Prognosis of vulval cancer with lymph node status and size of primary lesion: A survival study

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ABSTRACT

Introduction: Squamous cell cancer of the vulva is a rare disease with an annual incidence of two to three per 100,000 women. Lymph node metastasis is the most important prognostic factor for the recurrence and survival in vulval carcinoma.

Materials and Methods: It is a retrospective study of 18 cases, operated in our institute from 2006 to 2009 and followed up till July, 2012. These patients were divided into two group of node positive and node negative and compared for recurrence and survival.

Result: Ten patients had lymph node metastasis and eight had no lymph node metastasis. Recurrence rate was 40% and 12.5% in node positive and negative groups, respectively. Adjuvant radiation when given to node negative bulky tumor showed no recurrence compared to one out of two in the non-irradiated group. Survival was only 25% in node positive recurrent cases.

Conclusion: Lymph node positivity added a great risk for future recurrence. Prophylactic radiation in node negative, bulky tumor is helpful.

Key Words: Node positive, radiotherapy, radical vulvectomy, vulval cancer

INTRODUCTION

Squamous cell cancer of the vulva is a rare disease with an annual incidence of two to three per 100,000 women.^[1] Carcinoma vulva accounts for 4% of total gynecological malignancies.^[2] Standard treatment for these patients is surgical excision of the tumor with unilateral or bilateral inguinal lymphadenectomy via separate incisions. Depending on the localization of the tumor on the vulva, the size of the tumor and uni- or multifocality of the lesion radical vulvectomy, hemivulvectomy, or wide local excision can be performed. Flap reconstruction may be required for closure of the primary defect. The localization of the primary tumor (encroaching midline vulvar structures or not) also determines whether a unilateral or bilateral inguinal lymphadenectomy by separate incisions is needed. Adjuvant radiotherapy is indicated in case when one or more metastases are detected at pathologic examination of

Address for Correspondence: Dr. Pankaj Deka, Department of Gynaecological Oncology, Dr. Bhubaneswar Borooah Cancer Institute, Gopinath Nagar, Guwahati - 781 016, Assam, India. E-mail: drpankajdeka@gmail.com the removed lymph nodes. The efficacy of this treatment strategy in general is quite good, especially with respect to the rate of disease control in the groins. The groin recurrence rate in patients with negative nodes is estimated to be 0-2%; while the figures for patients with positive nodes are more variable, the risk is estimated to be 5-10%.^[3]

MATERIALS AND METHODS

It is a retrospective study of 18 cases of vulval cancer operated at our institute, from 2006 to 2009 and followedup till July 2012. All the patients underwent primary surgery with triple incision [Figure 1] resulting in complete tumor regression. Adjuvant radiotherapy (50 Gy in 25 fraction) was given to the patients depending on their lymph node status and size of the primary lesion. These patients were divided

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into two group: Lymph node positive and node negative groups depending on histopathology. These two groups were compared for recurrence and survival. Only those cases that underwent primary surgery at our institute and completed their adjuvant therapy were included for the study.

RESULTS

Vulval cancer is a disease of old age, 50% of cases in our study were above 60 year. All the cases presented with itching and ulceration around the vulva. 55.55% of patients were multiparous and associated with comorbid conditions like diabetes mellitus, hypertension, heart disease, tuberculosis, etc. Comorbid conditions did not seems to play any significant role in lymph node metastasis and as metastasis or recurrence [Table 1].

Clitoris was the most common site of involvement in our study and 14 patients had clinically enlarged groin nodes. Only two patients had tumor size less than 2 cm. Primary



Figure 1: Surgical photo showing triple incision in radical vulvectomy

Table 1: Evaluation of other prognostic factors

lesions were proliferative (10), ulcerative (5), and infiltrative (3) type and all three varieties showed equal pattern of node positivity and recurrence [Table 1]. International Federation of Gynecology and Obstetrics (FIGO) staging was done. 11.11% cases were in stage I, 33.33% in stage II, 33.33% in stage III, and 22.22% in stage IV as per the histopathology report. Table 2 states the nodal status and recurrence according to the age of patient, tumor size, and stage of the disease.

Histopathologically, 14 patients were of well-differentiated variety, 2 moderately differentiated and 2 were poorly differentiated. One important observation is that, both the poorly differentiated cases showed lymph node metastasis and had recurrence later on. Most of the women (15 cases) had depth of invasion more than 1 mm. Nine out of the 15 cases showed positive lymph node and four of them showed recurrence. Most common complication after surgery was wound gapping and it was seen in six cases in our study. The most common chronic complication was lymphedema of lower limbs, seen in seven cases.

Recurrence was seen in five patients, details are mentioned in Tables 3 and 4. Recurrence rate in the node negative group was 12.5%. On the other hand in node positive group, 40% of patients had recurrences. Only one patient was successfully treated for her recurrence in node positive group by surgical excision of the local recurrence. The sole recurrence in node negative group was treated successfully with radiotherapy.

DISCUSSION

The outcome of vulval carcinoma depends mainly on inguinal lymph node status and clinical tumor diameter. Woelber *et al.*, demonstrate that lymph node metastasis

Factors	Туре	Number	Node+ve	Recurrence	Node - ve	Recurrence
Type of the lesion	Proliferative	10	5	2	5	1
	Ulcerative	5	3	1	2	0
	Infiltrative	3	2	1	1	0
Histopathology	WD	14	7	2	7	1
	MD	2	1	0	1	0
	PD	2	2	2	0	0
Depth of the lesion	>1 mm	15	9	4	6	1
	<1 mm	3	1	0	2	0
Margins	+ve	2	0	1	0	0
	-ve	16	10	3	6	1
Comorbid conditions	DM	3	1	0	2	1
	HTN	2	1	1	1	0
	Other	4	2	1	2	0

DM: Diabetes mellitus, HTN: Hypertension, WD: Well differentiated, MD: Moderately differentiated, PD: Poorly differentiated

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		No. of points	Node		Recurrence		Treatment received
			Positive	Negative	Node +ve	Node – ve	
Age	<40 years	2	_	2			Sx-Surgery
	41-60 years	7	2	4	1	1	Sx+RT
	>60 years	9	7	2	2	_	Sx+RT
Tumor size <2 cm 2-4 cm	<2 cm	2	_	2		1	Sx
	2-4 cm	9	4	5	1	_	Sx+RT
	>4 cm	7	6	1	2	_	Sx+RT
Stage	I	2	_	2		1	Sx
	II	6	_	6	_	_	Sx+RT
	III	6	6	_	2	_	Sx+RT
	IV	4	4		2	—	Sx+RT

Table 2: Nodal status and recurrence according to age, tumor size, and stage

RT: Radiotherapy

Table 3: Details of patients with recurrence

Nodal status		Recurrence $(n = 5)$	Site of recurrence			Survival after treatment
			Local	Groin	Distant	for recurrence
Node positive, post RT (n=10)		4	1	2	2	1
Node negative	RT received (n=6)	Nil	_	_		_
	RT not received (n=2)	1	—	1	—	1

RT: Radiotherapy

Table 4: Demographic detail of recurrent cases

Node +/-	RT received or not	Disease-free survival	Treatment for recurrence	Outcome after treatment for recurrence
+	Received	1.5 years	Surgery	Surviving with 1 year follow up
+	Received	1 year	Palliative care	Died
+	Received	6 months	Palliative care	Died
+	Received	4 months	Palliative care	Died
_	Not received	3 years	RT	Surviving with 1 year of follow-up

RT: Radiotherapy

to the groin is the most important prognostic factor for disease-free and overall survival, while all other analytical factors remain secondary. Patients with unilateral lymph node metastasis had a five-fold increase risk of recurrence compared to node negative patients; in case of bilateral lymph node involvement, the risk was 17 times higher.^[4] Other factors that have consistently been correlated with outcome include histopathology, depth of invasion, tumor thickness, and the presence or absence of lymphovascular space invasion (LVSI).^[5] These features tend to be correlated with one another, and all are predictive of lymph node metastasis. In the study of Woelber et al., age, nodal status, tumor classification, depth of invasion, and margin involvement were statistically significant predictors for disease-free and overall survival by univariate analysis. Recurrence free and overall survival decrease with increasing tumor size, invasion depth, and margin involvement was noted. In multivariate analysis, lymph node status and age were the only independent prognostic

factors for disease-free and overall survival.^[4] Homesley *et al.*,^[6] reported 5 years survival rate of 91% for patients with negative inguinal lymph node and 75%, 36%, and 24% for patients with one or two, three or four, and more than five positive nodes, respectively. In our study the survival is 87.5% in node negative group and 70% in node positive group. Survival rate correlation with number of positive nodes could not be calculated in our study because of insufficient data. Brooks *et al.*, found significant difference in 5 years disease-free survival when node negative patients underwent thorough lymphadenactomy with more than 10 nodes compared to less than 10 nodes.^[7]

The depth of invasion is defined as the measurement of the tumor from the epitheliostromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.^[8] Hacker *et al.*, shows no lymph node metastasis in 34 patients where depth of invasion is <1 mm.^[9] According to Woelber *et al.*, adjuvant radiotherapy when given to node negative or only one positive node patients a statistically significant difference is found in disease-free survival.^[10] In our study adjuvant radiation was given on the basis of lymph node metastasis and size of the primary tumor. There is an obvious difference in disease-free survival in lymph node positive and negative group with 60% and 87.5%, respectively. But primary size of the tumor is not an important prognostic factor in our study because even tumor of less than 2 cm presented with recurrence. Another important observation in our study is that adjuvant radiotherapy is helpful in the cases of vulval cancer irrespective of the size and lymph node status.

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