

Carcinoma vulva: Ten years experience in a teaching institution of North India

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ABSTRACT

Introduction: Vulvar carcinoma is primarily a disease of post-menopausal women. Surgery is a primary treatment strategy. Chemotherapy and radiotherapy are a part of multimodal therapy. Presently, there is a shift towards neoadjuvant chemotherapy or radiotherapy so as to decrease the surgical morbidities. **Objective:** To study the surgical outcome and prognostic factors in Ca vulva patients. **Methodology:** A retrospective analysis of 19 vulvar cancer patients, surgically treated at a teaching institution of Punjab (2009–2019). **Results:** Mean age of the patients was 60.95 years. Ulcerative swelling (89.5%) over labia majora (73.7%) was the main presenting symptom. Radical vulvectomy-bilateral IFLN dissection was performed in 74% patients, hemivulvectomy-unilateral IFLN dissection in 21% patients and wide local excision in one patient. Squamous cell carcinoma was detected in all, and one had verrucous carcinoma. Thirty-seven per cent patients had FIGO stage III disease, 31.5% - stage II and 31.5% - stage I. On HPE, 78.57% (11/14) patients had positive nodes and two had ECS. Only 5/9 (55.5%) cases could receive PORT. Seven patients defaulted follow-up. Two developed nodal metastasis, and seven women developed recurrence. One patient with regional recurrence faced demise during RT course. In 10/19 regular follow-up patients, four are alive and disease free, five patients are on palliative chemoradiation, and one is undergoing adjuvant radiotherapy for regional recurrence. Estimated 5-year overall survival is 83.33%. **Conclusion:** Tumour stage, nodal positivity and nodal ECS were poor prognostic factors. Radical surgery-extensive groin node dissection causes significant morbidity; hence, studies evaluating the role of neoadjuvant treatment are needed so as to modify current treatment practices. HPV vaccination as a preventive measure and a thorough and extensive evaluation of patients with suspicious signs in vulvar disease is needed.

Keywords: Radical vulvectomy, radiotherapy, sentinel lymph node biopsy, squamous cell carcinoma

Introduction

Vulvar carcinoma is one among the rare female reproductive tract malignancies accounting for approximately 5% of female genital cancers.^[1] GLOBOCAN 2018 ranks vulvar cancer at 33rd position,^[2] and it accounts for 0.3% of all cancers among Indian women.^[3] Despite its rarity, it poses several challenges for gynaecologists and oncologists. The

cancer develops most frequently in post-menopausal women with median age of occurrence at 67 years.^[4] Advanced age, smoking, immune-compromised status and chronic skin diseases of the vulva such as lichen sclerosis, VIN (vulvar intra-epithelial neoplasia), Erythroplasia of Queyrat and human papillomavirus (HPV) infections are the major underlying risk factors.^[5] Immunization with quadrivalent HPV vaccine has been shown to be protective against vulvar carcinoma.^[6]

Vulvar cancer presents with varied features, ranging from a small nodule which later ulcerates, to small warty cauliflower

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growths on vulva. Women complaining of long-standing pruritus vulvae lesions over the perineum should be suspected of vulvar cancer.^[7]

FIGO 2008 laid down the revised surgical staging for carcinoma vulva on the basis of site and size of primary tumour, tumour extension, involvement of groin lymph nodes and tumour metastasis.^[8]

Treatment is decided on the basis of FIGO surgical staging and associated co-morbidities. Management involves surgical resection of the tumour, radiotherapy and chemotherapy. Patients with early stage disease (stage IA) are often managed with surgery alone, i.e., wide local excision.^[9] Adjuvant radiation therapy (RT) is offered to patients with close or positive margins or with more than one inguinal lymph node metastases to reduce the loco-regional recurrence and improve survival.^[10]

Surgical management of vulvar cancer from FIGO stage Ib includes resection of the loco-regional disease along with groin dissection commonly using triple incision technique.^[9,11] The most important prognostic factor is the presence and number of inguinal node metastases, other being extra-nodal tumour extension, tumour diameter, depth of invasion, tumour thickness, lympho-vascular space invasion, margin status, tumour grade and age.^[5]

Radiotherapy and chemotherapy^[12] are the additional or alternate treatment modalities for the management of vulvar cancer, especially for locally advanced and metastatic disease. Many patients who present in late age and have associated co-morbid conditions or patients with far advanced disease, distant metastases may not be suitable for aggressive treatments like radical surgery or chemoradiation. In such patients, definitive RT is an option for achieving remission.^[13]

Carcinoma vulva is predominantly seen in developing nations, but there is paucity of literature from India. Moreover, being a rare disease only a few prospective randomized trials are available. With this study, we aim to add our experience to the existing literature so that there can be advancement in treatment strategies chiefly targeting the morbidity and psychosexual sequelae associated with the disease course and the current management option, i.e., extensive groin dissection. This study focuses on the surgical treatment options, prognostic factors, post-operative complications, failure pattern and survival rates among patients with carcinoma vulva. On the basis of the results and surgical outcome, we believe that practitioners dealing with cases of vulvar lesions/ailments should keep a high index of suspicion of VIN or vulvar cancer so that the disease can be detected at the earlier stages. Through this study, we wish to spread patient awareness especially in developing nations about the HPV vaccination as a preventive measure and need for timely consultation and intervention in vulvar diseases for best patient outcome.

Materials and Methods

The present series is a retrospective analysis of cases diagnosed with carcinoma vulva who were surgically treated at Guru Gobind Singh Medical College & Hospital, Faridkot, Punjab, over a period of 10 years (2009–2019). The data was collected from medical record room of the hospital and follow-up records from the Outpatient Department of Obstetrics and Gynaecology and Radiotherapy. Nineteen patients with histologically proven diagnosis of vulvar cancer were treated surgically in our facility in a time frame of 10 years. Detailed study for demographic profile, presence of risk factors, stage of disease at the time of presentation, treatment modalities employed and disease outcome in terms of disease-free interval, complications and survival was done. Each patient's relevant investigations including pathological and radiological findings were noted. In our study, the type of surgical management ranged from wide local excision (WLE), hemivulvectomy (HV) to radical vulvectomy, with or without unilateral/bilateral inguofemoral node dissection and iliac node dissection was required. The data thus collected was analysed using appropriate statistical tests. Post-operative radiation therapy (PORT) was planned for indications such as positive or close (<8 mm) margins, lympho-vascular invasion and depth of tumour invasion >5 mm. Patients with more than one involved inguinal node, extracapsular extension or gross residual nodal disease were considered for PORT to both groins and the pelvis. Cases with carcinoma vulva not suitable for surgery (due to advanced age, associated medical co-morbidities or advanced stage) were managed with definitive RT or palliative RT (as found eligible) and were not included in the study.

Post-operative follow-up was done every three months for first two years, every six months for next three years and then yearly. Patients were evaluated for any symptoms indicating recurrence.

Results

The mean and median age of patients were 60.95 and 60 years, respectively (range: 39–105 years; SD: 13.91). All the patients were multiparous and had low socioeconomic status [Table 1]. The chief presenting complaints were ulcerative swelling (89.5%), pruritus (73.7%), pain (31.6%) and discharge (15.8%) in the genital area. The most predominant site of disease was labia majora extending to labia minora (73.7%, n = 14) followed by clitoris (21.05%, n = 4) and mons pubis (5.26%, n = 1). Four patients had clinically palpable inguinal lymph nodes, and seven patients had positive inguofemoral nodes on CT scan. Anaemia was the most common associated co-morbidity with 26.3% (n = 5) patients requiring preoperative blood transfusions. The mean haemoglobin was 10.7 (range: 7.6–14.3; SD: 1.8382). Three patients were hypertensive, and one had diabetes mellitus [Table 1]. Radical vulvectomy with bilateral inguofemoral lymph node dissection was done in 74% (n = 14) patients, and hemivulvectomy with unilateral inguofemoral lymph node dissection was done in 21% (n = 4) patients. Only one patient (5.26%) had undergone wide local excision [Table 2].

All patients had pathological R0 resections except one with positive margins. On histopathological examination, all the patients were found to have squamous cell carcinoma except one who was detected with verrucous carcinoma. On FIGO staging, majority of our patients had stage III disease (37%, n = 7) followed by stage II (31.5%, n = 6) and stage I (31.5%, n = 6) [Figure 1]. Among the patients who underwent bilateral inguinofemoral lymph node dissection (73.86%; n = 14), 78.57% (11/14) were found to be node positive and 21.42% (3/14) were found to be node negative [Table 3]. Patients who underwent U/L inguinofemoral lymph node dissection tested node negative on HPE. Adjuvant radiotherapy was indicated in total of nine patients (47.4%; 9/19) for the following indications: margin positivity in 1 patient, ECS (extracapsular spread) in two patients and more than one node positive in six patients. Only five out of nine (55.5%) patients received adjuvant radiotherapy because it was declined by two patients, and one patient with ECS had succumbed before radiotherapy could be administered and one patient with ECS was lost to follow up [Table 3].

Post-operatively 58% (n = 11) patients had developed wound infections at the site of inguinal incision which was conservatively managed with analgesics and antibiotics. Seroma formation

was seen in 53% (n = 10) cases and leg oedema in 10% (n = 2) patients [Table 4]. Conservative management was adopted involving multiple sittings of seroma aspiration and compression therapy for leg oedema cases. The complications had extended the mean hospital stay of patients up to 1.5 months.

Seven patients had defaulted in the follow-up period. At a median follow-up of 24 months (range: 6–48), a total of seven (31.57%) women had developed recurrence, five with local and two with regional recurrence. All the cases of local recurrence and one patient with regional recurrence had presented within 1 year of primary surgery and were subjected to adjuvant radiotherapy. Out of these, the patient with regional recurrence was in a chronic debilitated state and had faced demise during RT course. Another patient with regional recurrence developed the disease 3 years after the surgery and is currently undergoing radiotherapy. Two patients had developed nodal metastasis, at 5 and 7 months, respectively post-surgery, and were treated with adjuvant radiotherapy with no evidence of disease till date [Table 3].

In our study, 10/19 are on regular follow-up. Out of these four are alive and disease free, five patients are on palliative chemoradiation without any evidence of disease, and one patient is undergoing adjuvant radiotherapy for regional recurrence.

The estimated 5-year overall survival (OS) for all cases using Kaplan–Meier analysis was 83.33% [Figure 2]. On univariate analysis using log rank test, nodal positivity was identified as significant prognostic factor for overall survival [Figure 3]. Given the small number of cases, multivariate analysis was not possible.

Discussion

The mean age of patients in the present series was 63.95 years, comparable to the study by Nandwani *et al.*^[14] where the mean age was 65.2 years. However, studies have reported tumour occurrence in young age group of 30–40 years as well.^[9] Development of vulvar cancer in young age group is due to HPV infection associated with high-risk sexual behaviour and increasing trends of smoking (tobacco intake) in young girls.^[15] Quadrivalent HPV vaccination should be promoted among both young girls and boys as one of the preventive measure against Ca vulva.

Table 1: Demographic profile

Parameter	Number
Mean age	60.95 years
Parity	
Nulliparous	00
Multiparous	19
Menopausal status	
Premenopausal	00
Post-menopausal	19
Co-morbidities	
Anaemia	05
Hypertension	03
Diabetes mellitus	01

Table 2: Type of surgery performed

Type of surgery	Number of patients	Lymph node dissection		
		Unilateral	Bilateral	None
Radical vulvectomy	14	0	14	0
Hemivulvectomy	04	0	0	04
Wide local excision	1	0	0	01
Total	19	0	14	05

Table 3: Post-operative outcome, follow-up and survival among patients

Type of surgery	No. of patients	Positive lymph node	Negative lymph node	Planned for post-op RT	Post-op RT received	Recurrence	Follow-up	Survival (5 years)
Radical vulvectomy with B/L LN dissection	14	11 (02 with extracapsular spread; 06 with >1 node involved)	03	09	05	06 (05 local -adjuvant RT given), 01 regional ds. - Adjuvant radiotherapy ongoing.	06 defaulted; 01 pt. with ECS died	NED in 7 patients
Hemivulvectomy with U/L lym	04	-	04	00	00	1. 01 (regional) 2. 02 (Nodal metastasis - received adjuvant RT)	1 died (regional recurrence);01 defaulted	NED in 02 patients
Wide local excision	01	-	-	-	-	-	-	NED in 01 patient

Table 4: Post-operative complications		
Complication	n	Percentage
Wound infections (inguinal incision)	11/19	57.89%
Seromas	10/19	52.63%
Leg oedema	2/19	10.52%

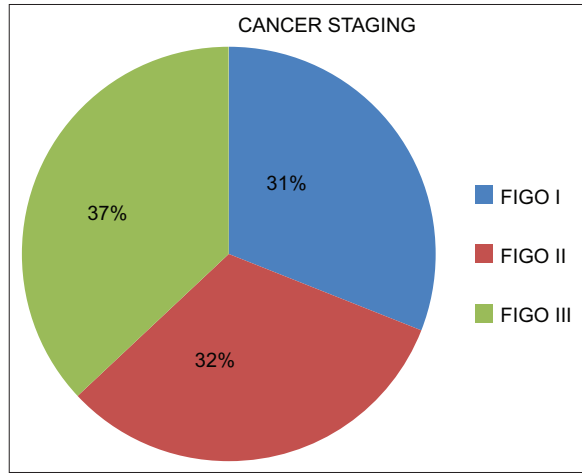


Figure 1: Distribution of the patients according to FIGO staging system

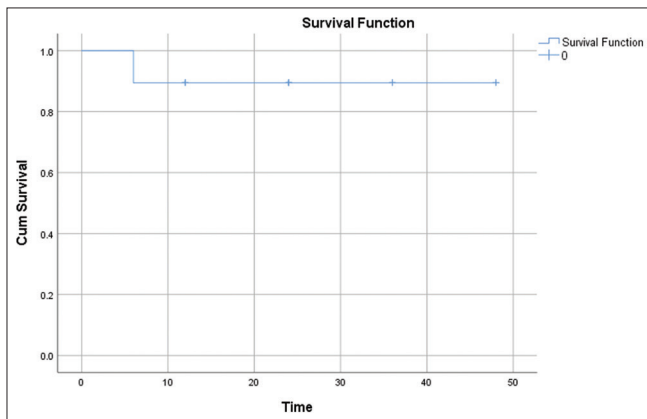


Figure 2: Kaplan–Meier curve—overall survival for all cases

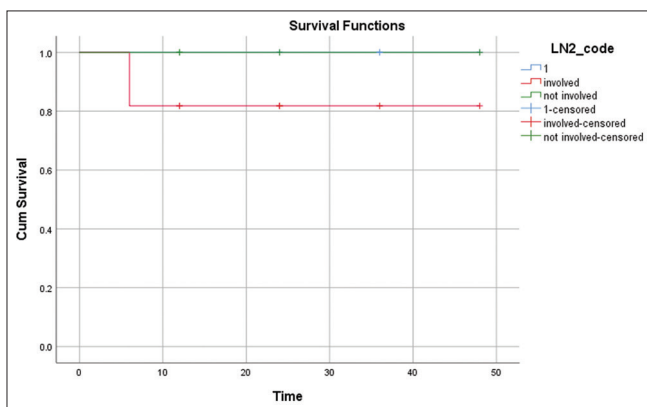


Figure 3: Overall survival of patients with and without pathological lymph nodes

Labia majora was the most common site of disease in our series as reported in the literature.^[5,9] In a study on 224 patients by

Hampl *et al.*,^[16] the tumour localization changed significantly from the labia to the area between the clitoris and urethra.^[9] We could not comment on such shift in location owing to small number of patients in our study. Histopathology of one of our patients suggested verrucous carcinoma which is a rare histological variant seen in less than 1% Ca vulva patients. The women had the vulval lesion from past 3 years and was managed on the lines of condyloma acuminata before getting referred to tertiary care facility. Similar observations have been reported by authors^[17,18] where vulvar condylomata patients refractory to medical management were later detected to be Ca vulva-verrucous type. Hence in such a clinical scenario, vulvar cancer should always be kept as one of the differential diagnosis.

Surgery involving cancer resection with adequate tumour-free margins along with IFLN (inguinofemoral lymph node) dissection is the mainstay of treatment.^[9,11] As per the FIGO guidelines,^[5,9] we resorted to wide local excision in patient with stage 1A disease with no evidence of disease till date. Luchini *et al.*^[19] and many other authors^[20-22] have illustrated that lymph node metastasis is one of the major prognostic factors. Considering that, either unilateral or bilateral inguinofemoral lymph node dissection was performed in all patients beyond stage IA who were planned for surgery as a primary treatment. Unilateral IFLN dissection was done for unilateral small lateral tumours with negative ipsilateral IFLN.^[23] The probability of positive bilateral nodes in case of negative ipsilateral nodes is <1%, in such cases unilateral dissection is appropriate. Recommendations are to remove at least 8 to 10 inguinofemoral nodes for an adequate staging.^[11] Homesley *et al.*^[24] in a series reported that 24% of patients with clinically negative nodes had positive nodes on pathology and 24% had it the other way round, suggesting that clinical examination is inadequate in assessing the nodal spread.^[11] In our study, 28% patients with clinically suspicious nodes had negative nodes and 36% with clinically negative nodes had positive nodes on pathology.

Singh *et al.*^[9] had employed frozen section technique for intraoperative analysis of the resected tissue and node so as to decide the further management. Literature^[25] documents that once tumour-free margins are detected using this technique, further dissection can be abandoned thus curtailing surgical morbidity. However, RCOG (2014)^[26] entails little use of frozen sections in surgical management of Ca vulva. Since frozen section is not available in our facility, we cannot share our experience.

The role of sentinel lymph node biopsy (SLNB) has been advocated in GROINSS-V aimed at significant reduction in post-operative morbidity by omitting lymphadenectomy in node negative patients. Groin recurrence rate was 2.3% in SLN-negative patients. In GROINSS-V II study, inguinal recurrence after radiotherapy developed in 1.6% cases with positive SLN concluding that radiotherapy can be an effective and less traumatic alternative to IFLND in patients with SLN metastases <2mm. SLN biopsy is a relatively newer procedure at present and need further clinical research.^[27]

Predisposing factors for post-operative complications in vulvar cancer are advanced age, poor nutritional status, presence of co-morbidities, risk of wound contamination by urine and faeces, wound dehiscence risk caused by sheer stress at groin creases on walking.^[26] Similar to our study, authors^[5,14,20] have mentioned wound dehiscence, infection, seroma collection, lymphocyst formation as the commonest complications and were managed in a similar way.

Extensive surgery with lymphadenectomy is also one of the predisposing factors for post-op complications. Rahm C *et al.*^[28] operated 182 patients with vulvar cancer, and the reported complication rates were 21.8%, 39.6% and 54.2% with vulvar surgery only, surgery with SLNB and surgery including IFLN dissection, respectively. The complication rate in our study is consistent with the findings of Rahm C *et al.*^[28]

Nowadays with the advent of neoadjuvant radio-chemotherapy, a more conservative surgical approach is followed in patients requiring extensive vulval procedures. Mahner S. *et al.*^[29] demonstrated improved survival in women treated with adjuvant groin radiotherapy for positive IFLN. Gynaecologic oncology group^[30] also reported similar results comparing IFLN radiation with node dissection in IFLN-positive patients.

In our series, while seven (37%) women defaulted to follow-up, 36% (n = 7) patients presented with tumour recurrence as compared to studies reporting the recurrence rate ranging from 23%^[31] to 29.3%.^[32] Six out of 11 patients (54%) with histological positive lymph nodes developed recurrence indicating node positivity to be a sole poor prognostic marker apart from other poor predictive factors in our study. Only 55% (5/9) node positive women consented for post-operative adjuvant radiotherapy. Non-compliance, unwillingness for post-operative radiotherapy were also the factors in addition to 'clinical poor prognostic markers' that resulted in high recurrence rate. Poor follow-up in Indian females is common due to factors like ignorance, low socio-economic status, lack of transportation and poor support system. Kumar *et al.*^[20] noted that these factors were responsible for high recurrence rate and poor prognostic outcomes in women with Ca vulva in Indian scenario.

The 5-year overall survival rate of patients under follow-up is 83.3% [Figure 2]. Small sample size and inadequate follow-up due to drop outs, thus interfering with calculation of recurrence and survival rate was the main limitation of our study.

Conclusion

Risk of vulval cancer can be lowered by adopting universal HPV vaccination in young boys and girls. The symptoms and gross appearance of vulval carcinoma are almost same in every patient except verrucous variant which is often confused with condyloma acuminata. Biopsy is confirmative in such cases. In carcinoma vulva, treatment should be tailored with multidisciplinary approach. Tumour stage, nodal positivity, and nodal positivity

with ECS were the significant prognostic factors for survival. Awareness about vulval self-examination, safe sexual practices, adherence to follow-up visits after primary surgery is much needed presently. Radical surgery with extensive groin node dissection is associated with significant post-morbidity; hence, further studies evaluating the role of neoadjuvant treatment are needed so as to modify the current treatment practices.

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.

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Conflicts of interest

There are no conflicts of interest.

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