Vulvar Sarcomatoid Squamous Cell Carcinoma: A Rare Entity

Abstract

Vulvar squamous cell carcinoma with sarcomatoid features is an extremely rare histological variant of squamous cell carcinoma with co-existence of both epithelial and mesenchymal features. A 70-year-old woman presented with genital lesions for 4 months with associated burning and pain. Examination revealed well-defined bilaterally symmetrical hyperpigmented plaques on labia majora, fleshy erythematous growth on labia minora. Biopsy from the fleshy mass was suggestive of sarcomatoid malignancy. However, immunohistochemistry was positive for cytokeratin AE1/AE3 and negative for desmin and smooth muscle actin. Biopsy from hyperpigmented plaque was suggestive of Bowens disease. On the basis of histopathology and immunohistochemistry findings, diagnosis of vulvar sarcomatoid squamous cell carcinoma with Bowens disease was made and patient was started on external beam radiation therapy. Sarcomatoid squamous cell carcinoma of vulva is very rare cancer that has an aggressive and fatal course. Diagnosis has traditionally been difficult due to a large ratio of sarcomatous to squamous cell component. Due to its rarity, there are no distinct guidelines to direct therapy and care.

Keywords: *Bowens disease, malignancy, sarcomatoid, squamous cell carcinoma, vulva*

Gayatri Gund, Akansha Chadha, Atul Dongre, Chitra Nayak

Department of Dermatology, Topiwala National Medical College and BYL Nair Hospital, Mumbai, Maharashtra, India

Introduction

Squamous cell carcinoma (SCC) with sarcomatoid feature is a histological variant of SCC with coexistence of both epithelial and mesenchymal features. Sarcomatoid squamous cell carcinoma (SSCC) is mainly found in the upper aerodigestive tract with the larynx being the most common site[1] and its occurrence in female genital tract is very rare.[2] Steeper *et al.*[3] reported the first case of vulvar SCC with sarcomatoid features. There are various hypotheses about SSCC but the most accepted is the transformation from the SCC component into a spindle cell cancer.[1] Diagnosis is essentially made on histopathological examination. Early diagnosis is important to increase the patient survival.

Here, we have described a case of vulval SSCC without metastasis.

Case Report

A 70-year-old multiparous, postmenopausal woman, present to our outpatient department with 4-month history of rapidly progressing, painful raised lesion on the genitals. There was no history of vaginal discharge and she had normal bowel bladder habits. She denied any addiction or high-risk sexual behavior. There was no major medical or surgical illness in the past.

Genital examination revealed well defined, firm, bilaterally symmetrical hyperpigmented plaques on both labia majora and fleshy erythematous growth on both labia minora [Figure 1a and b]. There was no evidence of oozing, bleeding, or ulceration and no significant inguinal lymphadenopathy. The cervix, vagina, and per rectal examination were normal. Her HIV, HBsAg, and anti-HCV antibodies were nonreactive and PAP (Papanicolaou test) smear showed normal cytology.

Histopathological evaluation of the biopsy from the hyperpigmented plaque on labia majora revealed acanthosis, some papillomatosis with full thickness keratinocyte atypia [Figure 2a]. On high power there was increased N:C (nuclear:cytoplasmic) ratio, nuclear hyperchromasia, and nuclear crowding but basal layer was intact [Figure 2b], consistent with Bowen's disease. Biopsy from fleshy mass on labia minora showed predominantly spindle-shaped cells infiltrating the

How to cite this article: Gund G, Chadha A, Dongre A, Nayak C. Vulvar sarcomatoid squamous cell carcinoma: A rare entity. Indian Dermatol Online J 2023;14:856-60.

Received: 28-Dec-2022. **Revised:** 20-Mar-2023. **Accepted:** 21-Mar-2023. **Published:** 05-Oct-2023.

Address for correspondence:
Dr. Atul Dongre, Department of Skin and V.D., OPD 14 (37), Second Floor, Topiwala National Medical College and BYL Nair Charitable Hospital, Dr A L Nair Road, Mumbai Central - 400008, Maharashtra, India.
E-mail: atul507@yahoo.co.in

Access this article online

Website: https://journals.lww.com/idoj

DOI: 10.4103/idoj.idoj_696_22

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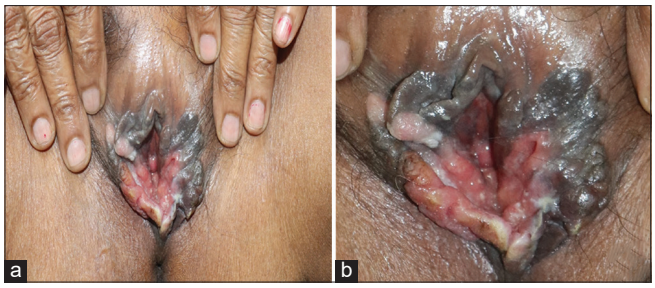

Figure 1: (a and b) Well defined, firm, bilaterally symmetrical hyperpigmented plaques on both labia majora and fleshy erythematous growths on both labia minora

dermis [Figure 3a and b] with storiform pattern and few atypical keratinocyte-like cells in the dermis [Figure 3c]. As spindle cell component was predominant, the tumor was initially thought to reflect leiomyosarcoma. However, on immunohistochemistry (IHC), these spindles cells were positive for cytokeratin AE1/AE3 [Figure 4] and negative for desmin [Figure 5a] and smooth muscle actin (SMA) [Figure 5b]. So, on the basis of histomorphology and IHC, diagnosis of sarcomatoid SCC was made. Magnetic resonance imaging pelvis and positron emission tomography (PET)-Scan was normal ruling out metastatic disease. The patient had received daily external beam radiotherapy for a month followed by brachytherapy of two sessions till date with improvement of lesions.

Discussion

Vulvar cancer represents only 3% to 5% of malignancies of female genital tract and 90% to 92% are of the squamous cell type.[4] There are several histological variants of SCC of vulva like adenoid squamous carcinoma, basosquamous cell carcinoma, sarcomatoid, and metaplastic carcinoma.[5]

SSCC is mainly found in upper aerodigestive tract with the larynx being the most common site. In female genital tract, cervix is the most common site and vulval disease is rare with incidence of 1%. This variant consists of admixtures of epithelial and mesenchymal looking cells and different terms are used to describe it, for example, carcinosarcoma, pseudo-sarcoma, and spindle cell carcinoma, to indicate its biphasic features.[6]

Risk factors for SSCC are same as for SCC which include human papilloma virus (HPV) infection, high-risk sexual behavior, cigarette smoking, immunosuppression, and precursors like Bowen disease in the genitalia.[1]

SSCC of female genital tract usually occur in postmenopausal women and present as ulcero-proliferative, friable, polypoidal, or necrotic mass with nonspecific symptoms like fatigue, anaemia, pelvic pain, weight loss, and loss of appetite; in small percentage the disease is asymptomatic. Due to its aggressive behaviour, most of the time patient presents in the metastatic stage.

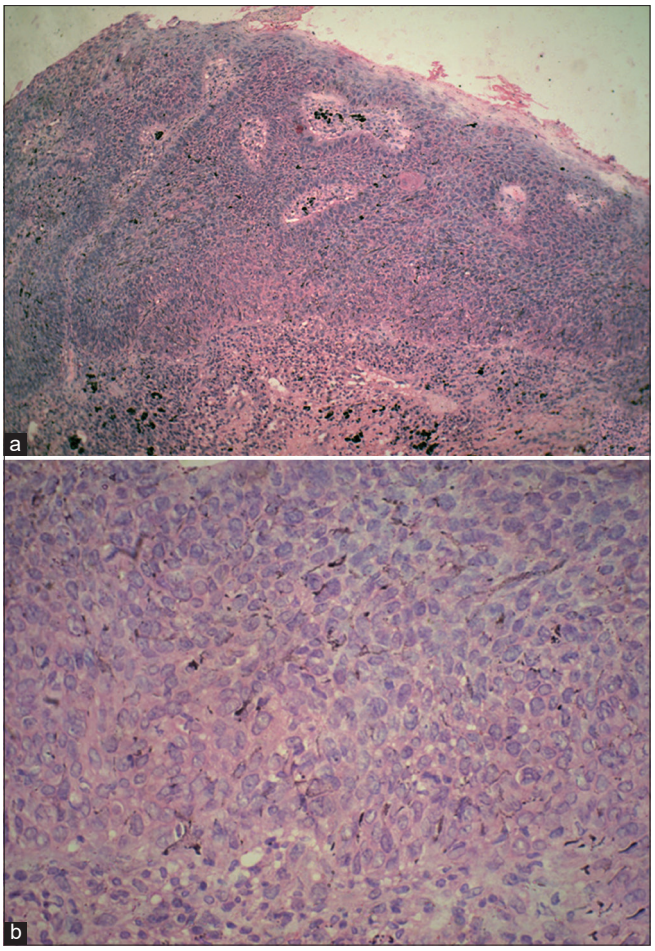

Figure 2: (a) Hyperpigmented plaque on labia majora revealed acanthosis, some papillomatosis with full thickness keratinocyte atypia (H and E, 100x) (b) On high power, there was increased N: C ratio, nuclear hyperchromasia, nuclear crowding with "wind blown" appearance. Basal layer was intact, consistent with Bowen's disease (H and E, 400x)

Histopathological diagnosis of SSCC rests upon demonstrating regions of classic SCC morphology merging with a prominent spindle cell component. When the spindle cell component is predominant without presence of classic squamous cells, the diagnosis is challenging and IHC is important to rule out other spindle cell malignancies. In our case, the spindle cell component was predominant and the lesions of Bowens disease present adjacent to the mass were clues to the diagnosis. Furthermore, immunohistochemistry of spindle cell was positive for cytokeratin AE1/AE3 and negative for SMA and desmin. As spindle cells were cytokeratin positive and SMA and desmin negative, it ruled out the other histological differentials of spindle cell tumor of vulva like amelanotic malignant melanoma, leiomyosarcoma, and malignant fibrous histiocytoma, arriving at the final diagnosis of sarcomatoid SCC. Usually, SSCC is positive for epithelial cell markers like cytokeratin and also for mesenchymal markers like SMA, desmin, and vimentin.[1] However, Lin *et al*. reported a case of SSCC with negative SMA,[7] like in our case. Many times it is seen that

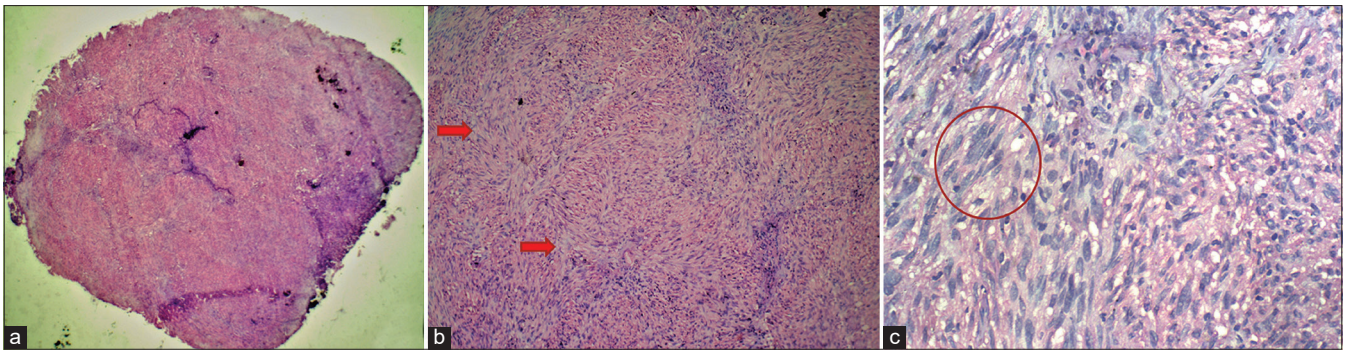

Figure 3: (a) Dermal infiltration (H&E, 40x) (b) Predominately shows spindle shaped cells in storiform pattern (Red arrow) (H&E, 100x) (c) Spindle shaped cells with storiform pattern and few atypical keratinocyte-like cells i.e., spindle cells (Red circle) (H&E, 400x)

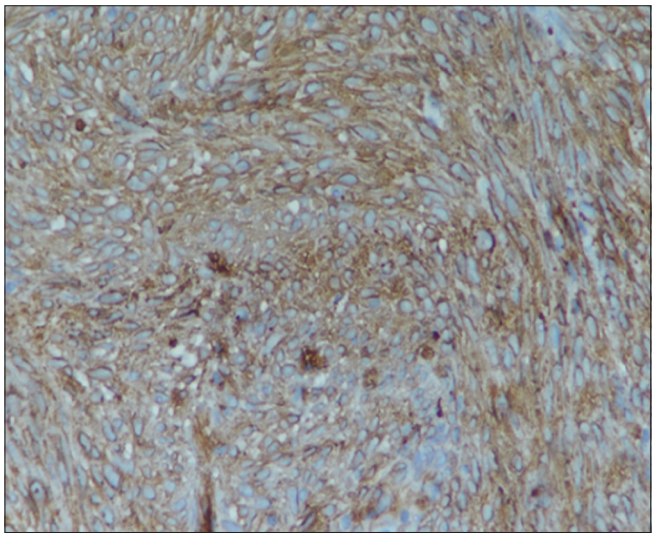

Figure 4: Spindle cell was positive for cytokeratin AE1/AE3 (IHC, 400x)

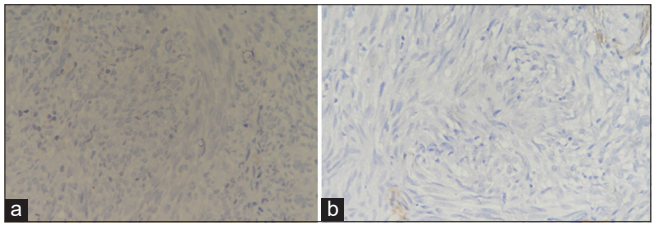

Figure 5: (a) Spindle cell was negative for desmin (IHC, 400x); (b) Spindle cell was negative for Smooth muscle actin (SMA) (IHC, 400x)

cytokeratin staining can be lost in spindle cells of SCC; hence, alternate stains like P63 and P40 which are more specific and can be helpful to confirm the squamous nature of the cells.

The comparison with other similar cases reported in the literature is depicted in Table 1.

Due to the rarity of this cancer, the International Federation of Gynecology and Obstetrics (FIGO) staging system that is used for SCC is also used for SSCC of the vulva, vagina, and cervix. This common staging system may not prove fruitful in the management of these patients as this variant is believed to be highly aggressive. As clinical staging ultimately guides therapy, a modified staging may be required.

These lesions are usually treated with radical surgery followed by radiation therapy and/or chemotherapy. Brown *et al*. (2003) successfully treated all stage I and stage II women with radiation therapy alone.[8] In our case, considering age of the patient and postoperative morbidity, anesthesia-related complications, and proven efficacy of radiation therapy, the patient was treated with daily external beam radiotherapy for a month followed by brachytherapy of two sessions without recurrence till date.

Good predicators of survival include younger age, early stage, and grossly carcinomatous elements and those who are diagnosed at stage-IV have survival rate of 5% at 5 years. Manglani *et al*. reported that superficial lesions and those with polypoidal growth have a low metastatic rate and good prognosis, while those with sessile configuration demonstrating merging of squamous to sarcomatous zones are associated with a poor prognosis.[9] But overall SSCC of vulva is a very rare cancer with an aggressive clinical course and is associated with poor patient outcome.[6,10]

Due to its rarity, there is no distinct staging or guidelines to direct therapy and care, so a collection and close study of these cases would be extremely useful in singling out and identifying the best treatment possible. As HPV is a risk factor of SSCC, with better screening modalities and use of HPV vaccine, one can expect the reduction in SSCC cases of female genital tract.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Table 1: Vulvar sarcomatoid squamous cell carcinoma- Review of literature

Authors	No of cases	Histopathology	Immuno histochesmistry	Inguino-femoral lymph node metastasis	Treatment
Way[10]	6	Unusual type epithelioma	NA	NA	Surgery
Gosling *et al*,[11]	2	Spindled squamous cell carcinoma	NA	NA	Surgery
Copas *et al*,[12]	1	Poorly differentiated spindled cell carcinoma	NA	+	Radical vulvectomy with bilataeral groin and pelvic lymph node dissection followed by radiochemotheray
Steeper *et al*,[3]	1	Pseudosarcomatous squmous cell carcinoma	Polyclonal antikeratin antibody demonstrating the epithelial nature of the sarcoma-like cells	NA	Radiation therapy followed by vulvectomy
LiVolsi *et al*,[5]	2	Carcinoma with sarcomatoid feature	NA	NA	NA
Santeusanio *et al*,[13]	1	Poorly differentiated carcinoma with sarcoma like feature	Sarcomatoid-looking cells stained positive for intermediate filament keratin polypeptides of stratified epithelium	+	Radical vulvectomy with bilateral femoral-inguinal lymph node dissection.
Parham *et al*,[14]	1	Mixed soft tissue sarcoma with atypical squamous cell	Tumour stroma cells positive for AE1/AE3, vimentin and desmin	NA	Local excision
Cooper *et al*,[15]	1	Sarcomatoid squmous cell carcinoma	Epithelial and spindle cells positive for cytokeratin AE1/AE3. Smooth muscle actin and desmin was negative	+	Radical vulvectomy with bilateral inguinal lymphadenectomy followed by radiotherapy
Choi *et al*,[2]	1	Poorly differentiated SCC with extensive sarcomatoid features	Spindle cells positive for cytokeratin AE1/AE3 and smooth muscle actin	-	Radical local excision with bilateral inguinal lyphadenectomy
Loizzi *et al*,[16]	1	Carcinosarcoma	Positive for vimentin, actin, and cytokeratin	-	Radical vulvectomy with central ingunal lymphadenectomy
Petrillo *et al*,[6]	1	Sarcomatoid squamous cell carcinoma	Positive for smooth muscle actin	+	Radical vulvectomy with bilateral inguinal lymphadenectomy followed by chemotherapy
Present case	1	Sarcomatoid squamous cell carcinoma	Cytokeratin AE1/AE3 positive, negative for desmin and smooth muscle actin	-	External beam radiotherapy for a month followed by brachytherapy

NA=Not available

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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