Invasive squamous carcinoma of the vulva in women aged less than 40 years: report of two cases and a third case diagnosed during pregnancy

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Summary

Purpose of investigation: Invasive squamous cell cancer of the vulva (ISCC) is a rare disease in young patients and in pregnant women. The purpose of this paper was to investigate this type of cancer in women less than 40 years old and to present three cases, one which was diagnosed in the third trimester of pregnancy. *Methods:* Three cases of invasive squamous cell cancer in women under age 40 among the retrospectively analyzed 52 vulvar cancer cases diagnosed between 1995-2002 were investigated. *Results:* Women aged 25, 39 and 31, respectively, had Stage 1, 2 and 3 ISCC of the vulva. The first two cases had been spared by surgery and radiotherapy. The third patient was diagnosed during the last trimester of pregnancy. Although she was treated by radical surgery and postoperative radiotherapy, she had a recurrence in the inguinal region at 36 months, and died of disease 12 months later. *Conclusion:* Vulvar ISCC in young women may occur in association with or without predisposing factors. Although HPV-related type is predominant in the literature, keratinizing type of carcinoma may also be seen in this group of patients. Biopsy from suspected lesions is of paramount importance.

Key words: Vulva; Vulvar cancer; Pregnancy; Young.

Introduction

Vulvar cancer is a rare disease, seen most often in older women, accounting for 3-5% of all gynecologic malignancies [1]. The most frequent histologic type is invasive squamous cell carcinoma (ISCC) comprising around 90% of the cases. Other types are basal cell carcinoma, melanoma, adenocarcinoma, Paget's disease and sarcomas. They all are rare in patients younger than 40 years old [2].

Invasive carcinoma of the vulva seems to derive from two separate entities [3]. The more common is a keratinizing carcinoma associated with lichen sclerosus, squamous hyperplasia, and p53 mutation in older women. The other is human papilloma virus (HPV)-linked warty or basaloid carcinoma in younger women. The latter patients appear to have a significantly better prognosis than the first group [4].

Vulvar cancer in women less than 40 years of age is not a thoroughly studied topic in the literature. An increase in the incidence of vulvar cancer, especially squamous type, has been recently reported [5, 6] and immunosuppression has been suggested to have a contributory role in this age goup [7]. In order to assist in future research and treatment recommendations in this group, we have discussed clinical and pathologic findings, treatment and outcomes of three cases of ISCC in women aged less than 40 years in a tertiary care university hospital setting.

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Materials and Methods

We conducted a retrospective review of the medical records of 52 women treated at our university for vulvar cancer from 1995-2002. In situ carcinoma cases were not included in these numbers. We identified six cases occurring in women less than 40 years of age accounting for 11.5% of all vulvar cancer cases. Three of these cases were ISCC and the rest were sarcomatous in origin. The relevant clinical data and follow-up information of ISCC cases were gathered. Since one of the cases was a pregnant women diagnosed to have cancer in the third trimester, association of pregnancy and vulvar ISCC is also discussed.

Results

The clinical data and outcome of cases are outlined in Table 1.

The first case was a 25-year-old woman who presented with a lesion 1 x 1.5 cm in size on the right labium major. After biopsy revealed that it was a squamous carcinoma, the patient had a radical vulvectomy with bilateral inguinofemoral lymphadenectomy. The tumor was a well-differentiated squamous cell carcinoma and eight lymph nodes were negative in terms of metastasis. Evaluated as having been treated for Stage I disease, she received adjuvant postoperative radiotherapy. After attending her regular follow-up visits, she was still free of her disease after five years.

The second case was a 39-year-old woman with chronic itching of the vulva. Her clinical examination revealed a 2.5 x 2 cm ulcerative lesion on the superior

Table 1. — *Details of the three vulvar ISCC cases*.

Case	Age	Stage	Grade	Therapy	Recurrence and site	Recurrence interval (months)	Survival* (months)	Outcome
1: ISCC	25	1	1	RV+BIL[1] and postoperative RT[2]	–	–	60	Alive
2: ISCC (keratinizing type)	39	2	1	RV+BIL[1] and postoperative RT[2]	+ local	90	114	Alive
3: ISCC + pregnancy	31	3	1	CS[3] RV+BIL[1] and postoperative RT[2]	+ Inguinal lymph nodes	36	48	DOD[4]

* Survival times for patients 1&2 are estimated up to the patients' last contacted date. [1] RV+BIL: radical vulvectomy and bilateral inguinal lymphadenectomy. [2] RT: pelvic radiotherapy. [3] CS: Cesarean section. [4] DOD: dead of disease.

portion of the left labium major, around 1 cm away from the clitoris. Radical vulvectomy with bilateral inguinofemoral lymphadenectomy was performed. Pathologic evaluation reported a grade 1 keratinizing squamous cell carcinoma with clear surgical margins of at least 2.5 cm in all directions, and 14 lymph nodes were all negative for disease. She received 28 fractions of pelvic radiotherapy postoperatively. Ninety months later she presented with a 3 x 1.5 cm recurrent ulcerative lesion at the former location of the clitoris. She underwent wide local excision and the defect was covered by bilateral subinguinal perineal flaps. The recurrence was a grade 2 lesion with focal pseudosarcomatous differentiation. Surgical margins were negative. After 24 months of follow-up, she had no evidence of recurrent cancer.

The third case was a 31-year-old pregnant woman, gravida 3, para 2, who presented at our clinic in the 31st week of gestation with a slowly growing lesion on the vulva. Her antenatal evaluation was normal, the fetus was appropriate for gestational age and no anomalies were detected during ultrasound. However, a 2 x 3 cm tumoral lesion on the right labium major extending to the clitoris was encountered. Biopsy revealed ISCC. The pregnancy was terminated and after one week definitive surgery comprising radical vulvectomy and bilateral inguinofemoral lymphadenectomy was carried out. The pathology reported that the tumor was a well differentiated squamous cell carcinoma but Stage 3 disease was present since there were unilateral positive inguinal lymph nodes. The surgical margins of the specimen were clear of disease. The patient had adjuvant pelvic radiotherapy treatment and was closely followed-up. At the 36th month of follow-up she had a recurrence in the inguinal region and despite salvage therapy, succumbed to her disease at 48 months.

Discussion

ISCC of the vulva is not commonly seen in young patients and most of the literature consists of small case series, with large series being rare [1, 8-10]. It has been reported that 3.3-15% of vulvar tumors occur in women less than 40 years old [1, 11]. Although our numbers are limited and derived from a single institution, this ratio is roughly in accordance with our result of 11.5%. Of note, two of the cases were associated with HPV while the other was a keratinizing carcinoma.

The coexistence of pregnancy and ISCC vulvar cancer is very rare and around 30 cases have been published to date [12, 13]. Due to the paucity of cases, a consensus on the treatment plan of these patients has not been established. In some patients definitive surgery was postponed until the postpartum period to avoid increased vascularity of the region, like in our case in which definitive surgery was performed one week after termination of the pregnancy. However the treatment was instituted promptly in our case and the decision to terminate the pregnancy in the 31st week of gestation was based on the patient's young age, presence of a midline structure and a lesion greater than 2 cm, availability of fetal intensive care, and demonstration of fetal maturation. Of the reported cases, nine were surgically treated during pregnancy and did not develop recurrence. Delaying the treatment until the postpartum period would have had grave complications and result in recurrence and death [14]. Our case turned out to have Stage III carcinoma, which undoubtedly negatively affected survival; she developed recurrence at the 36th month after the operation and eventually succumbed to her disease. Since there was no delay in the definitive treatment of our patient, whether the effect of delivery and/or early puerperium itself may worsen the prognosis of the disease is subject to discussion and should be further investigated.

Although it has been suggested by Bakou *et al*. [15] that vulvar cancer in pregnancy and by Carter *et al*., [9] that vulvar cancer in the young may be associated with immune system failures, there was no evidence of defective immune function in any of our patients. This finding suggests that mechanisms other than known causes of immunodeficiency could be operating to result in ISCC. One of the largest population-based series to date by Al-Ghamdi *et al*. also reported that immunocompromised hosts accounted for only a small percentage of young patients with vulvar ISCC [10]. It is also interesting to note that Ogunleye *et al*. have published an ISCC diagnosed and treated during pregnancy which recurred, just 11 weeks after surgery, at the 34th week of gestation. They concluded that although their case did not have any immune deficit, vulvar ISCC may recur in the setting of pregnancy and should be carefully followed-up [16].

Conclusion

Vulvar ISCC in women less than 40 years of age may occur in association with or without predisposing factors. Although HPV-related type is predominant in the literature, keratinizing type of carcinoma may also be seen in this group of patients. Although very rare, vulvar lesions during pregnancy or in the young may indeed be a carcinoma; therefore consideration for biopsy is of paramount importance. If diagnosis of vulvar cancer is confirmed, treatment should be started without delay.

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