Spectrum of vulvar lesions: patient’s anxiety, clinician’s concern and pathologist’s diagnostic challenge

Dharitri M. Bhat, Vrushali A. Mahajan*, Dinkar T. Kumbhalkar, Waman K. Raut

Department of Pathology, Government Medical College, Nagpur, Maharashtra, India

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*Correspondence:
Dr. Vrushali A. Mahajan,
E-mail: drvrushi.mahajan@gmail.com

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ABSTRACT

Background: A wide variety of inflammatory, premalignant and malignant lesions can occur on the vulva. Some of the lesions are limited to the vulva, while some also involve other parts of the body. Although vulvar diseases can cause a significant issue in the patients, they are less commonly discussed than those of cervix, uterus and ovary. Most of the asymptomatic lesions remain un-noticed, and are seen during routine gynecological checkups. Common complaints in symptomatic lesions are lumps, discomfort, itching and pain. Since the symptoms are nonspecific; determining the location of the lesion can assist with the diagnosis. Being a genital part with skin covering on outer aspect and mucosal lining inside, it is associated with various dermatological, nutritional, and hormonal as well as sexually transmitted diseases. The present study thus was conducted to categorize vulvar lesions based on their histological diagnosis and also to study the morphological spectrum of precursor lesions for malignancy.

Methods: Present study includes all types of vulvar lesions sent for pathological study in the Department of pathology, at GMC Nagpur over the period of one year.

Results: Total 34 lesions were studied including a wide diagnostic range from inflammatory, dermatological to benign, premalignant and malignant. Inflammatory lesions including various infections and LSA (Lichen sclerosus atrophicus) were the most commonly seen lesions along with collection of neoplastic lesions.

Conclusions: Proper diagnostic categorization of the lesions is essential for initiating therapy and reducing patient’s anxiety. Morphology of these lesions along with their diagnostic significance is discussed.

Keywords: Human papilloma virus, Lichen sclerosus atrophicus, Vulvar lesions, Vulvar intraepithelial neoplasia, Vulvar amoebic ulcer

INTRODUCTION

A wide variety of lesions occur on the vulva. Some of the disorders causing these lesions are limited to the vulva; while others also involve skin or mucocutaneous membranes elsewhere on the body. The vulva is sensitive to both physiologic and pathologic changes, as well as to the sex hormones. Hence in addition to hormone related changes, vulvar skin is known to show various dermatological manifestations, sexually transmitted diseases, precursor lesions and malignancies. There is virtually no form of dermatitis that has not been reported to involve the vulva. Classification of inflammatory dermatoses of the vulva uses the same terminology applied to dermatoses affecting nonvulvar skin. Lichen Sclerosus (LS) is a common chronic inflammatory dermatosis that frequently involves the vulva and can cause considerable tissue destruction. It is occasionally associated with vulvar intraepithelial neoplasia (VIN) of the differentiated type and invasive squamous cell carcinoma. Apart from these lesions, variety of cystic lesions and benign tumors also occur.
commonly on vulva. They may present as nodular masses or may remain asymptomatic. The complexity of vulvar diseases stresses the necessity of a multidisciplinary approach for the study of these lesions.² Some of these lesions may be asymptomatic and others may show significant symptoms with overlapping clinical features. They may cause discomfort in the patient at the same time may be challenging for the clinician. Although pertinent clinical history, physical examination and diagnostic tests help to narrow down the diagnosis in most of the cases, biopsy is often needed in cases where a diagnosis cannot be made confidently on visual inspection and by non-invasive methods or if the lesion dose not resolve after standard therapy.³ The incidence of vulvar squamous cell carcinoma (SC C), the most common vulvar cancer in women, is increasing worldwide.⁴ Growing evidence has established two major types of vulvar intraepithelial neoplasia (VIN), which correspond to two distinct oncogenic pathways to vulvar squamous cell carcinoma (VSCC). Despite the increasing prevalence, this disease is commonly misdiagnosed by physicians. Unfortunately, late-stage vulvar SCC has a poorer prognosis compared with early vulvar neoplasia and requires aggressive therapy such as radical surgical intervention. Therefore, early diagnosis by physicians is critical to reduce both the mortality and morbidity rates of vulvar SCC.⁵

METHODS

The present study is a descriptive observational study carried out in a tertiary care centre of Central India over a period of one year (January 2017 to December 2017). It includes samples from vulvar lesions of total 34 patients; sent for pathological examination from surgery/gynecology or dermatology departments to the department of pathology. The patient’s clinical data including age, chief complaints, general physical and local examination, relevant other investigations and various clinical differential diagnoses were also noted. The types of specimens received were scrape smears, punch biopsy of vulvar lesions, and excisional biopsies. The scrape smears (3) from ulcers were processed with various cytological stains including Hematoxylin and Eosin, PAP and Giemsa. The biopsy samples (33) were processed routinely and Hematoxylin and Eosin staining was performed on formalin fixed paraffin embedded tissue. Special histochemical stains were performed wherever indicated. The informed consent was taken from each patient before taking clinical photographs and other procedures. The identity of the patients was not revealed anywhere.

RESULTS

The study included total 34 patients with vulvar lesions. The patient’s age ranged from 18 to 63 years with peak incidence in 3rd decade of life (11 cases, 32.35%). Most common presenting complaints were itching and/or papule, patch over vulva. Other symptoms were nodular and warty growth, ulcer, pain, pigmented lesions, and vulvar discomfort. Involvement of labia majora was more frequent than minora, although in few cases both were involved. Out of the total 34 cases included in the study, 50% (17 cases) were of Non neoplastic category and the rest were Neoplastic and Precursor category including benign and malignant neoplasms as well as Vulval intraepithelial lesions. The non-neoplastic group was further subdivided into infectious and non-infectious inflammatory lesions and a miscellaneous category (Table 1 and Figure 1).

A spectrum of lesions was observed ranging from infections to malignancy. Viral lesions amongst the infective category were Condyloma Accuminatum (2 cases) presenting as warty polypoidal lesion near vaginal introitus [Figure 2(A)], Molluscum Contagiosum (2 cases) presenting as typical umbilicated pearly white nodules [Figure 2(B)] and one superficial ulcerative lesion (Herpetic ulcer) over labia majora in immunocompromised patient [Figure 2(C)]. Other infective lesion was very unusual; presenting as large destructive, foul smelling ulcer involving both majora and minora which was diagnosed as Amoebic ulcer.

Commonest non-infective condition seen in the study was Lichen Sclerosus Atrophicus (8 cases) accounting for 23.52% of the total. These patients were most commonly perimenopausal to post-menopausal with vulvar discomfort or itching and dysuria. Clinical examination revealed typical wrinkled whitish patch to plaque like lesion. Two cases of Hidradenitis Suppuritiva were detected which presented with painful reddish nodular swelling over labia majora. A single case of Bartholin cyst was diagnosed in a young female who presented with nodular cystic swelling in post-erolateral aspect of vaginal introitus. It was categorized in miscellaneous group.

Amongst the benign neoplastic category, we found tumours like Hidradenoma Papilliferum (3 cases), Aggressive Angiomyxoma (2 cases), Angiokeratoma (2

Figure 1: Distribution of vulvar lesions.

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>18%</td>
</tr>
<tr>
<td>Noninfectious inflammatory</td>
<td>29%</td>
</tr>
<tr>
<td>Benign tumors</td>
<td>26%</td>
</tr>
<tr>
<td>Precursor lesion</td>
<td>12%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>3%</td>
</tr>
</tbody>
</table>
cases) and one case each of Angiomyofibroblastoma and Lipoma. Hidradenoma Papilliferum presented with well circumscribed nodular mass in or around the interlabial sulcus. Cases of aggressive Angiomyxomas, Angiomyofibroblastoma and Lipoma [Figure 2(D)] presented with nodular painless masses of variable size and consistency. Two cases of Angiokeratoma was part of the study. The lesions were raised, papular to nodular, reddish blue in color with mild itching on labia majora. Histopathology was diagnostic in all these lesions.

Four cases of vulvar Intraepithelial Neoplasia (VIN) were seen of which one case was of VIN I and 3 cases of VIN III. In the first case patient was 35 years asymptomatic female in whom thickened plaque over vulva was noticed on routine screening. Simultaneous Pap smear showed features of LSIL. Biopsy from the vulvar plaque was taken, and showed features of VIN I. Amongst the VIN III group; we had a case of 26 years old ICH (immunocompromised host) female who presented with multiple small pigmented maculopapular lesions over vulva [Figure 2(E)] which on biopsy turned out to be Bowenoid papulosis. Thickening and pigmentation of both labia [Figure 2(F)] was noted in a 45 years female which on histopathology were diagnosed as Bowen’s disease.

### Table 1: Distribution of vulvar lesions.

<table>
<thead>
<tr>
<th>Distribution of vulvar lesions</th>
<th>Number of cases</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonneoplastic conditions (a+b)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Inflammatory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1 Infections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Human papilloma virus (condyloma accuminatum)</td>
<td>02</td>
<td>06</td>
<td>17.64%</td>
</tr>
<tr>
<td>2. Molluscum contagiosum</td>
<td>02</td>
<td>02</td>
<td>5.88%</td>
</tr>
<tr>
<td>3. Herpes simplex virus</td>
<td>01</td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td>4. Entamoeba histolytica</td>
<td>01</td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td>A2 Non infectious</td>
<td></td>
<td>10</td>
<td>29.41%</td>
</tr>
<tr>
<td>1. Lichen sclerosus atrophicus</td>
<td>08</td>
<td>08</td>
<td>23.52%</td>
</tr>
<tr>
<td>2. Hidradenitis suppuritiva</td>
<td>02</td>
<td>02</td>
<td>5.88%</td>
</tr>
<tr>
<td>B. Miscellaneous</td>
<td></td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td>1. Bartholin cyst</td>
<td>01</td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td><strong>Neoplastic and precursor conditions (C+D+E)</strong></td>
<td></td>
<td>17</td>
<td>50%</td>
</tr>
<tr>
<td>C. Benign tumors</td>
<td></td>
<td>09</td>
<td>26.47%</td>
</tr>
<tr>
<td>1. Hidradenoma papilliferum</td>
<td>03</td>
<td>03</td>
<td>8.82%</td>
</tr>
<tr>
<td>2. Aggressive angiomyxoma</td>
<td>02</td>
<td>02</td>
<td>5.88%</td>
</tr>
<tr>
<td>3. Angiokeratoma</td>
<td>02</td>
<td>02</td>
<td>5.88%</td>
</tr>
<tr>
<td>4. Angiomyofibroblastoma</td>
<td>01</td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td>5. Lipoma</td>
<td>01</td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td>D. Precursor lesions</td>
<td></td>
<td>04</td>
<td>11.76%</td>
</tr>
<tr>
<td>1. VIN 1 (vulval intraepithelial neoplasia 1)</td>
<td>01</td>
<td>01</td>
<td>2.94%</td>
</tr>
<tr>
<td>2. VIN3 (including 01 case each of Bowens disease and Bowenoid Papulosis)</td>
<td>03</td>
<td>03</td>
<td>8.82%</td>
</tr>
<tr>
<td>E. Malignant tumors</td>
<td></td>
<td>04</td>
<td>11.76%</td>
</tr>
<tr>
<td>1. Squamous cell carcinoma</td>
<td>02</td>
<td>02</td>
<td>5.88%</td>
</tr>
<tr>
<td>2. Spread of squamous cell carcinoma from cervix</td>
<td>02</td>
<td>02</td>
<td>5.88%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>

Primary squamous cell carcinoma of vulva was diagnosed in two premenopausal cases (50 and 47 years). One presented with an ulceroproliferative growth of 3 x 3 cm size over vulva with blood stained discharge. Second patient had an ulcerative growth of size 4x 3 cm over right side of vulva with necrosis and slough at the base of ulcer. Cervix and vagina were normal. Inguinal lymph node on the same side was enlarged. Histologically both of them were keratinizing squamous cell carcinomas (KSCC). The inguinal lymph node FNAC showed metastasis of KSCC. Another case was of a 42 years female who was operated for carcinoma.
cervix; on radiotherapy and presented with ulcer over vulva. Scrape smears from the ulcer showed diagnostic malignant keratinized squamous cells confirmed later on biopsy. In one case a 48 year old female presented with bleeding per vagina for 3 months. On examination there was a large cauliflower like growth over cervix involving vagina and extending over medial aspect of vulva more on left side. Biopsy from the vulvar extension confirmed SCC.

A: Condyloma Accuminatum- Polypoidal lesion near the vaginal introitus (pointed by arrow); B: Molluscum Contagiosum- Multiple, discrete, pearly white, nodules over vulva; C: HSV ulcers- Large superficial ulcer over vulva which is slightly covered with slough; D: Lipoma- Pedunculated skin covered nodule in the right vulva; E: Bowenoid Papulosis- Multiple small pigmented maculopapular lesions over vulva; F: Bowen’s Disease- Thickening of both labia majora and minora with irregular and warty surface.

Figure 2: Clinical features of various vulvar lesions.

A: Condyloma Accuminatum (10X)- Microphotograph showing hyperplastic epithelium with presence of koilocytes; B: Molluscum Contagiosum (10 X)- Microphotograph showing classic Henderson Peterson bodies in the epithelium; C: Scrape smears from HSV infection (40X) (PAP stain) Microphotograph showing typical nuclear changes with nucleomegaly, nuclear inclusions and overlapping in squamous cells. [Inset- Multinucleation in squamous cells]; D: Scrape smears from Entamoeba histolytica infection (100 X)- Microphotograph showing Trophozoites of the organisms. [Inset- PAS positivity for the organisms]; E: Lichen Sclerosus atrophicus (10X)- Microphotograph showing atrophic epithelium with flattening of the rete ridges and loss of adnexal structures; F: Hidradenitis suppuritiva (10X)-Microphotograph showing dense inflammatory infiltrate in the dermis surrounding the adnexal glands.

Figure 3: Microphotographs (All H and E stain) of various vulvar pathological lesions.
Figure 4: Microphotographs (All H and E) of various vulvar pathological lesions.

DISCUSSION

Vulvar lesions not only cause anxiety in the patients, but are often a matter of concern for the treating clinicians due to overlapping clinical features. They are a diagnostic challenge for the pathologists. Commonest symptom in these lesions is vulvar itching; however, other symptoms like pain, swelling, bulge or mass may be seen depending on the lesions.8 Association of certain precursor lesions with malignancy and other overlapping clinical features in these lesions make biopsy mandatory for final diagnosis to decide therapeutic approach, especially in dermatoses and suspected cases of VIN.9 Punch biopsy after clinical local examination and selection of proper site is indicated in dermatoses.10 For other lesions like mass or localized lesions with bulge, excision of the mass is preferred. Tying SK mentions use of toluidine blue for selection of dysplastic tissue similar to cervix.6 In our study, 3 samples were scrape smears due to ulcerative nature of the lesions 14 were punch biopsies and 19 were excision biopsies as per the type of the lesion.

The age range in our study varied from 18 to 63 years with peak incidence in 3rd decade. A significant number of postmenopausal patients were also seen in our study.13 On categorization, we found that (17/34) 50% of the lesions were non-neoplastic. In this, 06 cases belonged to infectious lesions as against 10 non-infectious and one miscellaneous lesion. Viral infections were the most common type. Two cases of condyloma were noted which showed typical nodular warty growth (Figure 2A), both were excised completely. Microscopy showed typical hyperplastic epithelium with presence of koilocytes. Dysplastic changes were limited to lower third of the epithelium only [Figure 3(A)]. One case of clinically suspected molluscum contagiosum [Figure 2(B)] showed classic Henderson Peterson bodies histologically [Figure 3(B)]. A known immuno-compromised patient on ART (Anti retroviral therapy) for 6 years had a large nonhealing ulcer over vulva extending posteriorly towards perianal region [Figure 2(C)]. Scrape smears from this ulcer showed dense inflammatory exudate and few epithelial cells with viral cytopathic effect such as multinucleation, nucleomegaly and ground glassing [Figure 3(C)]. This was labeled as herpetic ulcer in view of cytologic findings in the given clinical setting. Herpes simplex virus infection is quiet common cause of genital ulcer.11 Another ulcerative lesion was a very unusual case where patient presented with large destructive ulcer involving labia and extending into vagina interiorly and perineal region exteriorly. She had a foul smelling, blood stained discharge and was emaciated although she was seronegative. Scrape smears showed only necrotic material, nuclear debris and dense exudate along with...
few large structures resembling histiocytes. On suspicion of trophozoite forms of amoeba, PAS staining was done [Figure 3(D)] and later they were confirmed on biopsy. This patient showed dramatic improvement to antiamoebic treatment with almost disappearance of the ulcers with good healing within a month. Although amoebic infestation is not uncommon in India, usually the lesions are limited to colon and liver. In western countries, amoebic infestation is a marker of immunosuppression. Lack of health education, poverty and poor genital hygiene predisposes to this infection in India. Morphological identification of amoeba trophozoites is the diagnostic feature as in this case. Presence of erythrophagocytosis in the trophozoites resembling histiocytes was the clue to diagnosis as in present case.

Amongst non-infectious lesions LSA was the most common (8/10= 23.52%). Similar to other studies its predominance was seen in older age group. O’keefe RJ el al found 25% of lichen sclerosus in their study of non neoplastic vulvar lesions whereas another study of histopathological review and classification of vulvar dermatoses showed 38.8% cases of lichen sclerosus. Here they found wiry collagen with lymphocyte entrapment in early LS. Zoon’s vulvitis was the most common differential diagnosis. Although we did not encounter with any such differential diagnosis, most of them showed typical atrophic epithelium with flattening of the rete ridges [Figure 3(E)]. Loss of adnexa was a common feature. Only single case showed dermal edema. Few cases showed sparse lymphocytic infiltration in superficial dermis. Growing evidence has established increased association of vulval Intraepithelial Neoplasia in association with lichen sclerosus. Biopsies in cases of lichen sclerosus are useful for confirmation of clinical diagnosis and to exclude early invasive malignancy.

Two cases of hidradenitis suppurativa were found in our study. Both patients were in 3rd decade. One patient had recurrent painful nodular swelling, while another showed reddened nodule. Advanced suppurative hidradenitis resulting from chronic, progressive, inflammatory involvement of apocrine sweat glands often fails to respond to conservative treatment and necessitates the need of histological diagnosis as in these cases [Figure 3(F)].

A single case of Bartholin cyst was included in miscellaneous category which presented as a firm tender mass over labia majora. On excision it was a fluid filled cyst lined by squamo-transitional epithelium. Few acute inflammatory cells were also seen. The lining epithelium may vary from squamous to mucinous columnar or transitional. Secondary infection may result in abscess formation. Harsh Mohan et al mentioned 27 cases of cystic lesions in their 5 year study on vulvar lesions, which included developmental to infective and non-specific cystic lesions too.

Amongst the neoplastic category, 9 benign neoplasms were seen (Table 1). The most common lesion was Hidradenoma Papilliforma. All were small nodular swellings showing a well circumscribed lesion composed of a cystic space containing papillary structures having delicate fibrovascular branching stalk. Scanner view of Hidradenoma Papilliferum is usually quiet characteristic. On higher magnification, two layered epithelium of outer myoepithelial and inner tubular were quiet diagnostic. The typical presentation of a dome shaped nodule, the classic location and the characteristic diagnostic features usually help in reaching out at the diagnosis. Harsh Mohan et al in their study found 3 cases of Hidradenoma Papilliferum with no diagnostic problem.

Other benign tumors in our study included 2 cases each of Aggressive Angiomyxoma and Angiokeratoma. Aggressive Angiomyxomas were seen as soft, bulky tumors in young patients. One of it was larger measuring approximately 8x6x5cm, polypoidal in shape with stretched overlying skin; whereas in the other case it measured 4x4x3 cm. Microscopy showed spindle to stellate cells embedded in loose myxoid vascular stroma with prominent thin walled capillaries [Figure 4(A)]. Mild nuclear pleomorphism and occasional nucleoli were seen. Myxoid stroma was highlighted by mucin stains. The term aggressive denotes high chances of local recurrence, hence wide local excision is essential.

Angiokeratoma is seen as multiple purple to dark red lesions on labia majora. In one patient, both sides were involved. Although the clinical appearance is quite characteristic, sometimes it can clinically mimic genital warts. Biopsy is essential for confirmation as it is known to be associated with Fabry’s disease. Microscopy showed hyperkeratotic epithelium with variable acanthosis, papillomatosis and dilated endothelial lined spaces separated by strands and cords of squamous epithelial downgrowth [Figure 4(B)].

We found a single case of Angiomyofibroblastoma. It presented as a well circumscribed nodule over right labia minora. Clinically this tumor is known to be confused with Bartholin cyst, leiomyoma or other benign tumours. It was grossly well circumcised, pink to red in color, firm in consistency and microscopy showed hypo and hypercellular areas of vascular, edematous stroma. Clustering of spindle tumor cells around blood vessels is peculiar of this tumor which helps to differentiate this from aggressive angiomyxoma, its differential diagnosis on histology [Figure 4(C)]. The tumor cells also show immunoreactivity for estrogen and progesterone receptors and vimentin. Other features that differentiate this tumor from aggressive angiomyxoma are poor circumscription, presence of occasional giant and atypical cells and myxoid stromal change in the later. We did not find any case of neurofibroma, leiomyoma, hemangioma and fibroepithelial polyp.

Vulva is a rare location for lipoma, however, when suspected, it needs to be differentiated from other fat.
containing tumors of the vulva including liposarcoma. Although rare, it occurs in the age group of 40 to 60 years. It usually presents as painless soft tissue mass [Figure 2(D)] which show typical well encapsulated tumor showing mature adipose tissue. Imaging modalities like ultrasound or CT are helpful in preoperative diagnosis of these lesions.23,24

Our study included three cases of VIN III and one case of VIN I. Vulvar Intraepithelial Neoplasia (VIN) is a pathological denomination coined by the International Society for study of vulvo-vaginal diseases (ISSVD) and adopted by the International Society of Gynaecological Pathology (ISGYP) and by the World Health Organization (WHO). It may be asymptomatic or may present with vulvar itching or plaque.25 There are two types of vulvar intraepithelial neoplasia (VIN): warty-basaloid (usual) and differentiated. Differentiated VIN is uncommon and seldom diagnosed prior to carcinoma and, traditionally, is not graded. There are currently three grading systems for warty-basaloid VIN: The WHO three grade system of VIN I-III, a two-grade system of low and high grade vulvar intraepithelial lesions, and the revised ISSVD classification which has no grading of VIN. According to the ISSVD, VIN I should be abolished and VIN II and III combined into a single category, simply termed warty-basaloid VIN.26 Two major types of VIN correspond to two distinct oncogenic pathways to vulvar squamous cell carcinoma (VSCC). While the incidence of VSCC has remained relatively stable over the last three decades, the incidence of VIN has increased. VIN of usual type (uVIN) is human papillomavirus (HPV)-driven, affects younger women and is a multicentric disease. In contrast, VIN of differentiated type (dVIN) occurs in post-menopausal women and develops independent of HPV infection. dVIN often arises in a background of lichen sclerosis and chronic inflammatory dermatoses. Although isolated dVIN is significantly less common than uVIN. dVIN bears a greater risk for malignant transformation to VSCC and progresses over a shorter time interval. On histological examination, uVIN displays conspicuous architectural and cytological abnormalities, while the morphological features that characterize dVIN are much more subtle and raise a wide differential diagnosis. On the molecular level, dVIN is characterized by a higher number of somatic mutations, particularly in TP53.16 In our study, one case of VIN I was seen and it was associated with CIN I that was confirmed on Pap smear. Studies mention that approximately 50% of these women have other neoplasias involving the genital tract, most often cervical intraepithelial neoplasia (CIN) and condyloma acumunata.18 Presence of koilocytes in the superficial layers of the epithelium and loss of polarity along with occasional mitosis above basal layer but limited to lower third of the epithelium was diagnostic of VIN I in this case [Figure 4(D)]. Increased incidence of VIN is mentioned in immune compromised patients and in patients known to have sexually transmitted diseases. Sometimes the lesions may be pigmented, multiple, papular, pruritic or verrucoid. Such lesions are termed as Bowenoid papulosis.27 Our study included one case of Bowenoid Papulosis seen in HIV positive patient [Figure 2(E) and 4(E)]. The lesions involving the nonkeratinizing epithelium over mucosal surface of the vulva are termed as Erythroplasia of Queyrat while similar pigmented lesions over the keratinized epithelium are preferentially called as Bowen’s disease. In our study, patient with Bowen’s disease showed thickened plaque like labial surfaces which were irregular and slightly warty [Figure 2(F)]. Microscopy in VIN III showed presence of abnormal cells with abnormal mitosis, multinucleation and dyskeratosis involving almost whole thickness of the epithelium [Figure 4(F)]. The terms Bowenoid Papulosis and Erythroplasia of Queyrat are based on the clinical appearances and location of the lesions rather than morphology. All of them show features of VIN III. The association of them with HPV infection has been proved.28 Early diagnosis of these precursor lesions helps further progression by initiating early treatment.6,29,30

Squamous cell carcinoma comprises about 90% of all vulvar cancers, the others being Melanoma, Paget’s disease, Bartholin’s gland tumour, Adenocarcinoma and Basal cell carcinoma.29 Strong evidence has accumulated showing that there are two different etiopathogenic pathways for the development of VSCC and VIN, one associated with HPV infection, and a second independent of HPV infection. These two different types of VSCC have different epidemiological, pathological and clinical characteristics, and should therefore be considered as two separate entities. Histologically, HPV-associated VSCCs are of the basaloid or warty type, and arise from VIN of the usual type. Whereas HPV-independent VSCCs are keratizing and associated with differentiated VIN and lichen sclerosus that frequently show mutations of p53.16 p16 (INK4a) and p53 immunostaining can be useful for classifying VSCC into HPV-associated or HPV-independent. p16 is considered a surrogate marker for HPV infection and will be positive in HPV-associated VIN. On the other hand p53 is marker for HPV independent VSCC and seen positive in those SCC which are secondary to dVIN. Although large, multicentre studies are needed to definitively assess the involvement of HPV in the prognosis of VSCC, most studies have not found clear differences in survival between HPV-associated and HPV-independent tumours.31

Out of the total 4 cases of Squamous cell carcinoma in our study, two cases were primary vulvar SCC without any evidence of any growth in other part of female genital tract. Both of them presented as ulcerated nodular growth and one of them complained of blood stained discharge. Unilateral Inguinal lymphadenopathy was also seen in one, which was proved as metastatic squamous malignancy on cytology. Both were postmenopausal patients. Early diagnosis in these cases would have been possible with routine gynecological examination. Lack of
health education and awareness usually results in late presentation of the patients in India.

In other two cases, one was already known case of SCC cervix on radiotherapy since last few months. She developed an ulcer over vulva. Scrape cytology and biopsy from the lesion revealed recurrence of squamous malignancy. In other case, patient had a large ulceroproliferative growth over cervix, extending into vaginal wall, more on one side with involvement of labia minora. This was also confirmed on histopathology. Such locally advanced vulvar cancers have not only poor prognosis but also are a therapeutic challenge for the treating oncologists.38

CONCLUSION

A spectrum of vulvar lesions can be seen which may be symptomatic or asymptomatic. Due to the overlapping features, they often cause diagnostic challenge for the pathologists and therapeutic challenge for the treating doctors. We have studied vulvar lesions over one year duration and categorized them on the basis of etiology as well as morphology. A wide range of all lesions including inflammatory, benign and malignant neoplastic, precursor lesions and some miscellaneous lesions were also noted. Since the incidence of vulvar cancer is gradually increasing since last few years, it is essential for a pathologist to be aware of the morphology and differential diagnosis of precursor lesions so that follow up and early detection of vulvar cancer can help in better patient survival. This was one year study; however, larger studies are needed for wider assessment of variation in morphological spectrum.

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REFERENCES


