

High-risk cutaneous squamous cell carcinoma with intravascular involvement recurs in a patient with systemic sclerosis



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INTRODUCTION

The classification and management of high-risk squamous cell carcinoma (SCC) of the skin is an evolving topic in dermatology. These tumors are associated with poor prognosis and higher rates of local recurrence and metastasis.¹ Standard treatment options include Mohs micrographic surgery with or without adjuvant radiation.¹ We present an unusual case of high-risk SCC in a patient with systemic sclerosis, in which intravascular growth resulted in vascular occlusion. Despite Mohs micrographic surgery and adjuvant radiation, the patient's tumor recurred 17 months later.

CASE REPORT

A fair-skinned female in her 70s with systemic sclerosis presented with a 6-month history of a nonhealing scaly lesion on the scalp. The patient did not have a history of skin cancer. She denied systemic symptoms apart from her scleroderma, which was being treated with 3000 mg mycophenolate mofetil (MMF) daily. Examination found a 2- × 3-cm soft, tender crusted nodule on the vertex scalp. Biopsy found SCC. The patient was referred for Mohs micrographic surgery, and the tumor was cleared in 4 stages. The second Mohs layer found tumoral SCC islands occluding a large-caliber vessel (Figs 1 and 2).

The defect was partially closed with a purse-string suture followed by xenograft. The tissue blocks were sent for permanent section, which found a poorly differentiated SCC, with a depth of 3.1 mm and

Abbreviations used:

MMF: mycophenolate mofetil
SCC: squamous cell carcinoma

perineural invasion involving a nerve measuring 0.1 mm in diameter. Because of the tissue processing from a Mohs cut to vertical sectioning, intravascular involvement was not initially observed on permanent sections. Fig 3 shows intravascular invasion of a vessel observed after the tissue was re-cut.

After discussion of the case with a multi-disciplinary tumor board, the otolaryngology was consulted for sentinel lymph node biopsy. Radiotracer uptake was seen at the injection site and immediately around the tumor defect, but no sentinel lymph node was identified. Computed tomography angiography of the head and neck and subsequent positron emission tomography scan found no evidence of nodal involvement or metastasis. Systemic chemotherapy with cetuximab was considered although not recommended given tumor clearance with Mohs micrographic surgery.

Radiation therapy was recommended because of several high-risk features and completed with 50 Gy in 20 fractions, leaving a large sclerotic and alopecic patch on the vertex and midscalp. The patient presented 17 months after completing radiation with a 1.5- × 1.5-cm soft, tender, and violaceous

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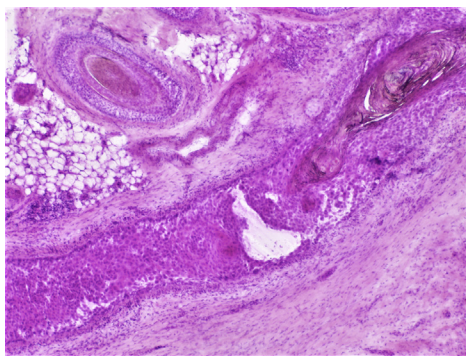


Fig 1. SCC of the skin, initial Mohs layer (processed frozen). In the subcutis, beneath the bulbs of the hair follicles (bottom right), a large-caliber vessel is noted that is completely filled with a proliferation of squamoid morphology cells and one large squamous eddy. Conspicuously absent is the present of normal luminal contents, such as erythrocytes or leukocytes. (Original magnification: $\times 40$.)

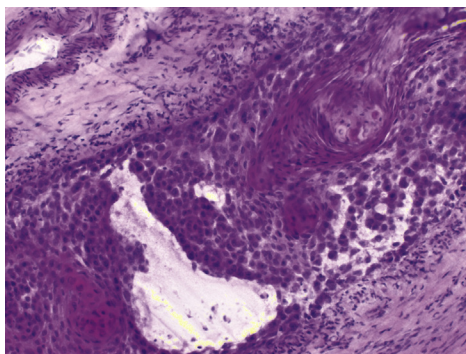


Fig 2. SCC of the skin. On higher magnification, the muscular lining of the vessel wall becomes visible, and the squamoid morphology of the intraluminal proliferation is verified with the cells showing abundant pale cytoplasm and basophilic oval-to-round nuclei. Evidence of keratinization is present with a large parakeratotic squamous eddy. (Original magnification: $\times 100$.)

nodule on the frontal scalp within the anterior border of the radiated area (Fig 4).

Excisional biopsy found SCC extending to the base of the biopsy. Subsequent Mohs micrographic surgery cleared the recurrent tumor in 2 stages. Permanent sections showed high-risk features to include involvement of subcutaneous tissue and perineural invasion involving a 0.12-mm-diameter nerve. This patient has not had a third recurrence although she now has a persistent, hyperkeratotic plaque overlying the most recent surgery site. Scouting biopsies found scar and actinic keratosis, which has not responded to 2 courses of 5 days of fluorouracil plus calcipotriene. This area is stable and considered consistent with postsurgical and radiation change in the setting of systemic sclerosis.

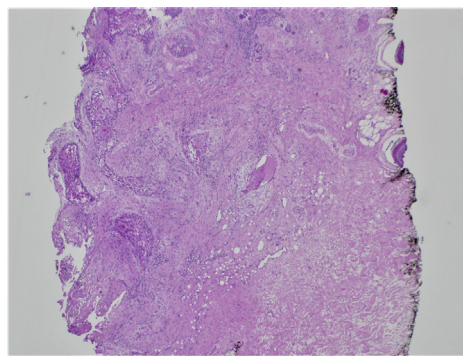


Fig 3. SCC of the skin, permanent section. A large-caliber vessel is noted at the center of the image, which is completely filled with a proliferation of squamoid morphology cells. (Original magnification: $\times 40$.)



Fig 4. SCC of the skin. Frontal scalp with 1.5- \times 1.5-cm soft, tender, violaceous nodule on the frontal scalp within the anterior border of the radiated area.

DISCUSSION

Although intravascular growth of cutaneous SCC is rarely reported, vascular involvement, along with perineural invasion and lymph node involvement, is acknowledged as a predictor for recurrence/metastasis.¹ To our knowledge, this patient represents only the third reported case of cutaneous SCC tumor thrombus occluding a vessel. Both cases detailed high-risk SCC patients, with vascular occlusion from tumor thrombus noted on Mohs slides. Mendese et al² described a patient who remained tumor free at 21 months, despite receiving neither radiotherapy nor adjuvant chemotherapy.² The second patient was treated with Mohs micrographic surgery followed by adjuvant radiation and remained tumor free at 12 months.³ Neither one of these patients had concomitant immunosuppression or systemic sclerosis.

A report by Boozalis et al⁴ summarizes an increased risk of both melanoma and nonmelanoma skin cancers in patients with morphea or systemic sclerosis. It is unclear if the underlying cause is the use of immunosuppressive agents or chronic inflammation.⁴ Although our patient is considered

immunosuppressed, MMF has been shown to have a lower risk of nonmelanoma skin cancer compared with other similar medications.^{5,6} MMF use in mice did not increase the rate of SCC versus placebo and even showed a decrease when added to higher-risk medications.⁵ This finding has not been conclusively demonstrated in humans and requires more investigation, but a nested case control study did find MMF to have an overall lower risk of SCC development than that seen with other immunosuppression.⁵

A review article by Zeineddine et al⁷ suggests that fibrosis in the setting of systemic sclerosis may serve as a nidus for cancer. These authors postulate that chronic inflammation may block lymphatic channels and lead to accumulation of carcinogens.⁷ Although this finding was initially studied in the context of pulmonary fibrosis and lung cancer, it could prove relevant to development of cutaneous SCC. Additionally, Rossi et al⁸ found a significant decrease of lymphatic vessel density in skin affected by scleroderma. They also recognized that the vessels present were dilated, suggesting lymphostasis.⁸ In cutaneous scleroderma, the presence of chronic inflammation and lymphostasis may affect tumor growth (confining its spread to local cutaneous structures) and limit utility of sentinel lymph node biopsy, as in our patient. Additionally, we hypothesize that the presence of cutaneous sclerosis itself may affect tumor growth patterns, with malignant cells following the path of least resistance, resulting in the unusual histologic findings on our patient's Mohs sections. The clinical implications of this phenomenon remain to be determined. Interestingly, there are no case reports discussing metastatic SCC in systemic sclerosis.

Our patient's local recurrence of a high-risk SCC with intravascular occlusion and perineural invasion may be a consequence of the known fibrosis and lymphostasis associated with systemic sclerosis as well as concurrent immunosuppression with MMF. It is unclear if fibrosis could confer protection from lymphatic tumor spread. We recommend close dermatologic surveillance in patients with systemic sclerosis to monitor specifically for disease recurrence and new cutaneous malignancies.

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