Multiple, disseminated cutaneous metastases of vulvar squamous cell carcinoma

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Cutaneous metastases of vulvar carcinoma are extremely rare and have been reported in six patients so far. Our patient, who is the seventh one, is a 38-year-old woman with a history of diabetes mellitus.

After detecting stage III squamous cell carcinoma of the vulva, she underwent radical vulvectomy and bilateral inguinal lymphadenectomy. She received 6000 cGy external beam radiation for positive margins. Six months later, she came back with multiple advanced skin lesions. Biopsy was performed and lesions were confirmed as cutaneous metastases.

For her palliation, some chemotherapy drugs were prescribed. She is on her sixth chemotherapy cycle, but these skin lesions are somewhat a preterminal event and there is no well-established treatment for this phase of disease.

Keywords: carcinoma, skin metastasis, squamous cell carcinoma of vulva, vulvar carcinoma.

Invasive squamous cell carcinoma (SCC) of the vulva represents 5% of all malignancies of the female genital tract and 95% of all vulvar malignant tumors.

SCC of the vulva is predominantly a disease of postmenopausal women, with a mean age of approximately 65 years. Incidence increases with age. However, there is a recent evidence of increased frequency in younger populations.

There is a long history of pruritus, usually associated with a vulvar dystrophy and Lichen Sclerosis et Atrophicus as pre-existing phenomena in some patients.

In older women, invasive SCC of vulva may extend to the vulva, perineum, and anal margins. Inguinal lymph nodes are the first place for metastases and then it may involve deep pelvic nodes. Hematogenous spread to distant sites includes the lungs, liver, and bones.

Five-year survival rate will be 90%, if there is no lymph node involvement and 25% if metastasis to deep pelvic nodes is present.

Cutaneous metastases can occur but extremely rare. Until now only six documented cases have been reported.

We describe another case of vulvar carcinoma with extensive multiple cutaneous metastasis. Regarding previously published cases, our patient is the youngest one with multiple focal skin metastases.

Case report

Our patient is a 38-year-old woman (G10—P10—LC6) with vulvar skin lesions who was referred to our gynecology oncology department with a diagnosis of invasive SCC in March 2002. Lesion was 5 cm in size.
diameter and on the right labia minor that extended to labia major and urethra superficially. Inguinal lymph nodes were not large or palpable. There were no report of distant metastases on chest X-ray, liver ultrasound or on abdomen and pelvic CT-scans (stage III, T3 N0 M0).

She has had diabetes mellitus since 2 years and was on glibenclomid since then.

She had chronic itching and burning sensation since 8 years. Because of large lesions she ought to undergo preoperative radiation, but because of logistical reasons and to reduce tumor size before surgery, she underwent neo-adjuvant chemotherapy by vincristine (1 mg/m²) and cisplatin (50 mg/m²) for two cycles and within 12 days interval. Fourteen days after completion of second cycle of chemotherapy, she underwent radical vulvectomy and bilateral inguinal lymphadenectomy with resection of 1.5 cm of urethra to have tumor free margins.

Tumor was diagnosed histologically as moderately differentiated SCC with marginal involvement and without lymph node involvement (Fig. 3).

After surgery she referred to radiotherapy for treating marginal involvements. Vulva was treated by a dose of 6000 cGy external beam radiation in 30 fractions.

Six months after radiotherapy, she came back with multiple, focal, disseminated violaceous nodules on the skin of the remaining parts of the mons, groins, lower abdomen, flank, and buttocks (Figs. 1 and 2).

Biopsy of the lesion showed metastatic well-differentiated SCC (Fig. 4). Because of itching and burning sensation, eosin solution was used on her lesions and she was treated by six cycles of cisplatin (100 mg/day) in 1 day and 5-FU (1 g/day) for 4 days.

Discussion

In females, cutaneous metastases occur most commonly from breast carcinoma, followed by colorectal carcinoma, melanoma, and ovarian carcinoma(8).
Cutaneous metastases from vulvar carcinoma have been reported just in a few patients (six patients); therefore it can be considered rare\(^{1,5-9, this\ case}\) (Table 1).

Cancer of the vulva represents with an average annual age-adjusted incidence rate of 1.2 per 100,000 women years and increases with increasing age to 20 per 100,000\(^{10}\).

In general, the management of patients with T2 and early T3 tumors consists of radical vulvectomy and bilateral inguinal lymphadenectomy. If the disease involves the distal of urethra or vagina, partial resection of these organs is required; alternatively it may be preferable to give preoperative radiation therapy to allow a less radical resection.

Distant between tumor and surgical margin is a significant predictor for local recurrences. Margin of 8 mm or less is associated with 50% recurrence rate\(^{3}\).

Local vulvar recurrences are most likely in patients with primary lesions larger than 4 cm in diameter\(^{11}\).

The reported rates of recurrence range from 15 to 37% after radical surgery\(^{12,15}\). Recurrence can be categorized into four groups: local, inguinal, pelvic, and distant. The patterns of recurrence in patients fail to respond to regional therapy for vulvar cancer are 61% in vulva and perineum, 23% in the groin, 16% in the pelvis, and 10% distant\(^{16}\). In this vulvar and perineal recurrences might be due to the lesion with more than 4 cm in size and marginal involvements.

Postoperative radiation therapy can be helpful to prevent local recurrence and improve survival in patients with involved or close margin (<5 mm)\(^{11,17}\). Because of this fact, our patient underwent radiotherapy.

![Figure 4](image)

*Fig. 4. Histology of the metastatic nodules in Figure 3 revealed metastatic squamous cell carcinoma (H&E, ×100).*

**Table 1.** Cutaneous metastases from vulvar cancer: literature survey

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age initial diagnosis</th>
<th>Medical history</th>
<th>Treatment</th>
<th>Stage</th>
<th>Nodes</th>
<th>Histology</th>
<th>Grade</th>
<th>First recurrence (months)</th>
<th>Location</th>
<th>Treatment</th>
<th>Second recurrence</th>
<th>Location</th>
<th>Treatment</th>
<th>Third recurrence</th>
<th>Location</th>
<th>Leg edema</th>
<th>Treatment</th>
<th>DOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghaemmaghami et al. (present)</td>
<td>2003</td>
<td>38</td>
<td>Diabetes mellitus</td>
<td>RVBGN + RT</td>
<td>III</td>
<td>Negative</td>
<td>SCC</td>
<td>II</td>
<td>7</td>
<td>Vulva, lower abdomen, buttocks, groins</td>
<td>CT</td>
<td>RT</td>
<td>8 months later</td>
<td>Vulva</td>
<td>S</td>
<td>6 months later</td>
<td>Vulva + pelvis</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Tjalma et al.</td>
<td>2003</td>
<td>73</td>
<td></td>
<td>RVBGN</td>
<td></td>
<td></td>
<td></td>
<td>III</td>
<td>9</td>
<td>Vulva</td>
<td>S</td>
<td></td>
<td>S + RT</td>
<td></td>
<td>3 months later</td>
<td>Thigh, calve</td>
<td>Yes</td>
<td>No</td>
<td>4 months later, lung metastases</td>
</tr>
<tr>
<td>Dudley et al.</td>
<td>1998</td>
<td>79</td>
<td>Br Ca</td>
<td>RVBGN + RT</td>
<td></td>
<td></td>
<td></td>
<td>I</td>
<td>5</td>
<td>Abdomen, limbs</td>
<td>CT</td>
<td>S</td>
<td></td>
<td>Thigh</td>
<td></td>
<td></td>
<td></td>
<td>?</td>
<td>?</td>
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<tr>
<td>Kulkarni et al.</td>
<td>1995</td>
<td>59</td>
<td>Negative SCC</td>
<td>RVBGN</td>
<td></td>
<td></td>
<td></td>
<td>I</td>
<td>8</td>
<td>Abdomen, vulva, thighs</td>
<td>CT</td>
<td>?</td>
<td></td>
<td>Abdomen</td>
<td></td>
<td></td>
<td></td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Tobias et al.</td>
<td>1995</td>
<td>57</td>
<td>Positive SCC</td>
<td>RVBGN</td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>5</td>
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<td>CT</td>
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<td></td>
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<tr>
<td>Santala et al.</td>
<td>1989</td>
<td>54</td>
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<td></td>
<td></td>
<td>II</td>
<td>8</td>
<td></td>
<td>CT</td>
<td>?</td>
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<td></td>
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<tr>
<td>Cianfran et al.</td>
<td>1996</td>
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<td>Positive SCC</td>
<td>RVBGN</td>
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<td>I</td>
<td>6</td>
<td></td>
<td>CT</td>
<td>?</td>
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DOD, dead of disease; RT, radiotherapy; RVBGN, radical vulvectomy and bilateral groin nodes dissection; SCC, squamous cell carcinoma.

Combination with Cisplatin (50 mg/m² on day 1) and 5 FU (1000 mg/m² 24 h x 4 days) during first and last weeks of therapy. Radiation doses of the vulva and groins ranged from 50 to 65 cGy (18).

Cutaneous metastasis from vulvar SCC have been described as non-tender, solid, red dermal nodules containing keratin pearls and partially cystic areas with tumor necrosis, hyperemic maculo-papular, nodular and pustular lesions showing anaplastic epidermoid cells in dermal lymphatic or other thin-walled vascular spaces and extending through the epidermis, and diffuse red inflammatory plaques and patches simulated toxic erythema composed of islands of distorted anaplastic squamous cells (1). Among females, approximately 75% of the cutaneous metastases found are on the anterior portion of the chest and abdomen, and metastases to the skin of the buttocks and/or hips are rare (7).

It seems cutaneous metastases were due to superficial lymphatic spread and not hematogenic ones, because even in the end stage of the disease there were no lung or hepatic metastases detected. In patients treated for vulvar cancer the draining lymphatic channels are mostly destroyed, either by surgery and/or radiotherapy or by the disease itself (9). In this case, diabetes mellitus is a predisposing factor.

The appearance of metastasis to the skin from an underlying malignancy must be considered an ominous sign (39). Treatment can be consisted of radiation, excision and/or chemotherapy. Also topical immunomodulators can be effective in these cases. But due to the limited number of cases, there is no well-established treatment or management of this condition.

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References


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