IADVL

IADVL SIG FEMALE GENITAL DERMATOSES
(IADVL ACADEMY) – NEWSLETTER

VULVOVAGINAL MALIGNANCIES - THE EVIL LURKING WITHIN

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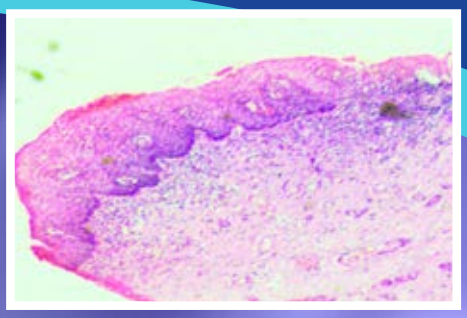
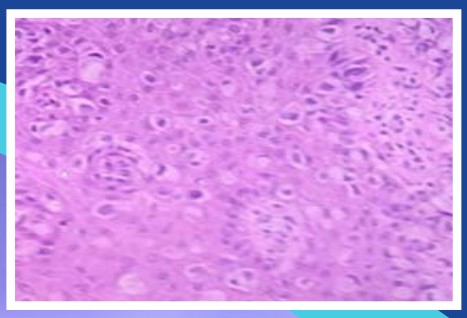
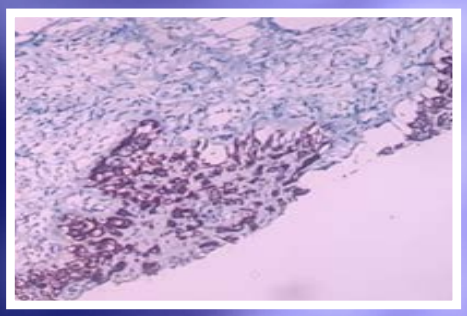
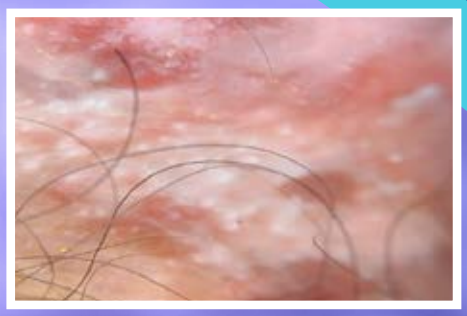

Dr Smitha Prabhu
Coordinator – SIG Female Genital Dermatoses

Dr Pragya Nair
Convener – SIG Female Genital Dermatoses

Dr. Nina Madnani
Advisor

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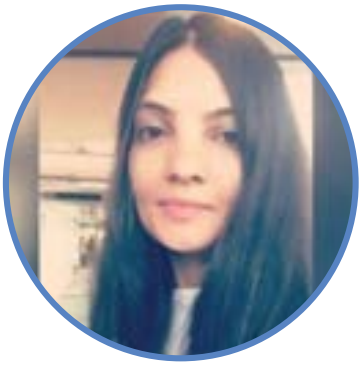

Dr. Nisha Chaturvedi

Dr. Vinitha Gopala krishna

Dr. Anup Kumar Tiwary

FOREWORD:

Dermatoses in and around the genital area remain much neglected until late due to the inherent hesitation and shame associated with revealing these so called “private parts” to outsiders. Most women tend to suffer in silence, rather than voice their despair. This is the norm even in innocuous vulvovaginal conditions like candidiasis, lichen planus, discharge or pruritus , and becomes most relevant when it comes to vulvovaginal malignancies, which indeed becomes the evil lurking within. Incidence of vulvovaginal malignancies is estimated to be 2.5–4.4 per 100,000 persons per year and vulvar malignancy is the fourth commonest malignancy in women. Though these may occur at any age, the incidence rises sharply after menopause. Squamous cell carcinoma is the commonest variant, followed by basal cell carcinoma, extramammary Paget’s disease and melanoma. Often, it is an initially premalignant lesion which subsequently becomes malignant and invasive. Hence diagnosis and adequate treatment at premalignancy stage goes a long way to improve the patient’s quality of life.

Recently, many updates have occurred in the various terminologies used for female genital malignancies and many well known terms from the past have been replaced. The whole spectrum of vulvovaginal malignancies have been encompassed under a couple of umbrella terms for ease of understanding the pathogenesis. Histopathology aided by IHC remains the gold standard of diagnosis. There also have been advances in management, still local wide resection remains the firstline modality in most cases.

Herein we focus some pertinent aspects of vulvovaginal malignancies.

We also have a case vignette corner, and a quiz session to further aid the understanding of this condition.

This newsletter tries to cover the most pertinent aspects of this vast topic.

Wishing for a fruitful reading

Dr. Smitha Prabhu S, Dr. Pragya Nair.

1. PREMALIGNANT VULVAR LESIONS: IMPORTANT SNIPPETS

Dr. Eswari L

MD DVL, FRGUHS Dermatosurgery, FAADV Dermatopathology
Associate Professor, Bangalore Medical college and research Institute, Bangalore

- Now termed Vulvar Intraepithelial Neoplasm (VIN)
- Older terminologies (sometimes still referred to): Bowen's disease, BowenoidPapulosis, Erythroplasia of Queyrat,, Squamous cell hyperplasia with atypia, atypical vulval dystrophy
- VIN is of 2 types: [i] VIN of usual type (uVIN), which is human papillomavirus (HPV)-driven (also known as classic, undifferentiated, basaloid, warty, Bowenoid type)and [ii] VIN of differentiated type (dVIN) which develops independent of HPV.
- uVIN charecteristics:
- tends to occur in young women, in the third to fifth decades of life.
- Risk factors: smoking, increase in sexual partners and immunosuppression
- Associated with pruritus and dysuria.
- White or erythematous macules or papules, coalesce to form verrucous plaques and may involve anywhere in the anogenital area (Figure 1).
- Less than 5% progress to Squamous cell carcinoma, with advanced age, radiotherapy and immunocompromised status being risk factors.
- Recurs in approximately 13–36% of patients, and few patients exhibit spontaneous regression of disease.
- Histopathology: hyperkeratosis or parakeratosis, acanthosis with club shaped rete ridges, with disoriented keratinocytes giving a wind-blown appearance just above the intact basal layer (eye liner sign). Hyperchromatic nuclei and mitosis are an important feature. (Figure 2)

d VIN Characteristics:

- typically occurs in post-menopausal women in the sixth to eighth decades of life, but can occur in younger patients.
- often associated with adjacent lichen sclerosus (LS) (Figure 3) and/or chronic inflammatory dermatoses.
- Clinicallypresents as focal greay white discolourations with rough surface, thick white plaques or elevated nodules. (Figure 3)
- dVIN has a higher risk of progression to Vulvar Squamous Cell Carcinoma (VSCC).
- Histopathology: acanthosis, occasional parakeratosis, and irregular elongation and anastomoses of the rete ridges. On high power, nuclear atypia is often confined to the basal and parabasal layers. There is premature keratinization, extracellular keratin and abortive squamous pearls within the lower layers of the epidermis. There is normal maturation in the superficial layers and retention of keratohyaline granules. The optimal biopsy should include the interface between the lesion and normal skin because dVIN often has an abrupt edge. There can be features of squamous cell hyperplasia (SCH) or lichen sclerosus (LS) in the adjacent skin

Comparison of the 2 types of VIN

uVIN	dVIN
More common	Less common
Younger age group	Older age group
Multifocal lesions	Unifocal lesions
Associated with HPV	Preexisting lichen sclerosus/ chronic inflammatory disease/ vulvar dystrophy
Low risk of progression to SCC P16 +, P53+, Ki67 full thickness	High risk of progression to SCC P16 –, P53 + or –, Ki67 confined to lower layers
HPV E6 inactivation of p53 HPV E7 inactivation of Rb suppressor gene	TP53 mutation in some cases

- **Immunohistochemical markers**

P16- correlates extremely well with high-risk HPV status. LS and SCH tend to be negative for p16.

P53- is positive in dVIN. It may be negative in few cases.

Ki67- dVIN show positive staining for Ki-67 in the basal and suprabasilar layers in contrast to the basal expression seen in LS, which can be a helpful distinguishing feature. The staining for Ki-67 in uVIN is much more conspicuous, and usually stains the full thickness of the epithelium

- **Differential diagnosis of VIN**

Lichen sclerosus- long term studies have shown that LS has a very low risk (1–3%) of progression to VSCC, and is not considered a premalignant lesion by most authors. The finding of basal nuclear atypia in otherwise ordinary LS has been referred to as atypical LS.

Squamous hyperplasia- SCH lacks atypia and has an organised proliferation of mildly enlarged but non-atypical keratinocytes and absent or minimal mitoses restricted to the basal layer.

Pseudoepitheliomatous hyperplasia- due to extramammary Paget's diasease- It is characterised by acanthosis, papillomatosis, dyskeratotic cells, and may show some nuclear pleomorphism.

Extramammary Paget's disease- should always be considered in the differential diagnosis of VIN. Classically, extramammary Paget's disease is positive for CK7, CAM5.2, CEA, PAS, mucin stains, GCDFP-15 and HER2, whereas VIN is positive for CK5/6 and p63.

Melanoma- should always be in the differential diagnosis of VIN. Neoplastic melanocytes may colonise the epidermis in the form of single cells, nests or more confluent groups, potentially mimicking VIN. Unlike VIN, melanoma is positive for S100, SOX10, HMB45 and MelanA.

Vulvalacanthosis with altered differentiation (VAAD) - This entity was first described by Nascimento and Crum. The triad of features that characterised VAAD included: (1)

acanthosis with variable verruciform architecture, (2) loss of the granular layer with superficial epithelial pallor, and (3) multilayered plaque-like parakeratosis. All cases of VAAD were HPV negative. VAAD was proposed as the precursor lesion to Verrucous Carcinoma (VC).

- **Assessment of coexistent invasion**

Early invasion usually presents as single cells or nests of eosinophilic keratinocytes with irregular or angulated contours, invading from the basilar epidermis or from the elongated rete ridges. A desmoplastic stromal reaction is a helpful feature, if present. Tangential sectioning of the rete ridges can mimic invasion; in this situation, the nests are evenly spaced, have rounded or bulbous contours and are not associated with stromal desmoplasia.

- **Treatment**

Based on the fact that not all VIN progressed to VSCC and on the recognition of the psychological and sexual morbidity of vulvectomies, less aggressive therapies like local excision, topical imiquimod, cidofovir or 5-fluorouracil, photodynamic therapy and laser ablation are being used

- Future of HPV associated neoplasia – significant reduction in incidence due to universal HPV vaccination

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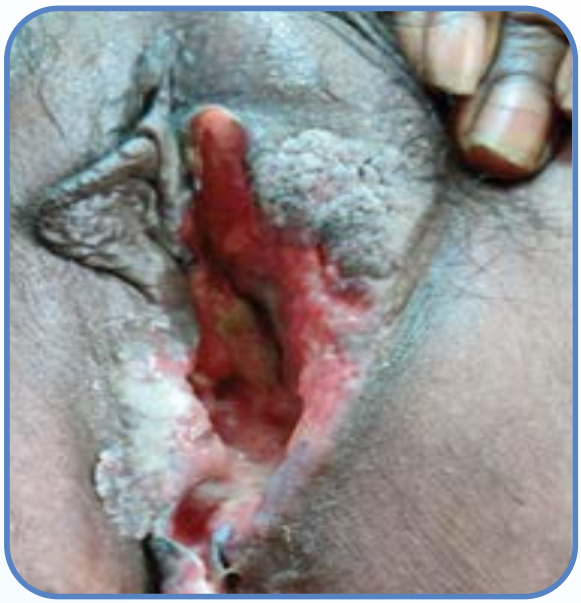

Figure 1: 53-year-old female with multifocal lesions and the verrucous plaques had features suggestive of uVIN

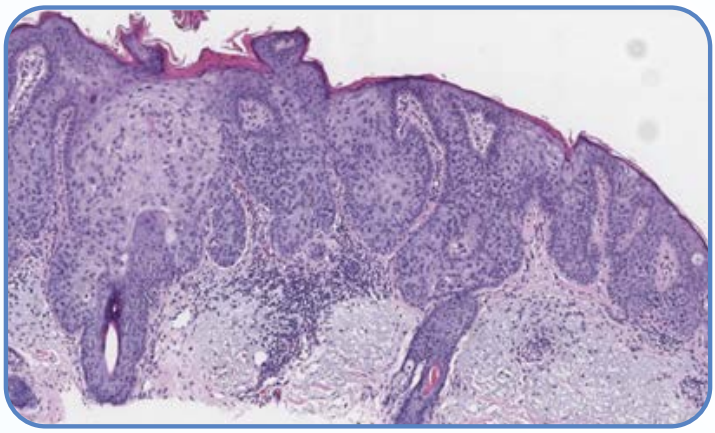

Figure 2: Focal parakeratosis, acanthosis with clubshapedreteridges, disoriented suprabasal keratinocytes with mitotic figures and intact basement membrane, Features of Squamous cell carcinoma in situ.

Figure 3: 75-year-old female who had features of VIN in a longstanding case of Lichen sclerosus

2. RISK FACTORS FOR VULVAR MALIGNANCIES

Dr. Nisha Chaturvedi

Consultant Dermatopathology Surya Hospital, DrIndu child health care centre , LNT health care centre, Mumbai.

Introduction-

Vulvar cancers (VC) comprise 5% of all malignancies of female genital tract and is the 4th most common gynecologic cancer.VC are of several types, the commonest being squamous cell carcinoma (90%). Melanoma, adenocarcinoma and sarcoma are rare. There are multiple factors which increase the risk of developing VC. Eliminating or minimizing these factors can not only aid in prevention but also limit the progression of the disease.

The following factors may raise the risk of developing VC

- Age- Risk of VC increases as women ages. Half of all cases of VC are seen in women over 70 years of age. HPV dependent VC are seen in premenopausal women whereas the HPV independent VC is seen in older women.
- Human papillomavirus (HPV)- HPV is associated with majority of cases with vulvovaginal malignancies. Multiple sexual partners, unprotected sexual contact (vaginal, oral or anal), prior sexually transmitted infections are some of the risk factors of genital warts. HPV subtypes 6 ,11,16, 18 and 31 are commonly associated with vulvar intraepithelial neoplasia.
- Cigarette smoking – Studies show cigarette smoking linked with three to six fold risk of vulvar malignancy.
- Lichen Sclerosus – Risk of squamous cell carcinoma is approximately 5% in patients with lichen sclerosus. Studies have shown that early detection and treatment of lichen sclerosus reduces the risk of squamous cell carcinoma.

- Chronic vulvar inflammation – Apart from lichen sclerosus, vulvar lichen planus can also be a risk factor for developing VC.
- Human immunodeficiency virus (HIV)- Women infected with HIV is at increased risk of developing VC and also more likely to get infected with HPV.
- Other genital cancer- Cervical cancer also increases the risk of VC. The same HPV subtypes are linked to both the cancers.
- Melanoma -Personal history of melanoma or dysplastic nevi on other body parts also have increased risk of developing VC.History of melanoma in the family also increases the risk of VC
- Women with history of Systemic lupus erythematosus and solid organ transplant also have an increased risk of developing VC due to immunosuppression and increased susceptibility to HPV infection.

Risk factors for recurrence –

Irrespective of the treatment modality used, data have shown that approximately 30% have shown recurrent disease. Recurrence post treatment was associated with positive margins, age>50 years, presence of lichen sclerosis/HPV, metasynchronous presence of cervical or vaginal intraepithelial neoplasia and immunosuppression. Wallbillichet al. demonstrated high rate of recurrence with smoking and treatment with laser ablation.

Prevention –

VC may be prevented by certain factors like avoiding sexual intercourse with multiple partners, practicing safe sex, stop smoking or use of tobacco, treatment of any pre-existing vulvar disease, regular gynaecological examination and administration of HPV vaccination.

HPV Vaccination is universal and is recommended at age of 11 to 12 years, and upto 26 years. CDC recommends that vaccination can start at the age of 9 years, and if given before 15 years, only 2 doses 6 to 12 months apart are sufficient, otherwise, 3 doses are required. There are 3 commercially available vaccines, the bivalent Cervarix which targets HPV 16 and 18, the quadrivalent Gardasil which targets HPV 6,11,16,18 and the nonavalent Gardasil which protects against HPV subtypes 6,11, 16, 18, 31, 33, 45, 52 and

58. In India, HPV Vaccine is approved for females, and is freely available. Gardasil is given at 0, 1, 6 months interval, and Cervarix at 0,2, 6 months.

- **Warning signs for patients:**

  1. Sudden growth
  2. Scaly plaque with itching/bleeding not responding to treatment
  3. Symptomatic lesions without definite diagnosis
  4. Chronic vulvar pruritus or pain
  5. Inguinal lymphadenopathy
  6. Change in color, texture or nodularity of pre-existing lesion

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3. MALIGNANCIES INVOLVING THE VULVAR REGION - A BRIEF OVERVIEW

Dr. Dhanashree Bhide

Consultant Dermatologist , KEM hospital , Pune / Deenanath Mangeshkar hospital Pune

Introduction-

Patients with vulvar dermatoses usually delay seeking medical advice due to anxiety and embarrassment. A simple symptom like pain and itching could be representative of underlying malignant conditions.

Vulvar cancer is one of the most common types of gynaecological cancers.Therefore a high index of suspicion ,thorough history and clinical examination ,supportive dermoscopy and a biopsy in all chronic conditions would help in early diagnosis and prompt treatment.The important vulvar cancers are squamous cell carcinoma, basal cell carcinoma, extra mammary Paget's disease and vulvar melanoma. The treatment requires interdisciplinary approach and referral to a dedicated cancer centre. Dermatologist may be the first point of contact and hence should be aware of signs and symptoms of these cancers so as to guide the patient on the right track.

A. Pigmented Basal Cell Carcinoma:

It is uncommon, low grade neoplasm in vulvar area classified as epithelioma rather than carcinoma, which rarely undergoes metastasis. It appear as pearly pink or flesh coloured mass with translucent sheen, occasionally pigmented showing brown or black colour. Other presentation can be in the form of nodules, polyps, ulcers or flat areas with pigmentary changes.

B. Squamous cell Carcinoma:

This is the most common form of vulvar malignancy and accounts for 80-95% cases, with rise in its incidence.

Risk factors

- In elderly women it is usually persistent long term inflammation (Lichen Sclerosus and Lichen Planus). Sixty % of vulvar SCC are associated with LS.It is important to treat and follow cases of LS as the risk of SCC can be 3-5% in untreated LS
- In young women- HPV infection, smoking, alcohol, cervical dysplasia, immunosuppression

Clinically it may have symptoms like itching, irritation or pain. The morphology of lesions is scaly plaque ,ulcer or ill-defined mass.

Three types have been identified

- Classic Bowenoid type :Keratoticverrucous nodule or masses
- Verrucous CA (Buschke Lowenstein tumor)-Large cauliflower like masses associated with HPV, locally invasive.
- Non HPV associated -Keratinising or differentiated SCC, presents with crust and associated with L S or LP.

If precursor lesion is VIN ,histologicallyuVIN(HPV dependent VIN) progresses to basaloid or warty SCC and dVIN(HPV independent VIN) progresses to keratinising SCC.

On IHC uVIN is positive for p16 and negative for p53 whereas dVIN is negative for p16 and positive for p53.

Some patients may show overlap.

Biopsy, Imaging ,Cystoscopy,Proctoscopy ,HPV testing in indicated cases should be considered. Pelvic examination, colposcopy and cytology is recommended in HPV associated cases.

Surgical removal in early stages whereas external beam radiation therapy with or without chemotherapy in advanced stages is recommended.

PD 1 and PD L1 blockers need to be tried in vulvar SCC. Cemiplimab PD1 blocker has been FDA approved for metastatic cutaneous SCC, however data in vulvar SCC is lacking.

C. Extra mammary Paget's Disease (EMPD): [Fig1-3]

It is a rare cutaneous malignancy accounting for 1-2% vulvar cancers. The lesions are non-specific and hence there is delay in the diagnosis with a median delay of 2 years. It mimics fungal infection, eczema or psoriasis and present after receiving multiple topical therapies. Symptoms includes pruritus, burning, tenderness and oedema. It is usually seen in apocrine gland rich sites, but Ectopic EMPD occurs in areas with poor apocrine glands such as cheeks, abdomen and external ear. EMPD can present either as primary or secondary disease.

Primary EMPD– Clinically present with erythematous scaly plaque with crusting, erosions, ulcerations, nodules, vegetative lesions and regional lymphadenopathy.Healing takes place with pigmentary changes. Vulva is affected in 65% patients.

The Paget's cells are thought to originate in epidermis at sweat gland level or from primitive epidermal basal cells and is not associated with underlying adenocarcinoma

Secondary EMPD- Lesions are seen close to underlying malignancy,perianal area if GI malignancy is present, andvulvar region in case of female genitourinary involvement.

The Paget's cells arise from epidermotropic spread of malignant cells either from underlying adenocarcinoma in dermal adnexal gland or within contiguous epithelium of ct.

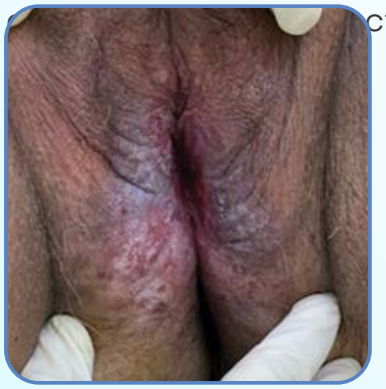

Figure 1: EMPD (Hyperpigmented scaly plaque with erosions,hypopigmentation, induration on both labia majora extending on labia minora)

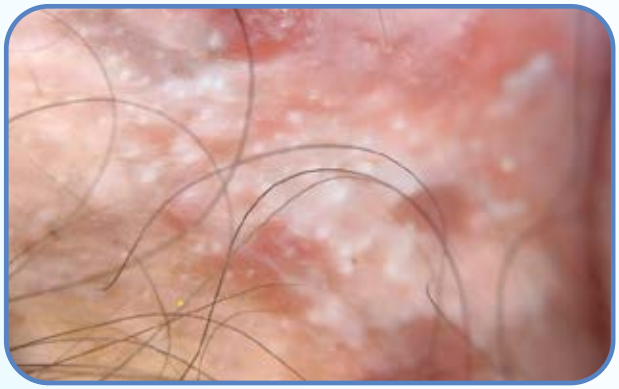

Figure 2: Dermoscopy of EMPD(White dots, thick white lines ,structure less white cloud like areas)

Figure 3: A.-HPE Fig 3 B CK 7 Positivity in EMPD

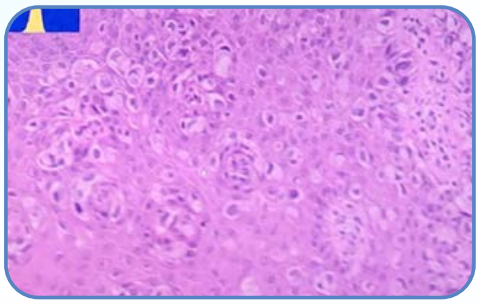

Figure 3: A

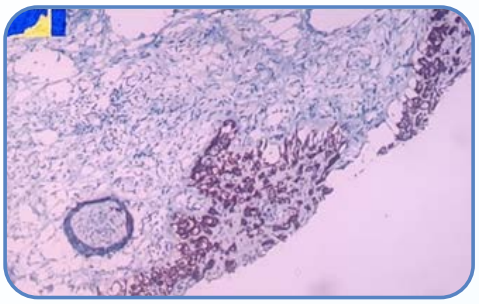

Figure 3: B

The exact pathogenesis is not clear. The proliferative neoplastic cell is a Paget's cell, concentrated in lower epidermis.

These are large round cells with abundant, pale staining, basophilic cytoplasm and large centrally situated nuclei with prominent nucleolus.

There are a wide range of IHC markers.

- CK-7/CK-20
  CK 7 has good sensitivity for Paget's cells in both mammary and EMPD
  CK 20 is more specific for EMPD.

  In primary EMPD-CK 7 is positive and CK 20 is negative whereas in secondary EMPD both CK 7 and CK 20 are positive.
- CEA. is quite sensitive for EMPD.
- HER 2 protein overexpression may be detected in 30-50% of EMPD- Associated with more aggressive and recurrent disease.

D. Vulvar Melanoma

Vulvar melanoma is usually seen in the later decades of life, the median age at diagnosis is 68. Almost 32% present with regional or distant metastases at diagnosis.Total 8-10% of genital malignancies are melanomas, being the second most common malignancy affecting vulva. A positive family history of melanoma or inherited dysplastic nevus are important aetiological factors.

Clinical Features: Colour is variable ranging from red, white ,blue or black. Irregularity in color, asymmetry and indistinct borders with size >7 mm are other features.

Patients can present with melanocytic lesion or vulvar mass, ulceration, with or without bleeding, pain and pruritus.

Common site is labia majora, especially the mucosal site. In light skin patients, amelanotic melanoma is seen in almost one fourth of cases.

Diagnosis

- Histopathology : Increased number of atypical melanocytes arranged in solitary units or as nests
- The AJCC staging system should be used for vulvar melanoma instead of the FIGO system used in SCC.
- Imaging is recommended in the evaluation due to the high rate of locally advanced disease and regional/distant metastases.
- MRI may help to delineate the local extension and aid in surgical planning.
- CT or PET-CT is used for the evaluation of distant metastases.

Surgery remains the mainstay of treatment for melanoma and shave biopsy should be avoided. Dacarbazine chemotherapy and interferon are some of the modalities tried.

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4. ESSENTIALS IN DIAGNOSIS AND MANAGEMENT

Dr. Sweta Rambhia

Medical Director &Consultant Dermatologist Just care dental care and skin clinic, Mumbai

DR. ISHITA PATANI Consultant Dermatologist at Patani Nursing Home Mumbai

DR. RAMYA JAYARAM Consultant GynecologistWomens Centre Coimbatore

Introduction-

Vulvar malignancies are rare, with an incidence of 3.7 and mortality rate of 1.3/100000 women. It predominately affects elderly women who have comorbidity , thus prove challenging while planning management. Dermatologist should be able to identify the premalignant cases at earliest,should refer to oncologist and reduce the disease burden.

Screening

Women with conditions that predispose to vulval cancer should be screened regularly for following signs and symptoms

- Intractable itch
- Pain or soreness
- An ulcer / visible growth / swelling
- Burning micturition
- Excessive Vaginal discharge or bleeding

The mainstayof diagnosis is clinical examination and diagnostic biopsy.

Examination

- Pre-biopsy photographs
- Lesion should be evaluated for size, location, morphology and background
- Vagina, urethra, and anus should be examined

Vulval Biopsy

Should be considered when there is

1) Change in vulval epithelium in post menopausal women

2) Swelling, polyp , change in colour or excessive bleeding from the lesion

Types of Biopsy

Incisional Biopsy – Ideal biopsy specimen should be large and also contain interface between normal and abnormal epithelium.

Excisional Biopsy –Contains abnormal epithelium usually taken in VIN (Vulvar intraepithelial neoplasia)

Diagnostic tests

1) Histopathology

It is Gold Standard: Diagnostic biopsies must be greater than 1 mm depth to allow differentiation between superficially invasive and frankly invasive tumours allowing pathological interpretation.

Types of tumors and their significance:

Squamous cell carcinoma	Accounts for 90%of vulval malignancies
Melanoma, Paget's disease, Bartholin Gland tumor, Adenocarcinoma and Basal cell carcinoma	Account for remaining 10 %
Infiltrative growth pattern	Shows higher recurrence
Lympho vascular space involvement	Higher recurrence rate
Presence of fibromyxoidstroma at invasive edge	Associated with poor prognosis

Mucin Stain can be done in Paget's Disease.

Sentinal Node biopsy need to be carried out.

1) Dermoscopy:

Dermoscopy is an underused utility till now with few case reports

Vulvar Cancers	Dermoscopy finding
Vulvar Melanoma	Multicomponent pattern composed of 1) Blue white veil 2) Irregular black dots 3) Atypical network or streaks 4) Vessels- Dotted , linear , irregular
Vulvar Basal Cell Carcinoma	1) Blue ovoid nests 2) Homogenous Shiny white area – peritumoral fibrosis 3) Vessel- fine reddish Arborising or linear vessel
Squamous cell Carcinoma	1) Irregular plaques with asymmetry of structure and color 2) Color seen – dull pink/ red with whitish areas / gray blue / brownish areas 3) Brown gray dots at periphery 4) Vessels –Dotted , Glomerular and linear in variable and patchy distribution
Paget's Disease	Vessels -dotted and glomerular vessel Milky red areas

Colposcopy:

- Vulva is visualised using a colposcope. Acetic acid (5 %) is applied to vulva for a period of 3 min followed by naked eye and vulvoscopic examination for acetowhite areas.
- It is not advised as a routine examination;
- It helps to identify the lesion and choose the biopsy site.
- For examination of cervix, the use of acetic acid is prerequisite, but for vulva, it is useful when genital condylomataacuminata, intraepithelial neoplasia, or early invasive cancer is suspected

Immunohistochemistry findings:	IHC finding
VIN	Staining for p53 and p16 , Ki67, EGFR
Micrometastasis in Sentinal nodes	AE1/AE3 (Cytokeratin)
Vulval Melanoma	KIT mutations 25% BRAF 26% and NRAS less common Routine stains and immunohistochemistry for melan A, S100 and HMB45 used to confirm a melanoma.
Vulval Paget's and Extramammary Paget's	Cytokeratin 7 and 20, carcinoembryonic antigen, gross cystic disease fluid protein 15, and uroplakin III are needed to differentiate between the 2 subtypes Neoplastic Cells of Paget's are positive for CAM 5.2, CEA, EMA and CK7. Diffuse CK20 positivity Suggestive of Secondary Paget's disease (Malignancy of urothelial or anorectal carcinoma.)

4) Radiological Investigation

MRI is considered the best imaging system for Vulvar malignancy staging.

CT Chest and PET CT may be advised for advance Disease.

For primary tumours • Size ≤2 cm confined to the vulva and/ or perineum, • Size ≤1 mm of stromal involvement	Imaging staging is not recommended.
Squamous cell carcinoma with · Stromal involvement >1 mm, · Tumour size >4 cm,	Pelvic MRI staging with inclusion of inguinal regions.
· Tumours with suspicious involvement of the urethra, vagina, or anus according to clinical evaluation.	
For tumours >2 cm and ≤4 cm, clinical staging	Pelvic MRI staging (include inguinal lymph nodes) Groin ultrasound (with FNAC/biopsy of suspicious lymph nodes if found)
For regional or advanced disease	CT chest, abdominal and pelvic CT (or PET/CT) with coverage of the inguinal regions Images with Intravenous contrast of portal-venous help to increase diagnostic accuracy

Treatment :

Prevention of VIN (HPV Related)

- Quadrivalent vaccine is protective against HPV genotypes 6, 11, 16, and 18
- 9- valent vaccine against 6, 11, 16, 18, 31, 33, 45, 52, and 58.

Treatment of Premalignant lesions / Low grade malignancy

- Topical Imiquimod-Premalignant disease of vulvar epithelium ,Basal cell carcinoma, Bowens disease and mild cases of Paget's disease.

- Cryotherapy –Premalignant and low grade malignancies.
- Intralesional and Topical5 fluorouracil (5 –FU) –Basal cell carcinoma and Squamous cell carcinoma and BowenoidPapulosis .
- Laser Ablation with colposcopy to control the depth of ablation– premalignant / low grade malignancies.

Surgical Management

- Early stage malignancy –Wide local excision.
- Late stage malignancy –Wide excision ,sentinel node biopsy and groin Treatment. Recurrences are commonly seen intwo years over in Vulvar and perineal region.

Radiotherapy

- It is frequently used with or without chemotherapyin the treatment of advanced stage vulval cancer.
- Preoperative radiotherapy is used for sphincter-preserving surgery.
- It has replaced surgery for histologically proven involved groin lymph nodes.
- A prophylactic dose (45–50 Gy) to be delivered to the primary and nodal sites .Tumour is subsequently boosted by a second phase of radiotherapy or brachytherapy, to a total dose of 65 Gy.
- It is contraindicated in verrucouscarcinoma as it can induce anaplastic transformation and increase likelihood of metastasis.

Chemotherapy

Neoadjuvant Chemotherapy has been used in

- Invasive Squamous cell carcinomato reduce the size of tumour before surgery
- Adjuvant setting, postoperatively, alone or concomitantly with radiation in node positive disease.
- Recurrent and metastatic disease.
    - It is offered depending on age, renal function and performance status.
    - Patients are treated with chemotherapy such as cisplatin, 5FU and bleomycin. Recently erlotinib and cetuximab have been used.

Follow up:

Vulval Cancer Fully Treated /Low Grade VIN	· Three monthly for 1st year · Six monthly for 2nd year · Yearly thereafter
VIN High Grade , Multicentric disease, Vin in immunocompromised,	· Three monthly in Specialist Vulval Clinics / Gyneco oncologist for 1 year · Six monthly thereafter for 1 year · Annual follow up lifelong.
Paget's Disease, Melanoma in Situ	Same as above

Recommended Reading :

- FIGO Staging 2009 Or Vulvar Cancer Staging Guidelines of European Society of Eurogenital Radiology .
- Surgical Guidelines for Various Stages of Vulvar Maligancies .
- Nikolić et al. Insights Imaging (2021) 12:131 https://doi.org/10.1186/s13244-021-01075-6
- Guidelines for the Diagnosis and Management of Vulval Carcinoma ROYAL COLLEGE of Obstretician and Gynecologist May 2014.
- Borghi A, Virgili A, Corazza M .Dermoscopy of Inflammatory Genital Diseases: Practical Insights, Dec 2019.
- Giorgi et all , Clinical and Dermoscopic Features of Vulvar Melanosis Over the Last 20 Years
- Use of topical imiquimod in the treatment of VIN : A case report and review of literature Int J Womens Dermatol.2016 Mar; 2(1); 35-38.
- Bornstein Et All ,2011 Terminology of the Vulva of the International Federation for Cervical Pathology and Colposcopy.

5. QUIZ: Choose the best Answer :

Dr Smitha Prabhu

Additional Professor, Dept of Dermatology and Venereology,
Kasturba Medical College, Manipal, MAHE, Manipal.

1. **This is not an adenocarcinoma:**
   a. Toker's cell malignancy
   b. Paget's disease
   c. Bartholin gland cancer
   d. Leiomyosarcoma
2. **The following IHC Marker is absent in Extramammary Paget's Disease**
   a. CK 5/6
   b. CK7
   c. CAM5.2
   d. CEA
3. **The following may progress to vulvar malignancy, if chronic**
   a. Syringoma
   b. Lichen sclerosus
   c. Condylomalata
   d. Angiokeratoma
4. **HPV infection is strongly associated with:**
   a. uVIN
   b. dVIN
   c. Bowen's disease
   d. Pagets disease
5. **Radiotherapy is contraindicated here:**
   a. ExtramammaryPagets disease
   b. Bowen's disease
   c. dVIN
   d. verrucous carcinoma

6. **Treatment of choice in VIN is;**
    a. Radiotherapy
    b. Vulvectomy
    c. HPV vaccine
    d. Intralesional 5-FU
7. **The following is true for uVIN**
    a. Seen in older females
    b. Is unifocal
    c. It is not associated with HPV infection
    d. Chance for progression to SCC is rare
8. **Gold standard for diagnosis of vulvar neoplasia is:**
    a. Colposcopy
    b. Histopathology
    c. Dermoscopy
    d. Imaging techniques
9. **Most common histological type of vulvar cancer is:**
    a. Adenocarcinoma
    b. Squamous cell carcinoma
    c. Sarcoma
    d. Basal cell carcinoma
10. **Extramammary Paget's disease of the vulva arising due to an anorectal neoplasia is classified as:**
    a. Primary Type I
    b. Primary Type II
    c. Secondary Type I
    d. Secondary Type II

6. VULVAR INTRAEPITHELIAL NEOPLASIA MASQUERADING AS SIMPLE EROSION

Dr. Athota Kavitha

Consultant Dermatologist , Dr. Paruchuri Rajaram memorial skin and laser centre, Guntur, Andhra Pradesh

Introduction-

A 50 year old female patient presented with vulvar pain of 4 years duration, and recurrent burning micturition. She had attained menopause 5 years back.There was no other significant medical history including diabetes mellitus or hypertension. She was being treated with steroid antifungal combinations, topical oestrogens, antispasmodics and NSAIDS by gynaecologists with no response.

Local examination revealed a reddish lesion involving the clitoris,vestibule and the periurethral area.(Fig 1) Labia majora, minora and the vulvar skin were normal.There was no inguinallymphadenopathy. Oral mucosa is normal.

Investigations: Complete blood picture was normal.HIV, HBSAg, HCV were negative.

Differential diagnosis of erosive Lichen planus and vulvar intraepithelial neoplasia (VIN) were made.

Dermoscopy showed whitish background with intense red areas and few polymorphic vessels. Biopsy was taken from 2 sites.Biopsy showed a moderately dense lichenoidlymphoplasmocyticinfiltrate with mild hyperplasia of the epithelium. The lower third of the epithelium showed mild to moderate nuclear pleomorphism with an increased number of mitotic figures above the basal layer unto the lower half .(Figure2a, b &c)

A diagnosis of Grade 2 VIN was made.

Treatment: Vulvectomy, being the treatment of choice in VIN, was performed in this case.(Fig 3)

Discussion: Vulvar premalignancies and malignancies are not uncommon, but present in

varied ways and are often not diagnosed early in the disease. Timely and accurate diagnosis of these cases is of utmost importance to prevent progression to malignancy and for prompt treatment.VIN is of 2 types with HPV viral infection being a precursor in usual VIN and lichen sclerosus the commonest precursor for differentiated VIN. Both these conditions were not present in this case.Vaginal burning,pain and frequency of micturition lead to misinterpretation of the case as Genitourinary syndrome of menopause(GSM). This case is a prime example for the clause that any area with severe redness or whitish plaques that were clearly demarcated from the surrounding normal skin ,and cases not responding to routine treatment should arouse the suspicion of VIN.

Figure 1:

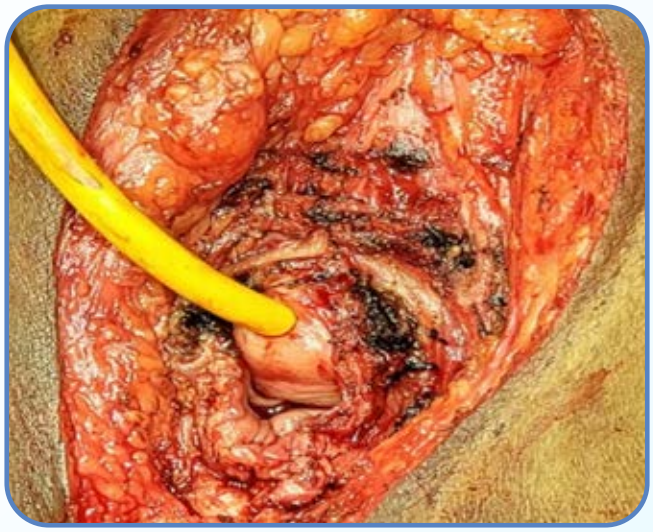

Figure 2:

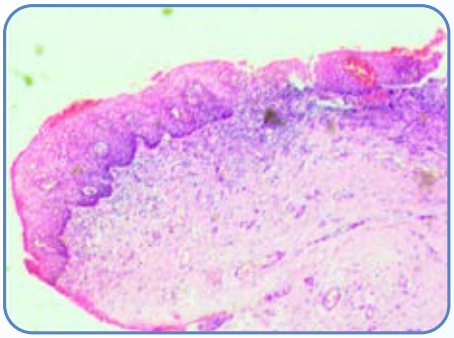

Figure-2a:
4X(H& E stain)

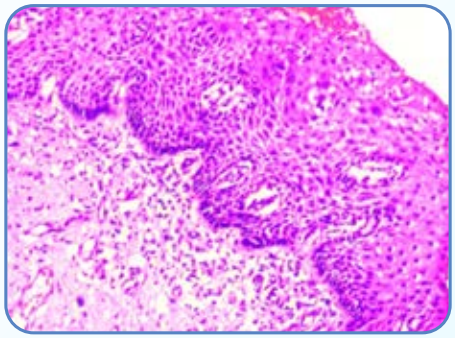

Figure-2b:
10X(H& E stain)

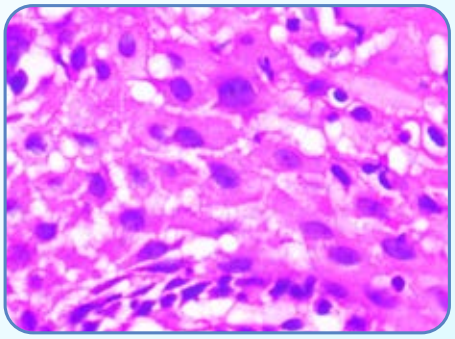

Figure-2c:
40X (H& E stain)

Answer to Quiz:

1. d	**2. a**	**3. b**	**4. a**	**5. d**
6. b	**7. d**	**8. b**	**9. b**	**10. c**

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