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Original Research Article

Histopathological spectrum of vulvar lesions on a remote Indian Island

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ABSTRACT

Introduction: A wide spectrum of normal, benign, premalignant, and malignant lesions may occur on the vulva. Symptoms of vulvar disorders may be non-specific. Empiric treatment of vulvovaginal symptoms is common but usually not helpful. Though the varied clinical presentation and diverse histopathological spectrum of vulvar lesions have amazed Pathologists, only a few studies have been reported in the literature. The present study consists of a histopathological spectrum of vulvar lesions.
Objectives of the Study: 1.To evaluate the histopathological spectrum of vulvar lesions. 2. To compare the incidences of non-neoplastic and neoplastic lesions of the vulva.
Materials and Methods: Present study includes all types of vulvar lesion specimens received in the Department of pathology over a period of four years.
Result: All thirty-nine vulvar biopsies received in the Department of Pathology were studied for histomorphologic features. The lesions were categorized as non-neoplastic, neoplastic. The neoplastic ones were further divided into benign, malignant, and premalignant. The age of the women ranged from 15 to 69 years (mean 36.18±12.71) with the maximum number of patients between 30 to 40 years of age. Non neoplastic lesions were more common (22; 56.4%) than the (17; 43.6%) neoplastic lesions. There were 15(38.5%) benign lesions while 2 cases (5.13%) were malignant. Among the non-neoplastic lesions, Bartholin\'s duct cyst was the most common histopathologic diagnosis (35.9%). The fibroepithelial polyp was the most common benign neoplastic lesion constituting 15.3%.
Conclusion: In the present study nonneoplastic lesions were more common than neoplastic lesions. Among the neoplastic lesions, benign neoplasms were more frequent than malignant lesions.

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1. Introduction

A variety of vulval lesions are seen in daily clinical practice. Women with chronic vulvar disorders have symptoms for many years before an accurate diagnosis is made and effective treatment is started. Most of the vulval conditions are diagnosed clinically on the basis of history and physical examination only.[1] The histopathological examination of the lesion is often necessary in clinically suspicious malignant lesions, the lesions with diagnostic dilemma and those lesions not resolved treatment after standard. We aim to describe the histopathologic spectrum of vulval diseases and document the frequency of neoplastic lesions of vulva among females of a remote Indian island.

2. Materials and Methods

The present study is a retrospective study carried out in a newly established medical college on a remote Indian island. The studied population comprehended all thirty-

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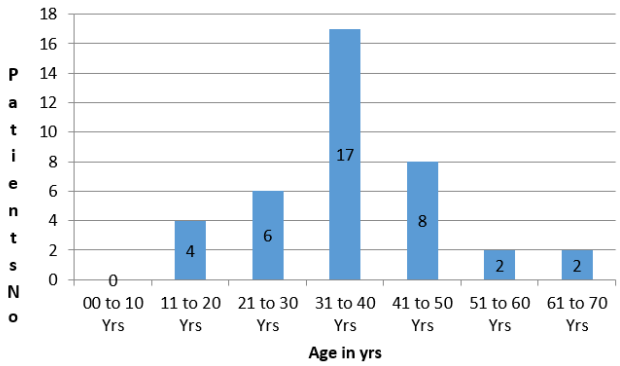
nine vulvar specimens received during the period of 2016 to 2019 with no exclusion criteria. The haematoxylin and eosin stained histopathological sections of vulvar biopsies received in the Pathology department were reevaluated and diagnosis was confirmed. The demographics and other relevant data were obtained from requisition forms, tabulated and analyzed in Microsoft Excel. This study was approved by the Institutional ethical committee.

3. Results

The age of the women ranged from 15 to 69 years (mean 36.18±12.71) with the maximum number of patients between 30 to 40 years of age. The age group distribution is shown in Graph 1.



Graph 1: Distribution of vulval pathology according to age group

Most common clinical presentation was swelling, nodularity. Itching and other rare presentations were white plaque, ulcer and discharge. Histopathological examination of thirty-nine vulval specimens showed spectrum of lesions as shown in Table 1.

There were 22(56.4%) non-neoplastic lesions while 17 cases (43.6%) were neoplastic. Amongst the non-neoplastic lesions, the most common histopathologic diagnosis was of Bartholin's cyst (14 cases; 35.89%). The next in frequency was of epidermal inclusion cyst (4; 10.26%). A diagnosis of lichen sclerosis et atrophicus was rendered in 2 cases (5.13%) where the biopsy revealed a band-like inflammatory infiltrate at the dermo-epidermal junction with atrophy of overlying epidermis. One case (2.56%) revealed nonspecific inflammation and was diagnosed as non-specific vulvitis. Sebaceous hyperplasia was noted in a 44 year female (2.56%) who presented with multiple asymptomatic small yellow papules. Microscopic examination of the lesion showed unremarkable epidermis and lobules composed of enlarged sebaceous glands around a centrally located sebaceous duct in the dermis. The cells were predominantly mature sebocytes having foamy, vacuolated cytoplasm and a central nucleolus with no atypical features (Figure 1).

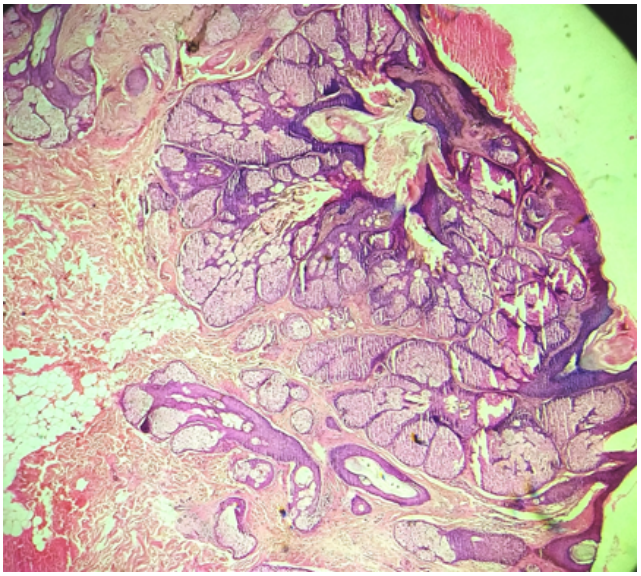


Fig. 1: Sebaceous Gland Hyperplasia Multiple, enlarged, Irregularly-arranged lobules of sebaceous glands (40X HE)

There were 15 (38.46%) benign neoplasms while only 2 cases (5.13%) were malignant. Among the benign neoplastic lesions, the most common tumor was fibroepithelial polyp in 6 cases (15.39%) followed by two cases (10.26%) of hidradenoma papilliferum. Microscopically, fibroepithelial polyps showed lesion with connective tissue stalk containing blood vessels and loose collagen covered by keratinized stratified squamous epithelium. Hidradenoma papilliferum on light microscopy showed a well circumscribed lesion composed of a cystic space containing papillary structures having delicate fibrovascular branching stalks. There were numerous tubules and acini lined by inner columnar epithelium with an outer compressed layer of myoepithelial cells.(Figure 2)

One case each of squamous papilloma, Condyloma acuminatum, haemangioma, lipoma, angiomyolipoma (Figure 3a,b), angiomyofibroblastoma and angiomyxoma was reported.

Angiomyofibroblastoma on microscopy revealed hypo and hypercellular edematous stroma with many thin walled blood vessels with plump, spindled and oval stromal cells around the blood vessels.(Figure 4)

Angiomyxoma on microscopy showed tumor composed of spindle and stellate–shaped cells in a myxoid matrix with many variable-sized thin-walled capillaries and thick-walled vascular channels.(Figure 5).

Among the neoplastic malignant lesions, one case (2.56%) showed Vulval intraepithelial Neoplasm III (VIN III) (Figure 6) while invasive Squamous cell carcinoma was seen in one case (2.56%).

Table 1: Histopathological spectrum of vulval lesions.

Non Neoplastic 22(56.4%)		**Neoplastic (n=17; 43.6%) Benign 14(38.46%)**		**Malignant & Premalignant and Borderline 2(7.69%)**	
Non-specific vulvitis	1(2.56%)	Condyloma acuminatum	1(2.56%)	VIN III	1(2.56%)
Lichen sclerosus atrophicus	2(5.13%)	Squamous papilloma	1(2.56%)	Squamous cell carcinoma	1(2.56%)
Sebaceous Hyperplasia	1(2.56%)	Hidradenoma papilliferum	2(5.13%)		
Bartholin's cyst	14(35.89%)	Fibroepithelial polyp	6(15.39%)		
Epidermal Inclusion Cyst	4(10.26%)	Lipoma	1(2.56%)		
		Hemangioma	1(2.56%)		
		Angiomyolipoma	1(2.56%)		
		Angiomyofibroblastoma	1 (2.56%)		
		Angiomyxoma	1 (2.56%)		

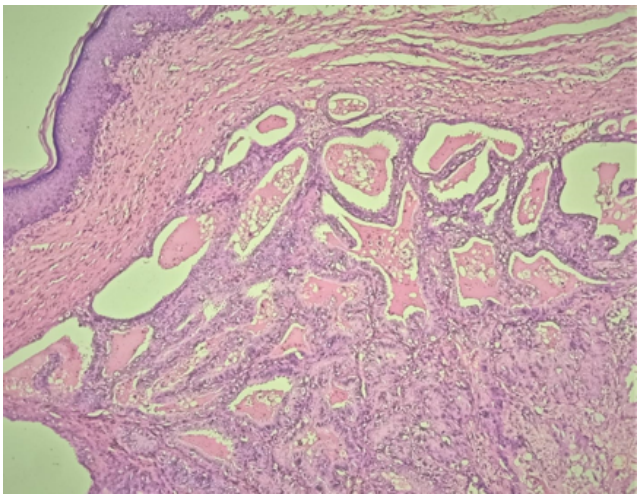


Fig. 2: Hidradenoma: papillae lined by double layer epithelium (40X; Hematoxylin & Eosin)

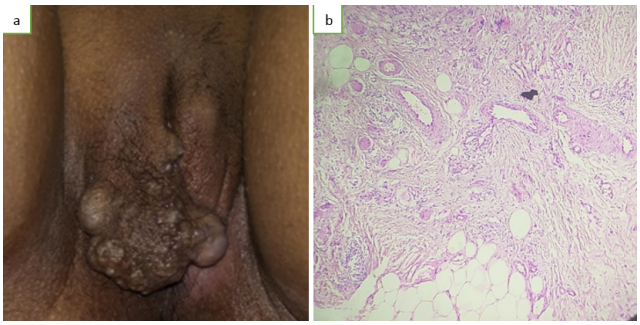


Fig. 3: Vulval growth involving labia majora and minora; b: Angiomyolipoma showing muscle fibers, blood vessels and adipose tissue. (40 X HE)

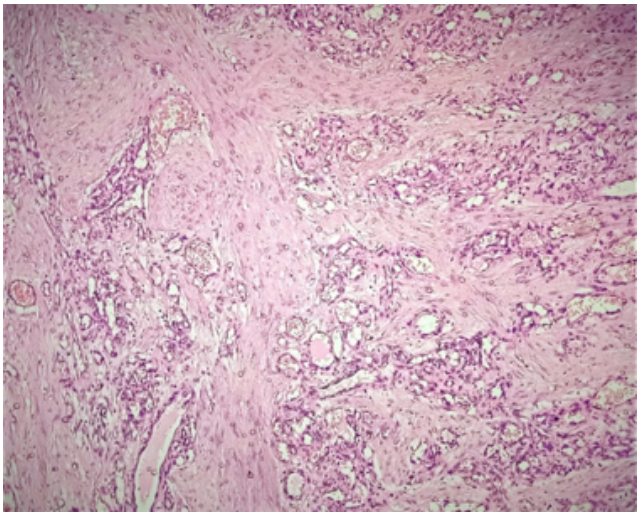


Fig. 4: Angiomyofibroblastoma showing hypo and hypercellular areas, vascular channels andspindle cells (40X; Hematoxylin & Eosin)

4. Discussion

Vulvar lesion is distressing for the patient and challenging for the clinician to treat. While some women are reluctant to address this sensitive issue with their physician, others – perhaps those with more severe symptoms may go from one doctor to another in search of effective treatment. The incidence of vulval skin disorders is not known. A community-based survey has estimated that 20% of women have vulval symptoms lasting more than 3 months during their lifetime.[2]

A wide variety of lesions occur on the vulva. The age range in our study varied from 18 to 63 years with maximum number (43.58%) between 31 to 40 years of age. in 3rd

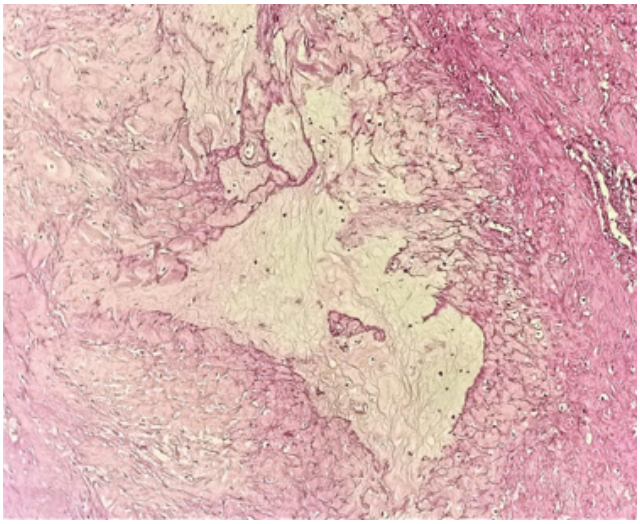


Fig. 5: Angiomyxoma showing myxoid matrix with thin-walled vascular channels (100X; Hematoxylin & Eosin)

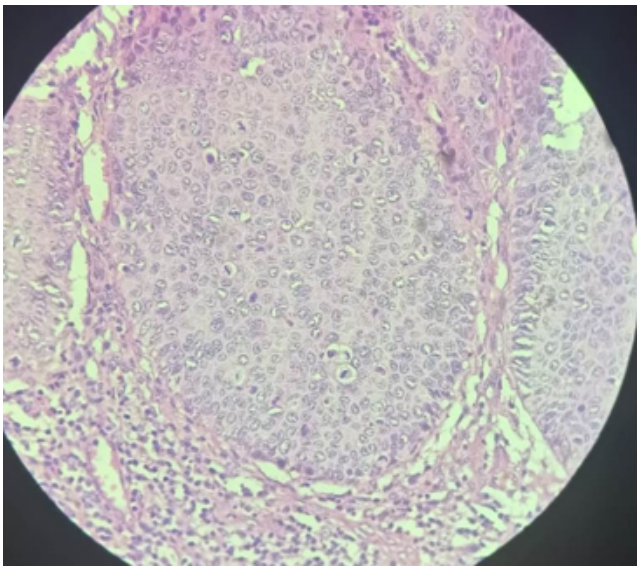


Fig. 6: VIN III: Complete disarray with nuclear pleomorphism (100X; Hematoxylin & Eosin)

decade as seen in other studies.[3] Most of the patients (38 to 46%) in other studies[4,5] were postmenopausal while in our study only 10.26% patients were post-menopausal.

Histological evaluation is must in establishing an accurate diagnosis as diagnostically different lesions may have similar gross characteristics. The non-neoplastic lesions were slightly more common than neoplastic lesions in present study which is somewhat similar to previous studies as shown in Table 2.

In present study, cystic lesions are more common amongst the non-neoplastic lesions. Bartholin's cysts were encountered in 14 cases accounting 35.89% while epidermal inclusion cyst accounted 10.26%. Bartholin's duct cyst is the most common cystic growth of the vulva.[8] Such high incidence of Bartholin's cyst is not reported by other studies. The incidence ranges from 1.5%[6] to maximum of 14.89%.[4] Bartholin's abscess results from an acute infection of the cyst or the gland. In our study we observed Bartholin's abscess in one case.

The vulval epidermoid cysts are seen rarely. They develop mostly as a result of implantation of superficial epidermal tissue into dermis or subcutaneous tissue following exposure to trauma or following episiotomy. Most vulval epidermoid cysts are localized on the clitoral region,[9] labia majora,[10] and very rarely seen in labia minora.[11] In the present study, all cases of epidermoid cysts were located in labia majora. One out of four patient had history of episiotomy 5yrs back while there was no history of trauma or any surgical intervention in other three cases. .

Lichen sclerosus was the most common non neoplastic lesion encountered in other studies.[3,4,7] In our study we had only two cases of lichen sclerosus seen in 40yrs and 66yrs old female. Lichen sclerosus has a bimodal distribution: pre-pubertal children and women with more advanced age.

We encountered one case of vulvar sebaceous gland hyperplasia (SGH) in a forty four year woman who presented with polypoid lesion involving left labium major. Sebaceous gland hyperplasia is a benign condition that originates in the sebaceous follicles and occurs most commonly on the forehead and cheek. Only a few cases of SGH are reported in the literature.[12,13]

Contrary to facial lesion of sebaceous hyperplasia, the vulvar lesions present in women of reproductive age and with variable clinical presentation from raised or elevated lesion to a large polypoid mass.[14] In our case the lesion was polypoid. Histopathologically, sebaceous hyperplasia is characterized as large, mature sebaceous lobules grouped around a central dilated duct, whereas Fordyce spots represent ectopic sebaceous glands without attached follicles. The histopathological differential diagnosis includes sebaceous adenoma and Sebaceous Carcinoma. Sebaceous adenoma has lobules with predominantly basaloid cells with interspersed mature sebaceocytes Sebaceous carcinoma is characterized by an infiltrative tumor composed of pleomorphic basaloid cells with focal sebaceous differentiation.

Benign tumours of the vulva are rare. They may be divided into those that are of epithelial origin (squamous and glandular) and those that originate from vulvar soft tissue (mesenchymal origin). In present study among the benign neoplastic lesions, the most common tumor was fibroepithelial polyp (15.39%) followed by two cases (10.26%) each of hidradenoma papilliferum and angiomyofibroblastoma. Other studies also reported FEP as the most common benign neoplasm.[4] The fibroepithelial

Table 2: Incidence of Neoplastic and non-neoplastic vulvar lesions

Author	Non neoplastic Lesions	Neoplastic lesions		
		Total	Benign	Premalignant and Malignant
Bhat DM[3]	50%	50%	26.47%	11.76%
Mohan H.[4]	55.29%	29.41%	15.88%	13.53%
Ozhan Ozdemir[6]	65.39%	34.60%	30.80%	3.80%
Gayatri Ravikumar[7]	69.6%	30.4%	11.27%	19.12%
Present Study	56.4%	43.6%	38.46%	5.13%

polyps (FEPs), which are also referred to as acrochordons or skin tags, are common lesions that typically occur in adults, especially obese women. They show a predilection for the neck, axillae, and groin and are rare in vulva .Vulval fibroepithelial polyp usually do not grow larger than 5 cm in diameter though few cases of giant vulval fibroepithelial polyp are reported.[15]

We came across one case of angiomyofibroblastoma in our study. Angiomyofibroblastoma (AMFB) of the vulva was first described by Fletcher et al. in 1992.[16] It is a rare, benign mesenchymal tumor that occurs in the subcutaneous tissue of the vulva of middle-aged women. Most of these tumors are grossly well circumscribed, homogeneous, tan to gray, rubbery in consistency and range in size from 0.5 to 1 cm. Angiomyofibroblastoma microscopically show alternating hypocellular and hypercellular areas having entrapped scattered capillary sized blood vessels admixed with spindled stromal cells. The stromal cells have a tendency for perivascular clustering. Their nuclei showed minimal atypia with sparse to absent mitotic figures. Multinucleated giant cells, plasmacytoid and epithelioid cells are also seen. It should be differentiated from similar lesion like aggressive angiomyxoma because of its different biological behaviour. Aggressive angiomyxoma typically present as large deep-seated masses with a "pushing" infiltrative border with entrapment of mucosal glands and nerves. The stromal cells are short spindle or stellate shaped within a loose myxoid matrix. Angiomyxoma have medium- to large-sized vessels with a muscularised, thick, and hyalinised wall whereas, the blood vessels of AMFB are thin-walled, venular or capillary-sized. Very few cases of angiomyofibroblastoma of vulva are reported in literature.[17] In our two year study we reported a single case of angiomyxoma in 34yrs old female The lesion was measuring 3.5x3 cm in. The diagnosis was provided on light microscopy after excluding differential diagnosis of myxolipoma, myxoid neurofibroma, and leiomyoma with myxoid change. Most of Aggressive angiomyxoma tends to locally recur in about 30%. In two yrs follow up our patient did not show any evidence of recurrence. On immunohistochemistry most of tumour cells are Desmin Positive and also express CD34 and factor XIIIa. The expression of both estrogen and progesterone receptors by tumour cells suggest hormone dependency.

Hidradenoma papilliferum, a benign neoplasm thought to be either of apocrine sweat gland or anogenital mammary-like gland origin, occasionally occurs on the vulva or perineum. It may be confused with adenocarcinoma by clinicians due to its tendency to ulcerate. On histopathological examination may mimic adenocarcinoma due to the closely packed glands. The characteristic two-cell layer seen on histology distinguishes it from malignancy. In our study we found two cases of Hidradenoma papilliferum accounting for 5.13% of total cases. Reported incidence of Hidradenoma papilliferum in other studies[3,4] ranges from 1,3% to 8.82%.

Other benign tumours in our study included each case (2.56%) of Condyloma accuminata, squamous papilloma, angiomyolipoma, Lipoma and haemangioma. Martignoni[18] first described an 'angiomyolipoma' involving the kidney in the year 1951.An angiomyolipoma is a non-malignant tumour that contains fat tissue, smooth muscle cells and blood vessels; the proportion of each component may be variable. Secondary to the kidney, the liver is the next common site of occurrence of angiomyolipoma. Cases have been reported involving other sites such as mediastinum, fallopian tubes, oral cavity and skin; hardly a few cases of vulval angiomyolipoma have been reported.[19,20]

Amongst two malignant neoplasms in our study, one (2.56%) was Vulvar Intraepithelial Neoplasm (VIN III) and another (2.56%) was well differentiated invasive squamous cell carcinoma. Vulvar intraepithelial neoplasia (VIN) is a high-grade intraepithelial precursor of invasive squamous cell carcinoma. Two different types of VIN have been defined: the common human papilloma virus (HPV) related type and the differentiated non-HPV-related type, the latter being associated with vulvar dermatoses, especially lichen sclerosus.[21] HPV-related VIN is the predominant clinical lesion (95%) with the highest frequency among younger women aged 20–35 years whereas the differentiated type of VIN (2–5%) most commonly occurs in elderly women.[22] These lesions clinically present as erythematous patches, or verruciform or even pigmented plaques. The number of cases reported in various series of vulvar lesions ranges from 1.9%[6] to 22.22%.[4]

Approximately 95% of malignant tumours of the vulva are squamous cell carcinoma (SCC), however only representing 5–10% of all gynecological cancers.[23] Chronic vulvar HPV infection with one or more of the oncogenic HPV types is involved in half of the cases of SCC, whereas lichen sclerosus and to a lesser degree other chronic dermatoses, such as lichen planus, are predisposing factors in the non-HPV-related cases. The frequency of oncogenic HPV associated vulvar squamous cell carcinoma is different between young and older women. HPV, usually type 16, is reported in less than one fifth of vulvar carcinomas in older women (mean age 77 years), whereas approximately four fifths of the vulvar squamous carcinomas identified in younger women (mean age 50 years) are HPV associated. The histopathologic type of invasive carcinoma also differs. In the older women vulvar squamous cell carcinomas are usually well differentiated and highly keratinized. In younger women, the tumors are usually warty or basaloid carcinomas. The female with SCC in our study was 65 yrs old and showed well differentiated keratinising squamous cell carcinoma. HPV screening was not done in the present case.

5. Conclusion

A variety of lesions occur in vulva ranging from inflammatory lesions to benign and malignant neoplasms. However, correct and rapid diagnosis often requires biopsy and histopathological examination in order to differentiate. In present study nonneoplastic lesions were more common than the neoplastic lesions. Among the neoplastic lesions, benign neoplasms were more frequent than the malignant lesions. Weaknesses of this study relate to its pool of patients, short duration of study and less number of cases. Also, being hospital study the statistics included in the study may not be representative of the general population.

6. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

7. Source of Funding

None.

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