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Vulvar carcinoma at King Chulalongkorn Memorial Hospital between 1994 - 2003

Tarinee Manchana*
Nakarin Sirisabya* Ruangsak Lertkhachonsuk*
Tul Sittisomwong* Apichai Vasuratna*
Wichai Termrungruanglert* Damrong Tresukosol*

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Objectives : *To determine the clinicopathological characteristics, outcomes of treatment and prognostic variables of vulvar carcinoma.*

Setting : *Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University*

Design : *Retrospective descriptive study*

Patients and Methods : *26 patients with vulvar carcinoma who received treatment at King Chulalongkorn Memorial Hospital between1994-2003. Patient charts were reviewed and clinicopathological characteristics were recorded. Disease free survival (DFS) and overall survival (OS) was analyzed by Kaplan-Meier curve and prognostic variables were analyzed by Log rank test*

* Department of Obstetric and Gynecology, Faculty of Medicine, Chulalongkorn University

Results : *Their median age was 58.5 years. The most common presenting symptom was recognized mass (42.3 %). The main treatment was primary surgery in 19 patients (73.1 %). Distribution of the stage of the disease was namely: 8 patients (30.8 %) in stage I, 9 patients (34.6 %) in stage II, and 9 patients (34.6 %) in stage III. The most common histological type was squamous cell carcinoma (76.9 %). Median DFS was 54 months, and median OS was 68 months. Age, menopausal status, parity, tumor size, type of treatment, histological type, lymph node involvement and positive margin had no significant effect on the recurrence and survival of the patient. The stage of the disease was the only significant prognostic variable; the median OS in stage I was 89 months; stage II, 42 months; stage III, 10 months ($p < .05$). The rate of 5-year survival according to the stage of the disease was 85, 56 and 32 %, respectively.*

Conclusions : *Vulvar carcinoma is the disease of advanced age patient and primary treatment is surgery. Most patients present with early stage and stage was the significant prognostic variable.*

Keywords : *Vulvar carcinoma, Prognostic variable, Disease free survival, Overall survival.*

Reprint request : Manchana T, Department of Obstetric and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

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ธาริณี แม่นชนะ, นครินทร์ ศิริทรัพย์, เรืองศักดิ์ เลิศขจรสุข, ตุลย์ สิทธิสมวงศ์, อภิชัย วสุรัตน์, วิชัย เติมรุ่งเรืองเลิศ, ดำรง ตรีสุโกศล. ประสบการณ์ 10 ปีในการรักษามะเร็งอวัยวะสืบพันธุ์ภายนอกของสตรีที่โรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2547 ก.พ; 48(2): 91 –9

วัตถุประสงค์ : *เพื่อศึกษาลักษณะทางคลินิกและผลทางพยาธิวิทยาในผู้ป่วย วิธีการรักษา ผลการรักษา รวมถึงปัจจัยที่มีผลต่อการมีชีวิตรอดของมะเร็งอวัยวะสืบพันธุ์ภายนอกของสตรี*

สถานที่ทำการศึกษา : *ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

รูปแบบการวิจัย : *การศึกษาบรรยายแบบย้อนหลัง*

ผู้ป่วยและวิธีการศึกษา : *ผู้ป่วยมะเร็งอวัยวะสืบพันธุ์ภายนอกของสตรี จำนวน 26 ราย ที่ได้รับการวินิจฉัยและรักษาที่โรงพยาบาลจุฬาลงกรณ์ ตั้งแต่ปีพ.ศ. 2537-2546 ข้อมูลต่าง ๆ ของผู้ป่วยจะถูกบันทึกแล้ววิเคราะห์โดย Kaplan-Meier method และปัจจัยที่มีผลต่อการมีชีวิตรอดโดย Log rank test*

ผลการศึกษา : *อายุเฉลี่ยของผู้ป่วย 58.5 ปี โดยอาการที่นำมาพบแพทย์มากที่สุดคือคลำพบก้อนที่อวัยวะสืบพันธุ์ ร้อยละ 42.3 ผู้ป่วยส่วนใหญ่ได้รับการรักษาโดยการผ่าตัดร้อยละ 73.1 ผู้ป่วย 8 รายพบในระยะที่หนึ่ง (ร้อยละ 30.8), 9 รายพบในระยะที่สอง (ร้อยละ 34.6) และ 9 รายพบในระยะที่สาม (ร้อยละ 34.6) ผลชิ้นเนื้อส่วนใหญ่เป็นชนิด squamous cell carcinoma ถึงร้อยละ 76.9 ระยะเวลาเฉลี่ยตั้งแต่ได้รับการวินิจฉัยจนพบการกลับเป็นซ้ำ (median disease free survival) 54 เดือน และระยะเวลาเฉลี่ยตั้งแต่ได้รับการวินิจฉัยจนเสียชีวิต (median overall survival) 68 เดือน ปัจจัยที่มีผลต่ออัตราการมีชีวิตรอดคือระยะของโรค โดยพบว่าผู้ป่วยระยะที่ 1 มี overall survival เฉลี่ย 89 เดือน ระยะที่สอง 42 เดือน และระยะที่สาม 10 เดือน ซึ่งมีนัยสำคัญทางสถิติ ($p < .05$) อัตราการมีชีวิตรอดที่ 5 ปีในระยะที่หนึ่งเท่ากับร้อยละ 85 ระยะที่สองเท่ากับร้อยละ 56 และร้อยละ 32 ในระยะที่สาม*

สรุปผลการศึกษา : *มะเร็งอวัยวะสืบพันธุ์ภายนอกของสตรีเป็นโรคที่พบมากในผู้ป่วยสูงอายุ การผ่าตัดถือเป็นการรักษาหลัก โดยส่วนใหญ่พบในระยะต้นและระยะของโรคเป็นปัจจัยสำคัญที่มีผลต่ออัตราการมีชีวิตรอดของผู้ป่วย*

คำสำคัญ : *ระยะเวลาตั้งแต่ได้รับการวินิจฉัยจนพบกลับเป็นซ้ำ*

Vulvar carcinoma is a rare gynecologic cancer, comprising only 3 - 5 %, mainly seen in elderly women.[1] Although vulvar tumor arises on visible external body surface and produces a typical symptom of pruritus and recognizable lesion in more than 90 % of patients, its diagnostic delay is frequent which may be from the patient or physician.[2, 3]

The traditional treatment of the disease has been radical surgery.[4] Recently, combined treatment (irradiation, chemotherapy, or chemoradiation) with less conservative surgery has been well established, a therapeutic alternative to extensive radical surgery especially in large locally advanced tumor.[5-8]

The objective of this study is to determine the clinicopathological characteristics, treatment and outcome including prognostic variables in patients with vulvar carcinoma who were treated at King Chulalongkorn Memorial Hospital during the period of 10 years.

Patients and Method

The charts of all patients who were diagnosed with vulvar carcinoma and treated at King Chulalongkorn Memorial Hospital between1994-2003 were reviewed. Accordingly, their age, parity, menopausal status, presenting symptom, duration of presenting symptom, size of tumor, location of tumor, treatment, pathological diagnosis, stage according to surgical staging (FIGO 1995) and clinical staging for patient who received radiation alone were recorded. Their disease free survival times and overall survival periods were analyzed by Kaplan Meier curve, especially, of the patients who followed up at least for 1 year, and their prognostic variables were analyzed by Log rank test, using SPSS for Windows (Version 11.5) statistical program.

Results

During the period of 10 years, 26 patients were diagnosed as having vulvar carcinoma. Their clinicopathological characteristics are shown in Table 1. The median age of the patients is 58.5 years (ranged 39 - 79 years). 76.9 % of the patients were parous and menopausal women. The most common presenting symptom was recognized mass (42.3 %) and the average time of the patient's recognition of the symptoms to the established diagnosis was 40 months. *Labia minora* was the most common location and the median size of the tumor was 3 cm (ranged 1.5-9 cm). Primary surgery was the main treatment in this study which included 19 patients (73.1 %). After the primary surgery, only 4 patients (21 %) received adjuvant radiation due to inguinal node involvement and, or positive margin. The classification according to the stage of the disease included, namely: Stage I, 8 patients (30.8 %); Stage II, 9 patients (34.6 %); and Stage III, 9patients (34.6 %). The most common histological type was squamous cell carcinoma (76.9 %). In this study, 21 patients were able to be analyzed for survival. Their median time of follow-up was 25 months (ranged 24 - 85 months); 10 patients (47.6 %) had tumor relapsed; and 8 patients (38.1 %) died (Table2, 3). Their median disease free survival (DFS) was 54 months and the median overall survival (OS) was 68 months. If we analyzed according to the stage of the disease, the median DFS and OS in stage I, II, III was 62, 54, 46 months and 89,42,10 months, respectively (Figure1, 2). The age, menopausal status, parity, tumor size which was larger than 2 cm, type of treatment, histological type, lymph

node involvement and positive margin had no significant effect for recurrent rate and survival of the patients. The stage of the disease was the only significant prognostic variable for overall survival ($p < .05$). In this study, the 5-year survival in stage I-III was 85, 56 and 32 %, respectively.

Table1. Clinicopathological characteristics.

		No. of patients	Percent
Age	≤ 50 years	6	23.1
	> 50 years	20	76.9
Menopausal status			
	Premenopause	6	23.1
	Postmenopause	20	76.9
Parity	Nulliparous	6	23.1
	Multiparous	20	76.9
Size	≤ 2 cm	5	19.2
	>2 cm	21	80.8
Presenting symptom			
	Mass	11	42.3
	Ulcer	6	23.1
	Pruritus	9	34.6
Location			
	Labia majora	5	19.2
	Labia minora	10	38.4
	Clitoris	7	26.9
	Mons pubis	1	3.8
	Posterior fourchette	1	3.8
	Bartholin's gland	2	7.7
Histological type			
	Squamous cell CA	20	76.9
	Melanoma	1	3.8
	Invasive Paget's disease	3	11.5
	Fibrosarcoma	1	3.8
	Adenoid cystic CA	1	3.8
Stage	1	8	30.8
	2	9	34.6
	3	9	34.6
Treatment			
	Primary surgery	19	73.1
	Radiation alone	3	11.5
	Chemoradiation then surgery	3	11.5
	Topical chemotherapy then surgery	1	3.9

Table 2. Detail of 10 relapsed patients.

	Stage	Histo	1st treatment	Margin	Site of relapsed	Relapsed treatment	Status	DFS (mo)	OS (mo)
1	1	Squamous	Surgery	-	Vulva	Excision	alive	62	103
2	1	Invasive Paget	Surgery	+	Vulva	Excision	alive	6	85
3	2	Adenoid	Surgery	+	Lung	Chemotherapy	alive	54	61
4	3	Squamous	Surgery	-	Lung	No	dead	9	10
5	2	Squamous	Radiation		Vulva	Brachytherapy	dead	14	16
6	2	Squamous	Surgery	-	LN	LN dissection	dead	9	25
7	2	Squamous	Chemoradiation then surgery	+	Vulva	No	dead	4	11
8	1	Invasive Paget	Surgery	+	Vulva	Excision	alive	21	31
9	3	Squamous	Chemoradiation then surgery	+	LN	No	dead	5	6
10	1	Melanoma	Surgery	-	LN	Interferon	dead	6	7

Table 3. Detail of 8 died patients.

	Stage	Histo	1st treatment	Adjuvant treatment	Site of relapsed	Treatment	DFS (mo)	OS (mo)
1	3	Squamous	Surgery	Radiation	Lung	No	9	10
2	3	Squamous	Surgery	Radiation	No	-	5	5
3	2	Squamous	Radiation	No	Vulva	Brachytherapy	14	16
4	2	Squamous	Surgery	No	LN	LN dissection	9	25
5	2	Squamous	Chemoradiation then surgery	No	Vulva	No	4	11
6	3	Squamous	Chemoradiation then surgery	No	LN	No	5	6
7	1	Melanoma	Surgery	No	LN	Interferon	6	7
8	3	Squamous	RV	No	No	-	12	12

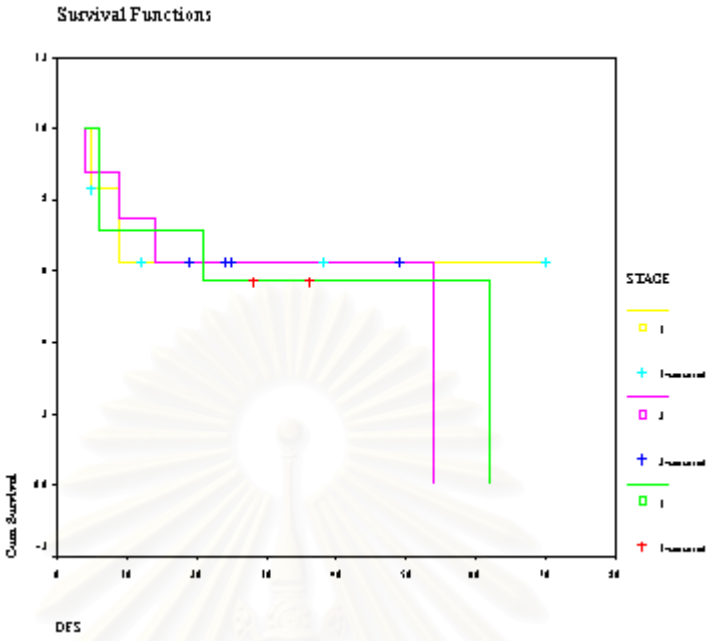

Figure 1. Disease free survival according to stage (p= .87)

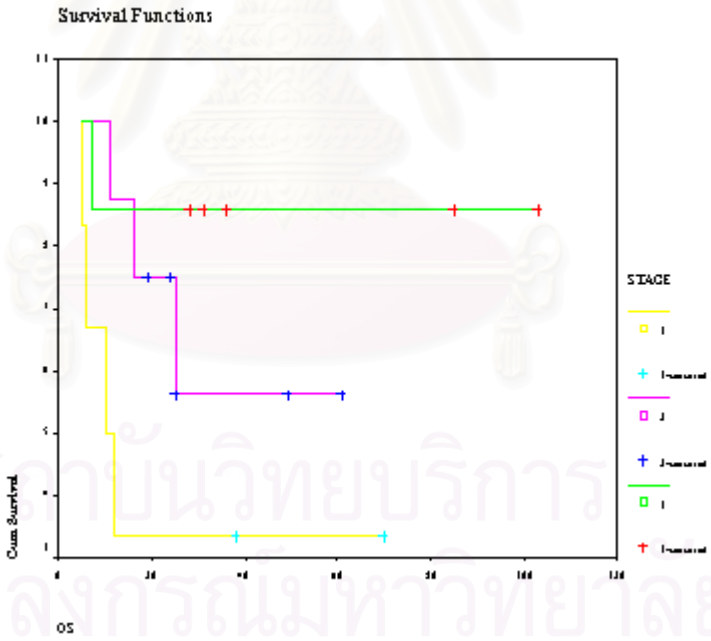

Figure 2. Overall survival according to stage (p= .035)

Discussion

Vulvar carcinoma is certainly a rare neoplasm, comprising only 1 % of all gynecologic malignancy in King Chulalongkorn Memorial Hospital. Only 26 patients in 10 years (averagely 3 patients per year). It is a disease of advanced age women, and approximately three-fourths of the patients present with early stage. The average time for the patient to recognize the symptoms to the establishment of the diagnosis was 40 months. The delay might be attributed from ignorance of the patient to recognize the symptoms, self-treatment and misdiagnosed by

the physician without establishing a pathologic diagnosis or biopsy at an incorrect site especially in elderly women.

Surgery is the main treatment of vulvar carcinoma; however, it may be impossible because the tumor is too large or being in advanced stage. The most recent therapeutic efforts have been focused on combined-modality treatment that combines radiation therapy or chemoradiation with less radical surgery. In this study, there were only 3 patients who received combined treatment, but their outcome was not impressive. In two-third of the patients, the tumor recurred and they died within a few months. This might due to their large tumor size at the delay of their treatment. Although chemoradiation might shrink the tumor, but generally it was not enough to bring adequate margin. One patient had local recurrence while another had inguinal node recurrence, both of which had no choice for further treatment. The advantage of combined modality treatment might be waited for a prospective randomized trial.

Regardless of initial treatment, recurrences can be categorized into three groups, namely: local, inguinal lymph node and distant metastasis. The treatment outcome in local recurrence is surprising well; 5-year survival after relapsed is approximately about 60-80 %. [9-10] But recurrence in the groin is almost universally fatal[11], in this study all patients who had groin node relapsed died within a few months after treatment. We found local recurrence as much as 47.6 % due to we include the patient with Paget's disease into this study which had very common for relapsing.

The major prognostic factors of the recurrence and death are, namely: stage, large tumor size (usually of more than 2 cm), lymph node metastasis, depth of tumor invasion and inadequate surgical margin.[2, 9,12-13] In this study, stage was the only significant prognostic factor ($p < .05$) and probably reason might be a small number of patients and a short duration time to follow, further study should be continued for proving other significant prognostic factors.

Early diagnosis may reduce both the morbidity and mortality. The reduction of delayed treatment requires a considerable effort in education of both the health care workers and the general public.

References

1. Ghurani GB, Penalver MA. An update on vulvar cancer. Am J Obstet Gynecol 2001 Aug; 185(2): 294 - 9
2. Piura B, Rabinovich A, Cohen Y, Friger M, Glezerman M. Squamous cell carcinoma of the vulva in the south of Israel: a study of 50 cases. J Surg Oncol 1998 Mar; 67(3): 174 - 81
3. Moscarini M, Carta G, Di Paolantonio L, Patacchiola F, Porzio G, Di Stefano L. Surgical treatment of invasive carcinoma of the vulva. Our experience. Eur J Gynaecol Oncol 2000; 21(4): 393 - 5
4. Levato F, Bianchi A, Lenzi B, Pansini F, Randazzo F, Ferretti S, et al. Surgical treatment of invasive carcinoma of the vulva. A reappraisal. Eur J Gynaecol Oncol 1992; 13(1Suppl): 99 - 104
5. Rotmensch J, Rubin SJ, Sutton HG, Javaheri G, Halpern HJ, Schwartz JL, Stewart M, Weichselbaum RR, Herbst AL.Preoperative radiotherapy followed by radical vulvectomy

with inguinal lymphdenectomy for advanced vulvar carcinomas. Gynecol Oncol 1990 Feb; 36(2); 181 - 4

6. Rodolakis A, Diakomanolis E, Voulgaris Z, Akrivos T, Vlachos G, Michalas S. Squamous vulvar cancer: a clinically based individualization of treatment. Gynecol Oncol 2000 Sep; 78 (3 Pt 1): 346 - 51
7. Balat O, Edwards CL, Verschraegen C, Delclos L. The long term results of radiotherapy with or without surgery in management of advanced vulvar cancer: report of 76 patients. Eur J Gynaecol Oncol 2000; 21(4): 426 - 9
8. Engleman MA, Small W Jr. Combined modality therapy in the treatment of gynecologic malignancies. Semin Oncol 2003 Aug; 30 (4 Suppl 9): 80 - 94
9. Maggino T, Landoni F, Sartori E, Zola P, Gadducci A, Alessi C, Solda M, Coscio S, Spinetti G, Maneo A. Patterns of recurrence in patients with squamous cell carcinoma of the vulva. A multicenter CTF Study. Cancer 2000 Jul; 89(1): 116 - 22
10. Rouzier R, Haddad B, Plantier F, Dubois P, Pelisse M, Paniel BJ. Local relapse in patients treated for squamous cell vulvar carcinoma: incidence and prognostic value. Obstet Gynecol 2002 Dec; 100(6): 1159 - 67
11. Hopkins MP, Reid GC, Vettrano I, Morley GW. Squamous cell carcinoma of the vulva: prognostic factors influencing survival. Gynecol Oncol 1991 Nov; 43(12): 113 - 7
12. Piura B, Rabinovich A, Cohen Y, Friger M, Glezerman M. Squamous cell carcinoma of the vulva in the south of Israel: a study of 50 cases. J Surg Oncol 1998 Mar; 67(3): 174 - 81
13. Fonseca-Moutinho JA, Coelho MC, Silva DP. Vulvar squamous cell carcinoma. Prognostic factors for local recurrence after primary en bloc radical vulvectomy and bilateral groin dissection. J Reprod Med 2000 Aug; 45(8): 672 - 8