Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2022;31:75-77
doi: 10.15570/actaapa.2022.10

In-transit metastasis of cutaneous squamous cell carcinoma: report of two cases

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Abstract

Transit metastases include metastatic foci of the skin and subcutaneous tissue located between the tumor and the nearest regional lymph node. Although transit metastases have been described for malignant melanoma, some cases of transit metastases have also been reported among primary cutaneous non-melanoma cancers. Treatment of patients with in-transit squamous cell carcinoma (SCC) is a multimodal approach for advanced staging imaging and therapy, including Mohs micrographic surgery, adjuvant radiation, and possibly sentinel lymph node biopsy and immunotherapy or chemotherapy. Here we report two cases of in-transit metastasis with primary cutaneous SCC.

Keywords: transit metastasis, clinical dermatology, cutaneous, squamous cell carcinoma, tumor

Received: 17 February 2022 | **Returned for modification:** 20 April 2022 | **Accepted:** 10 May 2022

Introduction

Cutaneous metastases are diagnostically important because they may be the first sign of an undetected internal malignancy or the first manifestation of metastasis from an adequately treated malignancy. Cutaneous metastasis from either primary skin or internal organ carcinomas is not common. In addition, in-transit metastasis is extremely rare in squamous cell carcinoma (SCC) (1). Histologically, metastases of malign epithelial tumors are generally located in the dermis or adipose tissue, and the epidermis is not involved (2). We present two non-immunosuppressed cases with numerous in-transit metastases of primary SCC in the pubic region and right femoral region because of its rarity.

Case 1

A 64-year-old man applied with a complaint of a crusted, ulcerated, non-healing wound on his perianal area. He had 9-year history of perineo-gluteal hidradenitis suppurativa (HS, Hurley stage 3) and was unrecovered despite long-term treatment with topical and systemic antibiotics and isotretinoin. After 2 years of treatment, the patient presented with a 14×10 cm ulcerated mass in an HS-affected area. The tumor rapidly and aggressively spread through the surgical wound within 2 months. In 2012 he had been diagnosed with cutaneous SCC, which was removed by surgery. Subsequently a tumor recurred in the perianal area, and he presented with right inguinal lymph node metastasis (Fig. 1a and b).

A skin biopsy specimen showed psoriasiform hyperplasia of the epidermis in concert with scattered atypical keratinocytes through all of its layers. In addition to these findings, malignant squamous epithelial cells were recognized in the lymphatic vessels. In addition to the epidermal changes, there were accompanying small islets of atypical squamous cells in the superficial reticular dermis (Fig. 2). We diagnosed the case as in-transit SCC, and the patient was referred to a tertiary hospital for further management. A large cutaneous excision was performed in combination

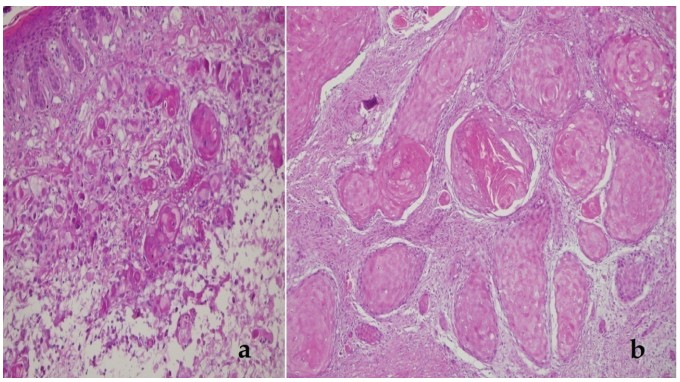

Figure 2 | Metastatic squamous cell carcinoma islets with a clear zone between the deposits and epidermis (H&E, a ×100, b ×200).

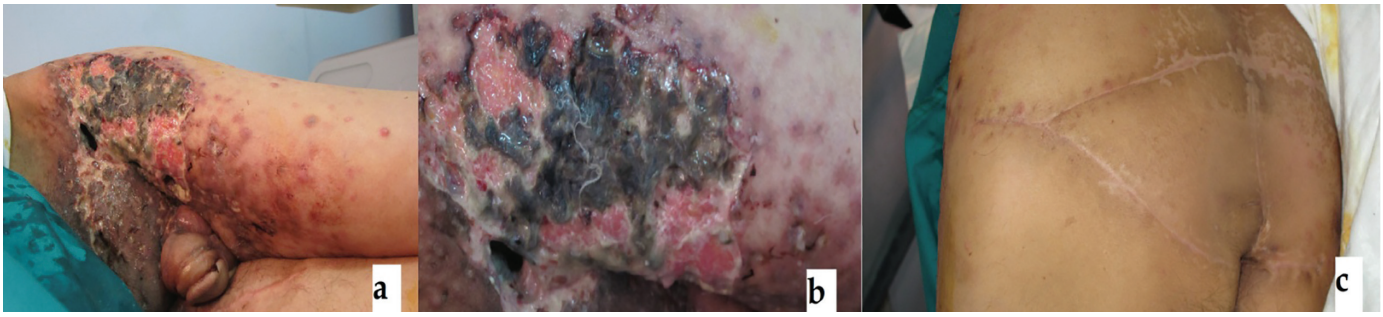

Figure 1 | a) Multiple ulcers with discharging serous fluid in the pubic, suprapubic, and scrotal region, b) ulceration and satellite ulcerations in the right groin area, c) postoperative image, incision on the posterior thigh and buttocks.

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with palliative chemotherapy (Fig. 1c).

Case 2

An 80-year-old female was admitted to a dermatology department with complaints of multiple papules and nodules in the right pubic region. According to the patient's statement, the lesions had been present for 3 months. She had complete right hemiplegia following a left-side cerebrovascular accident 7 years earlier. Her background medical issues included morbid obesity, diabetes, and atrial fibrillation. Dermatological examination showed nodular and tumoral lesions with a wide base that were hard and tender on pressure, varying in size from about 1 to 5 cm in the lateral part of the right thigh (Fig. 3). In superficial tissue, ultrasonography showed hypoechoic multiple diffuse thickenings possibly compatible with malignant infiltration under the skin and subcutaneously in the proximal right femur. Fine-needle aspiration biopsy of the inguinal lymph node followed by CT scan for staging confirmed the diagnosis of primary cutaneous SCC (Fig. 4). Histologically, the primary lesion was poorly differentiated with perineural invasion. A biopsy taken from one of the nodules showed a metastatic deposit as dermal proliferation of highly atypical cells arranged in cords, which infiltrated the dermis but spared the epidermis. Immunohistochemical staining of cytokeratin-14 (CK-14)

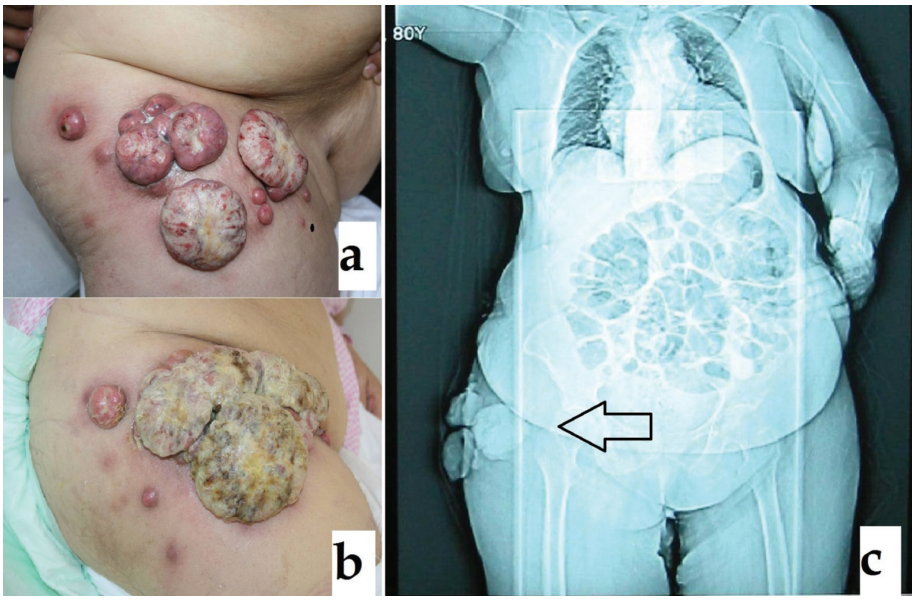

Figure 3 | a) Nodular and tumoral lesions with a wide base, hard, tender on pressure, varying in size from about 1 to 5 cm in the lateral part of the right thigh, b) rapid growth of the lesion after 2 weeks, c) primary cutaneous squamous cell carcinoma with right inguinal and right iliac lymph node metastases confirmed by CT scan.

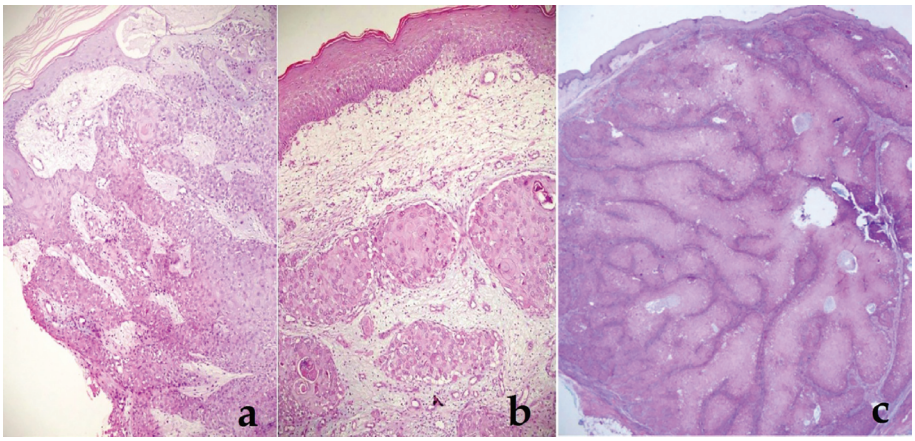

Figure 4 | a and b) The surface of the primary tumor is connected to the epidermis and consists of keratinocytes with extensive eosinophilic cytoplasm, c) frozen section histopathology showing squamous cell carcinoma foci with lymphovascular invasion (H&E, original magnification ×100).

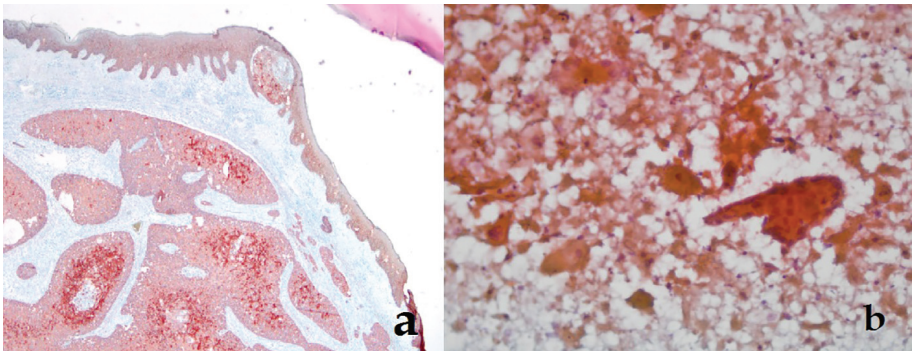

Figure 5 | a) Immunohistochemical staining positive for cytokeratin-14 and b) smooth muscle actin.

and smooth muscle actin (SMA) was positive (Fig. 5). A diagnosis of SCC with in-transit cutaneous metastasis was made, and the patient was referred for adjuvant radiotherapy. However, her disease continued to progress, and she died 8 months after her initial presentation to the dermatology department.

Discussion

Although SCC is more common in areas exposed to ultraviolet rays, such as the head and neck, it can also be rarely seen in other anatomical localizations. In-transit metastasis from primary skin SCC and visceral cancers is very rare (3). It is generally seen in between 0.65 and 2% of cases (4). In-transit metastases have also been reported in prostate, lung, ovarian, breast, and bladder cancers and in melanoma (5).

All SCCs seen in immunocompromised patients have a tendency to metastasize to distant sites. Ninety percent of metastatic SCCs usually occurs within 3 years of diagnosis of the primary tumor (1). Therefore, metastasis occurred in a much shorter time in both of our patients. In the first patient, the tumor embolism may have already been located in the lymphatic channels at the time of the inguinal node dissection, and removal may have been the cause of malignant transformation in HS, and therefore this may have led to early recurrence. In the second patient we hypothesize that the presence of diffuse lymphedema in the legs secondary to hemiplegia accelerated the progression of metastasis.

Although reports of in-transit metastases from primary cutaneous SCC have been reported in a few cases, Carucci et al. conducted a multicenter study of 21 patients, 15 of whom were iatrogenically immunocompromised transplant recipients. At a mean follow-up of 24 months, 33% of the transplant patients did not show any evidence of disease compared to 80% of the nontransplant patients (6). A similar study was performed by Ma et al. with a multicenter case series of 31 patients, of whom the majority (68%) were immunocompetent. The prognosis was poor, and the 5-year survival was approximately 13% (7).

Although our patients were not immunosuppressed, their advanced age, poor differentiation of the tumor, and tumor size larger than 2 cm caused the development of in-transit metastatic SCC.

In the literature, histological differentiation of the primary tumor and transit metastasis were reported to be mostly well differentiated, whereas poorly differentiated or undifferentiated tumors were mostly classified in the high-risk SCC group. Transit metastases invade the skin via lymphatic vessels and/or nerves. Dermal and subcutaneous tumoral infiltration without epidermal invasion are the histopathological findings of metastasis (8). In our cases, the histological differentiation of both primary tumor and in-transit metastasis was poor.

Treatment options identified for in-transit metastasis include surgical excision, radiotherapy, amputation, intralesional or systemic chemotherapy, oral retinoids, and immunosuppressive drugs (9). The first patient was referred for further treatment to the same tertiary care hospital where he had undergone surgery, but he was lost to follow-up. The recurrent tumor in our second case was treated with radiotherapy, but the worsening of the patient's health condition and the presence of infection did not allow continuation of radiotherapy, and she died of sepsis 8 months later.

Conclusions

Transit metastasis from cutaneous SCC is a distinct manifestation of metastatic SCC more commonly described in transplant recipients, and it is associated with a poor prognosis in this group, even in immunocompetent patients. SCC must be a diagnostic consideration in the context of chronic inflammatory wounds such as HS. Patients with in-transit SCC require a multimodal approach to further staging imaging and treatment, including surgery, adjuvant radiation, and possibly sentinel lymph node biopsy and immunotherapy or chemotherapy.

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