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Case Series

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Vulvar Cancers and Precancerous Lesions - Surgical Management with Reconstructive Strategies: A Case Series of 4 Patients

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Abstract

Vulvar cancer constitutes 5% of the malignancies of the female genital tract and 95% of the vulvar cancers are squamous cell carcinoma, followed by melanoma, sarcoma and basalioma. Pruritus is the most common and long-lasting reported symptom of vulvar cancer, followed by vulvar bleeding, discharge, dysuria, and pain. Diagnosis is confirmed by biopsy. The gold standard treatment of vulvar cancer is radical vulvectomy, with wide local excison of the lesion ensuring clearing margins along with enbloc resection of the inguinal lymph nodes. Vulvar intraepithelial neoplasia is a non-invasive squamous lesion, a precursor of vulvar squamous cell cancer. Clinically vulvar precancerous lesions may be flat, elevated, papulated or raised with the presence of ulcers or erosions. A thorough examination of the vulva, perineum, perianal, and anal regions, including the cervix and vagina, is essential to look for multicentricity. A good biopsy from the suspicious areas is confirmatory of diagnosis, and multiple punch biopsies should be performed for large, multicentric, and multi-colored lesions. Excisonal surgery is the treatment of choice for vulvar precancerous lesions of any type. we report 4 cases of vulvar lesions, 2 of which are vulvar cancer and two precancerous lesions of the vulva which we have diagnosed and treated in our center.

Keywords: ***Vulvar Neoplasms, Squamous Cell Carcinoma, Vulvar Intraepithelial Neoplasia, Human Papillomavirus Infections, Vulvectomy.***

Introduction

Vulvar cancer constitutes 5% of the malignancies of the female genital tract and is 4th in order of the cancers that affect the female genitalia after cancers of uterus, ovary and cervix. Ninety five percent of the vulvar cancers are squamous cell carcinoma, followed by melanoma, sarcoma and basalioma. Vulvar cancer can be classified into two groups according to predisposing factors: the first type correlates with an HPV infection and occurs mostly in younger patients. The second group is not HPV associated and occurs often in elderly women without neoplastic epithelial disorders. Pruritus is the most common and long-lasting reported symptom of vulvar cancer, followed by vulvar bleeding, discharge, dysuria, and pain. The confirmation of diagnosis is attained by a biopsy. The gold standard treatment of vulvar cancer is radical vulvectomy, with wide local excison of the lesion ensuring clearing margins along with enbloc resection of the inguinal lymph nodes [1]. A more conservative approach is a wide local excision of the lesion followed by sentinel lymph node biopsy of the inguinal station.

Vulvar precancerous lesions or Vulvar intraepithelial neoplasia (VIN) is a non-invasive squamous lesion that is a precursor of vulvar squamous cell cancer (**Table 1 & 2**) [2]. Differentiated VIN (dVIN) or DEVIL (Differentiated Exophytic Vulvar Intraepithelial Lesion) and usual VIN (uVIN) are the classifications of VIN. While dVIN is associated with other vulvar inflammatory disorders, such as lichen sclerosis, the more prevalent uVIN is associated with an underlying human papillomavirus infection. Patients with differentiated VIN have an increased risk of developing invasive malignancies.

Table 1: The 2015 International Society for the study of vulvovaginal disease terminology of vulvar squamous intraepithelial lesions.

LSIL of the vulva (vulvar LSIL, flat condyloma, or HPV effect)
HSIL of the vulva (VHSIL, VIN usual type)
dVIN

LSIL, low grade squamous intraepithelial lesion; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion;

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VHSIL, vulvar high-grade squamous intraepithelial lesions; VIN, vulvar intraepithelial neoplasia; dVIN, differentiated-type vulvar intraepithelial neoplasia.

Table 2: The 2020 World Health Organization tumor classification

	Classification
HPV-associated squamous intraepithelial lesions	Low-grade squamous intraepithelial lesion of the vulva High-grade squamous intraepithelial lesion of the vulva
HPV-independent VIN	Differentiated vulvar intraepithelial neoplasia Differentiated exophytic vulvar intraepithelial lesion Vulvar acanthosis with altered differentiation

Low grade squamous intraepithelial lesions (LSIL) are widespread in the general population and do not progress to invasive malignancies [3,4]. Conversely, VHSIL, which are 2.5-8.8 times more prevalent than LSIL per 100,000 women annually, have the potential to progress to invasive cancers [5-7]. Clinically vulvar precancerous lesions may be flat, elevated, papulated or raised with the presence of ulcers or erosions. A thorough examination of the vulva, perineum, perianal, and anal regions, including the cervix and vagina, is essential to look for multicentricity. A good biopsy from the suspicious areas is confirmatory of diagnosis, and multiple punch biopsies should be performed for large, multicentric, and multi-colored lesions. Excisonal surgery is the treatment of choice for vulvar precancerous lesions of any type, though high potency topical corticosteroids and ablative procedures may be tried in LSILs.

Here we report 4 cases of vulvar lesions, 2 of which were vulvar cancer and two precancerous lesions of the vulva which we have diagnosed and treated in our center.

Case Reports

Case 1: A case of Squamous cell carcinoma of the vulva

A 90-year-old female presented to us with pruritis and reddish ulcer over the right vulval area for one month duration. She had no comorbidities. On examination, a 2x2cms reddish indurated ulcer with elevated edges was seen on the right labia minora not extending till the urethral opening (Figure 1a). There was minimal discharge over the ulcer site. An incisional biopsy confirmed squamous cell carcinoma. Positron emission tomography (PET) scan showed an fludeoxyglucose (FDG) avid heterogeneously enhancing ill-defined soft tissue density lesion at the right vulvar region measuring 2x1.7x1.7cms, Standardized Uptake Value (SUV) 33.6. An FDG avid right inguinal lymph node of size 0.9x0.8cms with SUVmax 14.5 and few subcentimetric lymph nodes were noted.

She underwent a radical right vulvectomy, wide local excison of the ulcerated area with clear margins. Primary closure of the wound edges was done using Trusynth plus neo antimicrobial triclosan coated polyglactin 910 sutures (Healthium Medtech, India) using the surrounding lax soft tissue (Figure 1b). A right Superficial inguinal lymph node dissection was done and oxidised regenerated cellulose (Clinicel fibrillar, Healthium Medtech, India) was used to achieve hemostasis from the lymph node beds. The histopathology was vulvar squamous cell carcinoma, not otherwise specified (NOS), measuring 2.4cms in maximum dimension with all margins free of tumour and 2 out of 12 resected inguinal nodes were positive for malignant deposits without any periadenitis. The primary wound area healed well, and she had no lymphoedema post inguinal dissection. She was subjected to post operative RT in view of lymph node disease.

Figure 1a: A 2x2cms reddish indurated ulcer with elevated edges on the right labia minora

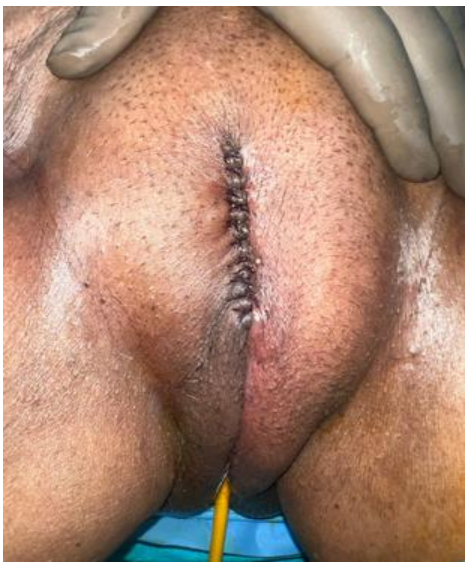

Figure 1b: Primary closure of the wound edges

Case 2: A case of Differentiated Vulvar intraepithelial lesion – dVIN or DEVIL

An 80-year-old lady presented to us with itching, soreness and cauliflower like lesion over the vulva for the last 6 months. She had no discharge from the lesion. She was diabetic and hypertensive. She had no previous vaginal disease. On examination, a whitish, proliferative, cauliflower-like growth with black speckles is seen involving both the labia majora and minora on either side (Figure 2a). The lesion on the right side was just extending till the urethral opening but not involving the urethra. clinically there were no palpable inguinal nodes.

Three incisional biopsies were attained from multiple sites of the proliferative lesion and were all diagnosed as differentiated vulvar intraepithelial lesion. The patient was subjected to an excisional surgery where the entire lesion was excised with a small margin of normal tissue. Oxidised regenerated cellulose (Clinicel knitted) was used to achieve the hemostasis of the surgical bed and primary closure was done using Trusynth plus neo antimicrobial triclosan coated polyglactin 910 sutures (Figure 2b). Foleys was

retained for 3 weeks in view of the sutures taken to the urethral opening on closure of the wound. The patient had no post operative wound complications. The final histopathology was confirmatory of Differentiated vulvar Intra epithelial lesion (Figure 2c). She was kept on 3 monthly observations without any further treatment.

Figure 2a: whitish, proliferative, cauliflower-like growth with black speckles is seen involving both the labia majora and minora.

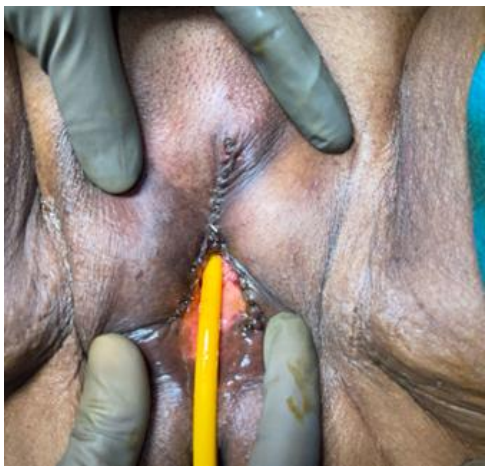

Figure 2b: Wound closure using Trusynth plus neo suture.

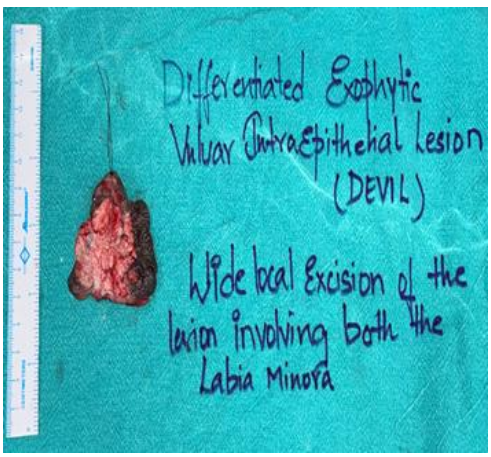

Figure 2c: Specimen of Differentiated vulvar Intra Epithelial lesion.

Case 3: A case of Pagets Disease of the Vulva

A 55-year-old female presented with complaints of whitish patch in the right vulval region for 2 months duration associated with history of itching. No known comorbidities. On examination, a whitish patch of size 2x2cms in the right vulvar region, with irregular margins was noted (Figure 3a). There was no surface nodularity. Incisional biopsy was suggestive of Paget's Disease. An upper gastrointestinal (GI) endoscopy, lower GI endoscopy, both breast mammogram and a whole-body PET CT was done to rule out Paget's disease elsewhere. A wide local excision of the lesion is done (Figure 3b) followed by VY transposition flap reconstruction of the defect (Figure 3c) using antimicrobial triclosan coated polyglactin 910 sutures (Trusynth plus neo) and oxidised regenerated cellulose (Clinicel knitted) was used to achieve the hemostasis of the surgical bed. There were no post operative wound complications. Patient was asked to follow up every 6 months for a period of 2 years.

Figure 3a: A whitish patch of size 2x2cms in the right vulvar region, with irregular margins.

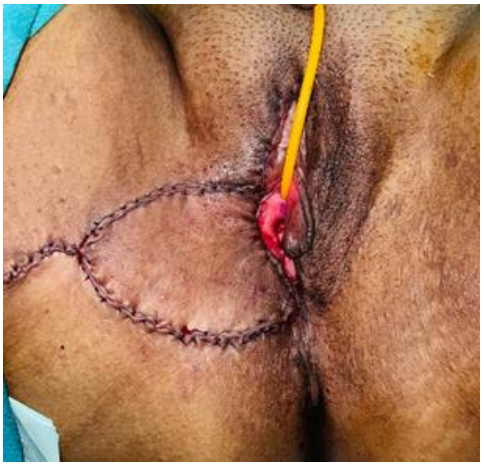

Figure 3b: Wide local excision of the lesion

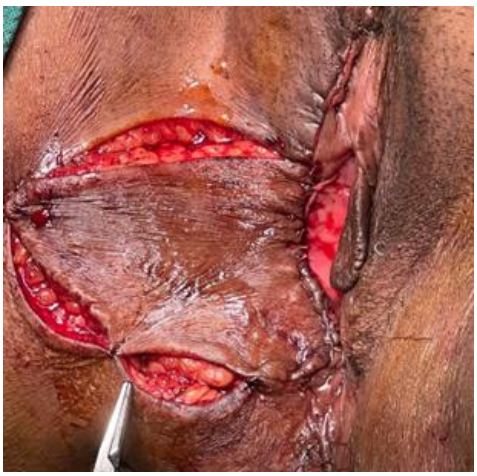

Figure 3c: VY transposition flap reconstruction of the defect

Case 4: A case of High grade squamous intraepithelial lesion of the vulva

A 61-year-old female presented with a whitish patch over the right vulvar region for past 2 months. She had history of itching over the lesion. On examination, there was whitish patch over the right labia of size 2x2cms with the surface being irregular and crusted (Figure 4a). An incision biopsy done from the edge of the lesion was suggestive of a High Grade Squamous Intraepithelial lesion. Whole body PET CT was suggestive of low FDG uptake [SUVmax 3] at the site of lesion with no significant inguinal or pelvic lymphadenopathy. Patient underwent an excision biopsy of the lesion with primary closure of the edges (Figure 4b & 4c) using antimicrobial triclosan coated polyglactin 910 sutures (Trusynth plus neo). Post operative histopathology was suggestive of HSIL. She was suggested a follow up every 6 months for 2 years.

Figure 4a: Whitish patch over the right labia of size 2x2cms with irregular and crusted surface.

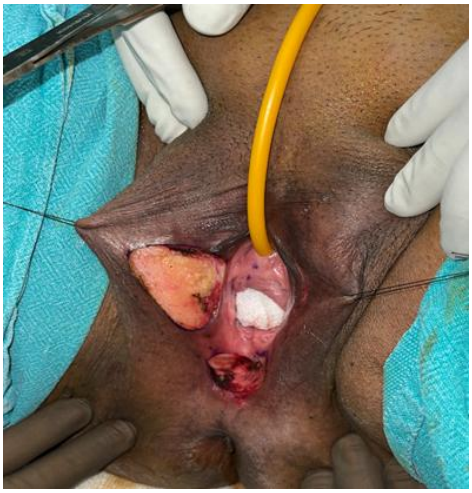

Figure 4b: Excision biopsy of the lesion.

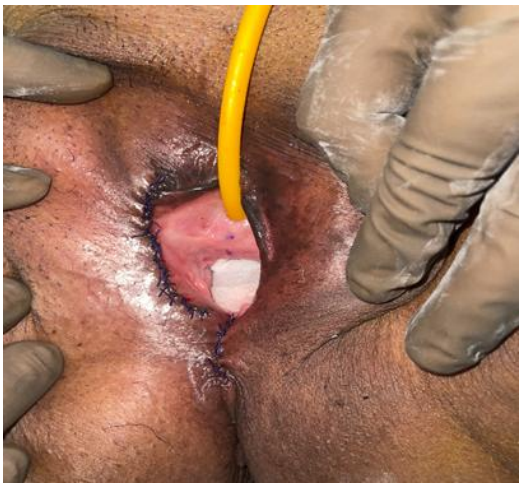

Figure 4c: Primary closure of the wound

Discussion

The vulva is comprised of the female external genitalia, which include the labia majora and minora, clitoris, vestibule, vaginal introitus, and urethral meatus. The vulva serves to direct urine flow, prevent foreign bodies from entering the urogenital tract, as well as being a sensory organ for sexual arousal. The internal pudendal artery and, to a lesser extent, the external pudendal artery are responsible for the blood supply. Most of the vulva is drained by lymphatics that pass laterally to the superficial inguinal lymph nodes. Vulvar cancer is the cancer of the vulva, and the most common type is the keratinizing squamous cell carcinoma followed by basalioma, melanoma and sarcoma [1].

There are two main pathological pathways that lead to vulvar SCC [2]: a) Keratinizing SCC usually occurs in older women and is often associated with lichen sclerosus and/or differentiated vulvar intraepithelial neoplasia (dVIN) and b) Warty/basaloid SCC generally occurs in younger women, is caused by persistent infection with oncogenic strains of HPV (particularly HPV 16, 18, 31 and 33), and has SIL as its precursor lesion.

Presenting symptoms and Diagnosis: while vulvar cancer may be asymptomatic, most women present with vulvar pruritus or pain or have noticed a lump or ulcer. They may also have abnormal bleeding or discharge, and many will have a history of vulvar symptoms due to underlying lichen sclerosus. Advanced vulvar cancer may present with a lump in the groin due to lymph node metastases. Any suspicious lesions are subjected to an incisional biopsy which is an office procedure. CT or MRI scan of the pelvis and groins may be helpful, especially for locally advanced tumors, to detect any enlarged lymph nodes in the groins or pelvis, erosion into underlying bone, or other metastases [3]. 18F fluorodeoxyglucose (18F-FDG) positron emission tomography with computed tomography (PET-CT) can more effectively assess and detect inguinofemoral lymph node involvement compared with CT.

Table 3: New (2021) FIGO staging for carcinoma of the vulva

Stage		Description of vulvar cancer – FIGO 2021
I		Tumor confined to the vulva
	IA	Tumor size ≤2 cm and stromal invasion ≤1 mm[a]
	IB	Tumor size >2 cm or stromal invasion >1 mm[a]
II		Tumor of any size with extension to lower one-third of the urethra, lower one-third of the vagina, lower one-third of the anus with negative nodes
III		Tumor of any size with extension to upper part of adjacent perineal structures, or with any number of nonfixed, nonulcerated lymph node
	IIIA	Tumor of any size with disease extension to upper two-thirds of the urethra, upper two-thirds of the vagina, bladder mucosa, rectal mucosa, or regional lymph node metastases ≤5 mm

	IIIB	Regional[b] lymph node metastases >5 mm
	IIIC	Regional[b] lymph node metastases with extracapsular spread
IV		Tumor of any size fixed to bone, or fixed, ulcerated lymph node metastases, or distant metastases
	IVA	Disease fixed to pelvic bone, or fixed or ulcerated regional[b] lymph node metastases
	IVB	Distant metastases

[a]*Depth of invasion is measured from the basement membrane of the deepest, adjacent, dysplastic, tumor-free rete ridge (or nearest dysplastic rete peg) to the deepest point of invasion.*
[b]*Regional refers to inguinal and femoral lymph nodes.*

Surgical Management of Vulvar Cancer

The gold standard of treatment for early vulvar cancers is radical wide local excision of the tumor. Associated preinvasive disease should also be excised to exclude any other areas of invasion, and to prevent new tumors arising in the so-called "abnormal field". While the surgeon should aim for surgical margins of 2 cm to achieve pathological margins of at least 8 mm (allowing for shrinkage of the fixed tissue), it is now recognized that many "recurrent" vulvar cancers are probably new tumors that have developed in the surrounding abnormal tissue, rather than recurrences due to inadequate margins [4]. The deep margin of the excision should be the inferior fascia of the urogenital diaphragm and, if necessary, the distal 1 cm of the urethra can be removed to achieve an adequate margin, without compromising urinary continence [5]. With most tumors, primary closure is possible, but consideration should be given to reconstructive surgery for closure of large defects, and for maintenance of vaginal function. When reconstruction is necessary, three of the most utilized flaps include the V-Y flap, rhomboid flap, and gluteus maximus myocutaneous flap [6].

The appropriate management of the groin lymph nodes is the most important factor in reducing mortality from early vulvar cancer, as recurrences in the groin are associated with poorer survival. The current standard involves resection of the primary tumor and lymph nodes through separate incisions [7]. Both the inguinal and femoral nodes should be removed, as inguinal node dissection alone is associated with a higher incidence of groin recurrence [8]. While some reviews have suggested that radiation alone can control microscopic groin disease [9], a small, randomized trial suggested that groin dissection, with postoperative irradiation for patients with positive nodes, is superior to groin irradiation [10]. All women who have Stage IB or resectable Stage II cancers should have an inguinofemoral lymphadenectomy. Patients who have tumors closer to (<2 cm) or crossing the midline, especially those involving the anterior labia minora, and those women who have very large lateral tumors (>4 cm), or positive ipsilateral nodes, should have a bilateral groin node dissection [11]. Indications for a sentinel node procedure, as per the GROINSS-V study [12]:

A. Unifocal tumors confined to the vulva
B. Tumors less than 4 cm in diameter
C. Stromal invasion more than 1 mm
D. Clinically and radiologically negative groin nodes

When an ipsilateral sentinel lymph node is not detected, a complete ipsilateral inguinofemoral lymphadenectomy must be done. In addition, if an ipsilateral sentinel lymph node is positive, a complete bilateral inguinofemoral lymphadenectomy is recommended [13]. Indications for pelvic and groin irradiation in patients with positive groin nodes [14]:

A. Presence of extracapsular spread.
B. Two or more positive groin nodes.

All patients who have a positive sentinel lymph node (one or more positive nodes), besides undergoing a full inguinofemoral lymph node dissection, should receive radiotherapy to the groins and pelvis. In terms of radiotherapy, radiation fields during external beam radiotherapy (EBRT) should include the inguinofemoral and external and internal iliac lymph nodes in most patients. If there are many or bulky positive inguinal nodes, or if pelvic node metastases are suspected, the upper border of the radiation field might be extended [15]. Patients with close (less than 5 mm) surgical margins may also benefit from postoperative radiotherapy, if it is not possible to re-excise the margins.

In cases of anorectal, urethral, or bladder involvement, tumor that is fixed to the bone or gross lymph node involvement, chemoradiation is recommended. Cisplatin mono, 5-FU, or also mitomycin C in combination with radiation therapy should be performed [1].

Vulvar precancerous lesions

Vulvar intraepithelial neoplasia (VIN) is a non-invasive squamous lesion that is a precursor of vulvar squamous cell cancer. Differentiated VIN (dVIN) and usual VIN (uVIN) are the classifications of VIN. While dVIN is associated with other vulvar inflammatory disorders, such as lichen sclerosis, the more prevalent uVIN is associated with an underlying human papillomavirus infection. Patients with differentiated VIN have an increased risk of developing invasive malignancies. Persistent infection with high-risk or oncogenic HPV (mostly HPV types 16, 18, and 33) typically cause of uVIN [16]. This subtype predominantly affects younger women and exhibits a multifocal pattern. Although less common, approximately 2-5% of all VIN lesions are of the differentiated type, dVIN has the highest potential for malignancy. It is linked to LS but is unrelated to HPV and typically affects older women.

To confirm the diagnosis, a biopsy of the most suspicious part of the lesion should be performed under local anesthesia. One or more lesions may be present, with keratotic, roughened surface, sharp edges and a papular, elevated appearance displaying white, red, grey, blue, or brown colors.

Excisional surgery is typically necessary for dVIN. Both surgical excision (ranging from superficial vulvectomy to wide local excision) and ablative therapy (argon beam coagulation, carbon dioxide [CO_2] laser vaporization, and cavitational ultrasonic surgical aspiration) are options for treating uVIN. To rule out malignancy, multiple representative biopsies must be performed first. According to van Esch *et al* [17], women who underwent surgery had a lower recurrence rate (48.8%) than that of patients who underwent laser ablation (56.0%) or combined laser and excision (66.7%). Medical therapy (imiquimod or cidofovir) may be considered as well for uVIN. Both vulvar cancers and precancerous lesions are followed up for a period of 2 years at 3 monthly intervals, and 6 monthly intervals for a period of 5 years to look for recurrence.

Conclusion

The management of vulvar cancers and precancerous lesions requires a multidisciplinary approach. Early detection through regular examinations and biopsies, followed by appropriate surgical treatment (wide excision or radical vulvectomy), significantly

improves outcomes. In addition, reconstructive techniques are essential for restoring the quality of life for patients undergoing extensive surgical procedures. Monitoring for recurrence, especially in high-risk groups like those with HPV-associated VIN or dVIN, remains a key aspect of post-treatment care. This case series underscores the importance of individualized treatment plans, addressing both oncological control and post-operative reconstruction to achieve optimal results for patients with vulvar malignancies and precancerous conditions.

Abbreviations

HPV- human papillomavirus
VIN- Vulvar intraepithelial neoplasia
dVIN- differentiated Vulvar intraepithelial neoplasia
uVIN- usual Vulvar intraepithelial neoplasia
DEVIL- Differentiated Exophytic Vulvar Intraepithelial Lesion
LSIL- low grade squamous intraepithelial lesion
HSIL-high-grade squamous intraepithelial lesion
VHSIL-vulvar high-grade squamous intraepithelial lesions
PET-Positron emission tomography
FDG-Fludeoxyglucose
SUV-Standardized Uptake Value
NOS-Not Otherwise Specified
CT- Computer Tomography
GI-Gastrointestinal
SCC- Squamous cell carcinoma
MRI-Magnetic Resonance Imaging
18F-FDG-18F fluorodeoxyglucose
FIGO-International Federation of Gynecology and Obstetrics
EBRT- external beam radiotherapy
5-FU-fluorouracil

Declarations

Ethical Approval and Consent to participate

NA and consent taken

Consent for publication

Taken

Availability of supporting data

Available on corresponding author upon a responsible request.

Competing interests

None

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