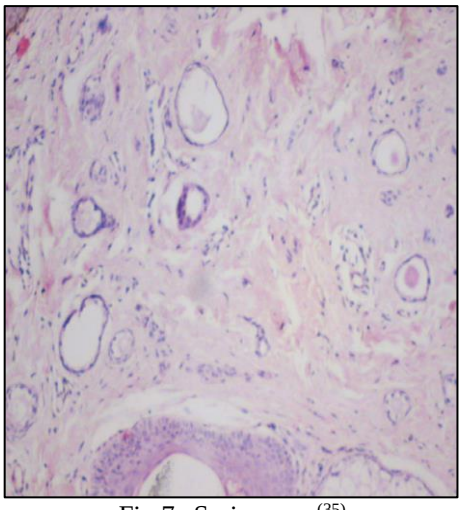

Fig 7c Syringoma [35]

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Microscopy showing dermis with multiple dermal structures

➢ *Fibroepithelial Polyp*

This is an epidermal vulvar growth which is thought to be influenced by the estrogen environment of the reproductive years, but the aetiology is not well defined as the condition has also been reported in a 68-year-old postmenopausal woman.[36] It presents commonly as a solid polypoid growth in the labia minora and often in association with other vulvar growths. It is commonly asymptomatic, but when it becomes larger, presenting with symptoms arising from the increasing size of the growth, the treatment is surgical excision.

Bahadar A et al reported a case of large painless polypoidal mass over the right labium in a 20-year-old.[37]. The mass was non-tender, non-pulsatile, and non-reducible. Treatment was by surgical excision. Histology confirmed the diagnosis of fibroepithelial polyp.

Fig 8a Fibroepithelial Polyp. [37]

Gross. Polyp with stalk from right labia majora 8b. Squamous epithelium overlying a polypoid mass with a hyalinised collagenous stroma.

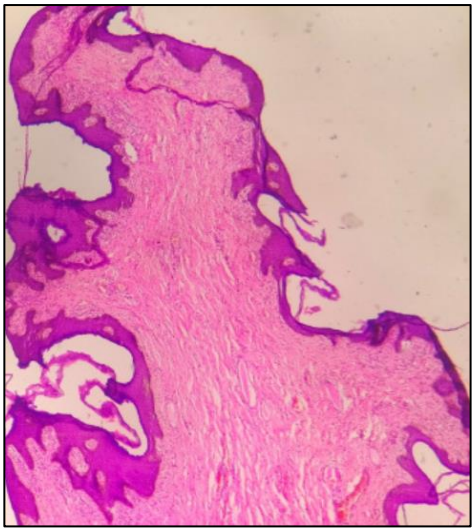

Fig 8b. Fibroepithelial Polyp. [37]

Microscopy. Squamous epithelium overlying a polypoid mass with a hyalinised collagenous stroma.

➢ *Infective Lesions*

Vulvar lesions caused by infectious agents include the condylomata lata caused by treponema pallidum, blisters of genital herpes and condylomata acuminata or genital warts which are caused by the human papillomavirus serotypes 6 and 11.[6]

Of all these, the genital warts are more persistent and quite distinct and easily recognized with the characteristic fluffy warty appearance. They can be treated with ablative agents like carbon dioxide laser or excised surgically.

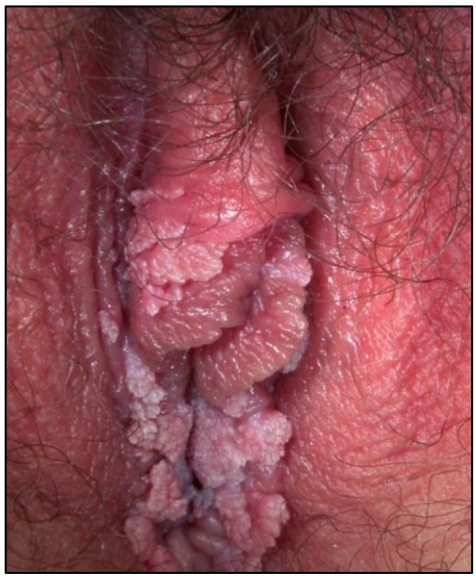

Fig 9a Condylomata Acuminata [38]

Gross image. Warty lesion on right labia majora

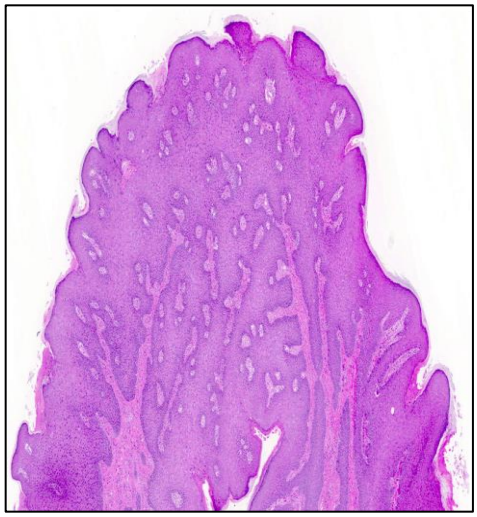

Fig 9b Condylomata Acuminata [39]

Microscopy showing acanthosis, papillomatosis, and basal fusion of broad papillae

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➢ *Pigmented Epidermal Lesions*

These include vulvar melanosis, lentigines and nevi. In vulvar melanosis, pigmented irregular macules appear on the vulva. The condition is benign and needs no treatment.(40) Microscopy shows hyperplasia of the melanocytes.

Fig. 10 Vulvar Melanosis. (41)

Hyperpigmentation less than 4mm is referred to as lentigo simplex. Larger lesions are termed vulvar melanosis.**(41)**

➢ *Mesodermal (Mesenchymal) Lesions*

Mesenchymal vulvar lesions include solid tumors like lipoma, leiomyoma, fibroma endometriosis all of which have been described from the specimens of vulvar excision surgeries. Their treatments are by excision as applicable with their occurrence in other parts of the body.

➢ *Leiomyoma*

Vulvar leiomyomas are rare tumors. They are reported to occur in the fourth and fifth decades of life.**(4)** Various histologic types have been described, which include spindled, epithelioid and myxoid neoplasms. Histologically, the differential diagnoses of vulvar leiomyoma include leiomyosarcoma, neurofibroma, dermatofibroma, and lipoleiomyoma.

Fig 11a Leiomyoma. (14)

Gross appearance after excision

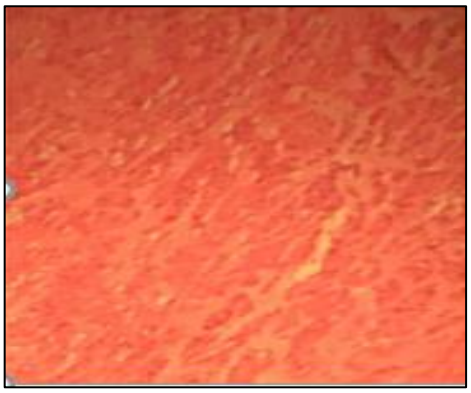

Fig 11b Leiomyoma (14)

Microscopy showing spindle shaped smooth muscle cells.

Leiomyoma and leiomyosarcoma have similar immunohistochemistry. Both stain positively for desmin, vimentin, and smooth muscle actin (SMA). They can be distinguished by using the criteria proposed by Nielson et al. (42)

According to Nielson et al, sarcomas are mostly more than 5cm in diameter, have up to and above 5 mitotic figures per 10 high power fields, exhibit cytologic atypia, and have unencapsulated, infiltrative borders. Neurofibromas differ from leiomyoma by being unencapsulated, having nerve sheath cells, fibroblasts, with the characteristic mast cells background, and showing areas of epidermal atrophy with indistinct rete ridges. Dermatofibroma shows proliferation of fibroblasts with thick mesh of collagen bundles, especially at the margins. Factor XIIIa stain is mostly positive for dermatofibroma. Lipoleiomyoma has a preponderance of adipocytes, in comparison with leiomyoma.

➢ *Vascular Lesions*

Vascular lesions occur in isolation as with capillary haemangioma or in association with other vulvar pathology. Hemangioma of the vulva is a benign lesion that can cause functional or emotional disability. Silva et al described the case of a 52-year-old female patient with a 3-year history of genital ulcer. She had undergone various treatments with creams and ointments. A diagnosis of vulvar haemangioma was eventually made from vulvar biopsy report and the lesion was surgically excised(43). Their report corroborates the diagnostic difficulty that can often be encountered with some vulvar lesions and the place of biopsy after a stepwise differential diagnosis is inconclusive.

Fig 12a Haemangioma (44)

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Gross appearance on left labia majora

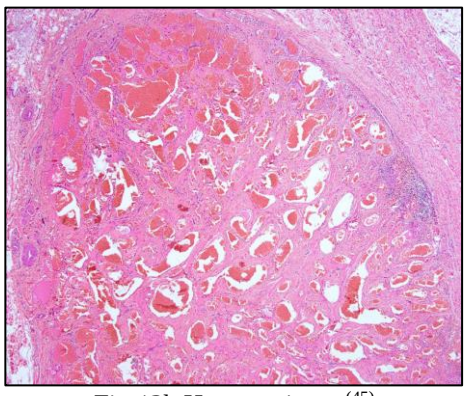

Fig 12b Haemangioma [45]

Microscopy showing numerous thin-wall vascular channels

➢ *Congenital Lesions*

Congenital vulvar lesions are cases of ambiguous genitalia and clitoromegaly which may make the assignment of the appropriate gender difficult, following the delivery of the infant. They may be due to congenital enzyme deficiency in the fetus (as in the case with congenital adrenal hyperplasia) or due to iatrogenic maternal exposure to androgen or its derivatives during pregnancy.

Another variety of vulvar lesion of congenital origin is the mucus cyst which arises from the remnant of the paramesonephric duct (the canal of Nuck from the processus vaginalis) which contains peritoneal fluid.[5]

➢ *Traumatic Lesions*

These often manifest as vulvar haematoma. Haematoma are more commonly the consequences of genital injuries at vaginal birth but it may occur in other genital injuries as non-obstetric events. Vulvar haematoma has been reported in a postmenopausal woman presenting with indistinct features and also as a vulvar swelling after intercourse.[15]

Generally, while the features of some vulvar lesions stand out clearly to permit "a spot diagnosis" others may be rigorous to determine, and the final diagnosis may not be made until after a histologic examination.

III. DISCUSSION

Benign vulvar lesions may not be as rare as clinicians may be tempted to believe.The true incidence may be unknown because the anatomic location of the organ can be a source of anxiety and reluctance about invasion of personal privacy and thus limit early and frequent presentation by the affected women[2]. Apart from common vulvar epithelial lesions that manifest with pruritus, the vulvar can also be the site of solid and cystic lesions easily recognizable in other organs of the body, but presenting diagnostic dilemma when they occur in the vulva[(4,5)]. Thus the need for histopathologic diagnostic workup when such symptoms present cannot be overemphasized.

An epidermal cyst of such nature has been reported where it was described as "a cyst in an unusual location" and presenting diagnostic difficulty because of such location[(25)]. A vulvar lesion may be of different structural composition. The lesion may be found to be composed of tissues of variable embryologic derivatives on histologic evaluation of the specimen,[(24)] which emphasis the place of a clinic-pathologic correlation in the management vulvar lesions.

In our literature review, vaginismus was reported as a complication of vulvar vestibulitis syndrome with the patient obtaining relief after local anaesthetic injection.[(23)]. Vaginismus is commonly seen as a "functional" sexual pain disorder which manifests as a recurrent difficulty in the woman allowing penile or a digital penetration of the vagina in spite of her wish or desire to do so. Because it evokes a sense of fear for vaginal penetration, there is the tendency to easily evaluate such patient's complaint along the line of psychological sexual dysfunction unless a thorough history of her vulvar health is included in such evaluation; thus this article recommends a need for open mindedness in the evaluation of such patient's presentation.

Similarly, a vulvar lesion can manifest with clinical presentation that can readily divert suspicion from the actual aetiology and may heighten anxiety about the possibility of a more "serious" diagnosis. In this article we cited a reported case of a "Vulvar haematoma masquerading as a Bartholin's duct cyst in a postmenopausal woman."[(15)] While Bartholin's duct cyst or any such pathology is relatively common in younger women of reproductive age group, the finding of such vulvar lesion in this sixty-six year old woman was a cause for concern and anxiety until the histology report of the biopsy specimen excluded malignancy. This again emphasizes the place of clinico-pathologic synergy in the evaluation of vulvar lesions.

Some of the authors of this article in another instance reported a case of leiomyoma arising from the Bartholin's gland as a vulvar tumor found in a young woman.[(14)] The gland was excised in whole as a definitive treatment for what was thought to be a recurrent cyst but the histology of the surgical specimen later reported a leiomyoma.

IV. CONCLUSION

Some lesions found in the vulva may consist of mixed tissue types, further contributing to the diversity of lesions observed in this region. The presence of such mixed structural compositions is indicative of the organ's unique developmental background.[24] The vulvar can be a location for lesions naturally expected to be domicile in some other organs of the female reproductive system.[14] It can be a source of anxiety when it presents as an unusual manifestation and in unusual site in some age group[15] and it can present a diagnostic challenge.[4] In all these, it is suggested that clinicians should have early resort to the synergy in a clinico-pathologic review so that no valuable time is wasted; a period that may be inadvertently allowed for the disease to fester.

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