Microcystic adnexal carcinoma of the glabella in a liver transplant recipient

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INTRODUCTION

Microcystic adnexal carcinoma is a rare malignant neoplasm first characterized in 1982.[1] Since the first report, at least 300 cases have been described in the literature, and it has been shown to have features of both eccrine ductal and pilosebaceous differentiation.[2] Although it has been suggested that photodamage and iatrogenic irradiation are contributing factors to the development of microcystic adnexal carcinoma, it is uncertain whether systemic immunosuppression confers an increased risk, as with other nonmelanoma skin cancers. Here we present a case of microcystic adnexal carcinoma in a liver transplant recipient. To our knowledge, this represents only the fourth case of microcystic adnexal carcinoma reported in transplant recipients and the first reported in a patient with liver transplantation.[3-5]

Abbreviations used:

BCC: basal cell carcinoma
SCC: squamous cell carcinoma

CASE REPORT

A 54-year-old woman with a medical history of liver transplantation (immunosuppressive regimen of tacrolimus 1 mg daily) 2 years before presented to the transplant dermatology clinic with a 1-week history of dysesthesias in a 1- to 2-cm patch overlying her glabella. She had been treated 2 weeks before and had no symptoms. Her dermatologic history included photodamage and actinic keratosis but no history of melanoma or nonmelanoma skin cancers. She had never been treated with voriconazole or azathioprine.

On physical examination, she had a 7-mm, subtle, light-pink, round macule on the glabella, with minimal scale (Fig 1). A 4-mm punch biopsy revealed atypical keratinocytes infiltrating between collagen bundles, with focal perineural invasion. The aggregates of tumor cells were cytokeratin 116 positive.

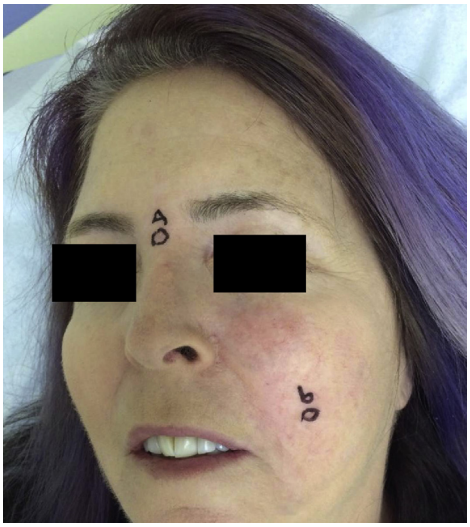

Fig 1. On initial clinical examination of the lesion, there was a 7-mm, subtle, light-pink, round macule on the glabella, with minimal scale (labeled *A* on the patient's face). She had exhibited only symptoms of dysesthesia before presentation.

The lesion was thought to be consistent with an infiltrative squamous cell carcinoma (SCC), and she was referred to the Yale surgical unit for Mohs micrographic surgery excision.

She underwent a single stage of Mohs micrographic surgery, whose results were sent for permanent section because perineural invasion was observed on the frozen sections. Definitive ductal

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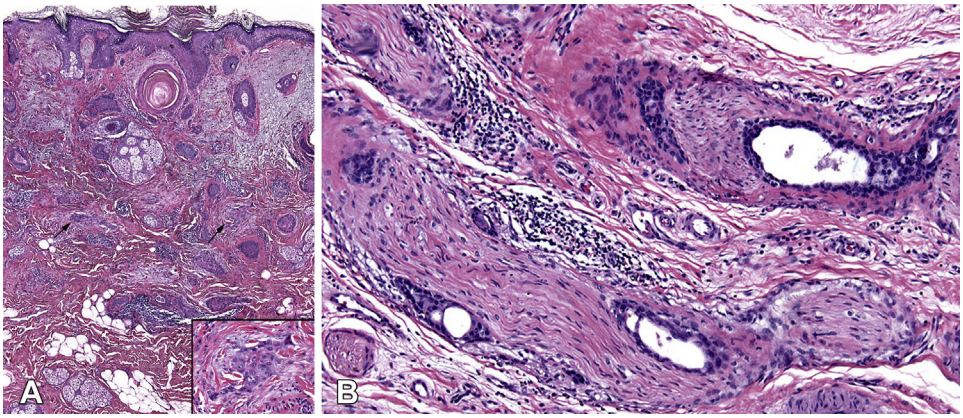

Fig 2. The original biopsy showed subtle islands of atypical squamous epithelium infiltrating the dermis, as indicated by the arrows, without obvious ductal differentiation; inset shows epithelium marked by arrow on the right. Ductal differentiation and extensive perineural involvement were noted in the re-excision. (Original magnifications: **A**, ×4; **inset**, ×20; **B**, ×10.)

differentiation was evident in the dermis and in perineural tumor (Fig 2). A staged wide local excision was performed, and after 3 stages, the margins were negative for carcinoma. Given the postoperative size of the defect and need for clinical monitoring for recurrence, healing by second intention was deemed to be the most appropriate method of closure (Fig 3). Result for magnetic resonance imaging of the head was unremarkable for deep tissue involvement or metastasis. Adjuvant radiation therapy was considered, but the idea was rejected because there is much debate in the literature regarding its benefit. Additionally, the lesion was close to the eyes, which was also thought to be a less ideal location for adjuvant radiation. The patient was followed at the Yale Transplant Dermatology Clinic every 3 months for total-body skin examination as well as review of systems, including neurologic symptoms such as changes in vision, headaches, paresthesias, skin pain adjacent to the scar, and progressive anesthesia on her face. In the subsequent months, she developed numerous basal cell carcinomas (BCCs) and SCCs away from the site of the microcystic adnexal carcinoma that required addition of sirolimus 3 mg daily, given its antineoplastic effects on nonmelanoma skin cancer. The patient is alive and generally well 45 months postoperatively, without any evidence of local invasion, metastasis, or recurrence.

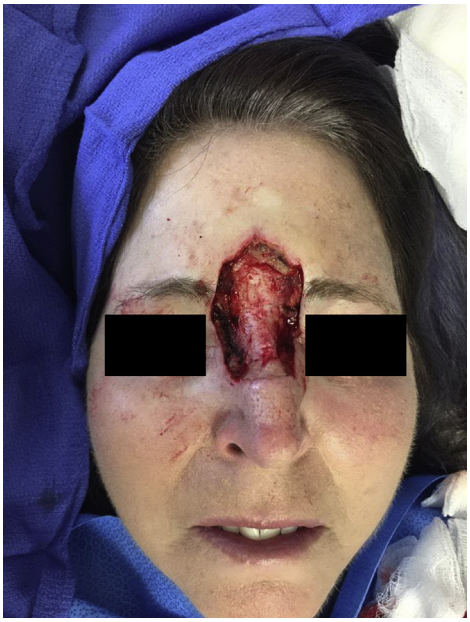

Fig 3. Final size of the lesion after a 3-stage wide local excision. The defect healed well by secondary intent and required no further intervention.

DISCUSSION

Microcystic adnexal carcinoma is a rare cutaneous neoplasm that typically presents in a deceptively indolent fashion on the head and neck, most commonly in women in the fourth through seventh decades of life. It often presents as a slow-growing pink papule or nodule that is often misdiagnosed on biopsy as BCC, SCC, desmoplastic trichoepithelioma, or syringoma.[6] Histopathologically, it was initially characterized by having islands of basaloid keratinocytes, sometimes with horn cysts, and abortive follicles in a desmoplastic stroma. It can also form ductal or glandlike structures that have a paisley-tie or tadpole shape. Deeper sections can show invasion of skeletal muscle and perineural invasion. Because of the depth of invasion, superficial sampling from

Table I. A summary of all the reported cases of microcystic adnexal carcinoma in transplant patients to date

Authors	Age	Sex	Transplant type	Site	Time after Txp	Immunosuppressive regimen	Treatment	Outcome
Birkby et al[3]	51	M	Renal	Lip	NR	Pred 12.5 mg and AZA (dose unreported)	WLE with 1 cm margins and radiation	Recurrence requiring hemimandibulectomy and radiation after 3 years
Snow et al[4]	63	M	Renal	Nasal Bridge/Root	25 y	Pred 5 mg QID and AZA 50 mg daily	MMS and extensive reconstruction	No recurrence at 1 year follow-up
Brookes et al[5]	66	F	Renal	Medial left Lower eyelid	18 mo	Pred and CsA (dose unreported)	MMS	Excision of medial half of lower eyelid with reconstruction
Stamey et al (current study)	54	F	Liver	Glabella	2 y	SLM 3 mg daily and TAC 1 mg daily	WLE with 1 cm margins	No recurrence at 22 months

AZA, Azathioprine; *CSA*, cyclosporine; *MMS*, Mohs micrographic surgery; *Pred*, prednisone; *SLM*, siroliumus; *TAC*, tacrolimus; *TXP*, transplant; *QID*, four times daily; *WLE*, wide local excision.

shave biopsy is a likely contributor to misdiagnosis because it frequently misses the more characteristic features.[1,6]

In regard to management, a limited number of studies have examined excision with simple margins versus Mohs micrographic surgery in management of microcystic adnexal carcinoma. The largest series to date suggests that the Mohs micrographic surgery procedure offered fewer total numbers of procedures required per patient, as well as the smallest average postoperative defect over simple margins. Microcystic adnexal carcinoma has rarely been reported to be metastatic to distant sites but is classically locally invasive, sometimes requiring extensive resection and reconstruction with postoperative radiation.[4] Recurrence rates in the literature are variable and larger case series have reported the rate after primary excision to range from 10.5% to 18%.[4,6,7]

To our knowledge, there have been only 3 other cases of microcystic adnexal carcinoma developing in solid organ transplant recipients. The first reported case was in 1989 on the lower lip of a renal transplant patient and led to significant local invasion of the mandible and bone marrow (Table I).[3] He subsequently underwent hemimandibulectomy followed by radiation therapy, without recurrence at 18 months. The second reported case, also in a renal transplant patient, was an invasive lesion of the nasal bridge into the muscle, bone, and nasal mucosa, requiring extensive reconstruction.[4] The final reported case in the literature was of a microcystic adnexal carcinoma of the medial left lower eyelid in a renal transplant patient, which was misdiagnosed as a chalazion. The lesion required extensive resection of the medial portion of the left eyelid with reconstruction but did not have bony or nodal metastasis.[5] All of these cases were locally aggressive or extensive. It is still unknown whether the impaired immunoresponse (caused by immunosuppressive regimens) in transplant patients may cause these tumors to be more aggressive. Although our patient's lesion did not invade muscle or bone, it did exhibit perineural invasion (an aggressive feature) and required a sizeable excisional defect.

In recent years, the increased risk of SCC and BCC in solid organ transplant recipients has become well established. However, in large follow-up studies of transplant patients, risk stratification was not performed for rarer nonmelanoma tumors such as adnexal and appendageal neoplasms. They were either not reported or grouped into a single category of unspecified neoplasms in these studies.[8,9] Given the relatively high frequency with which microcystic adnexal carcinoma is misdiagnosed on histology as SCC, BCC, or other appendageal neoplasms, it is

possible that these tumors were mischaracterized or misdiagnosed in some patients in these large studies, leading to an underrepresentation of microcystic adnexal carcinoma in the literature. Because our case represents only the fourth ever described in transplant, and the first in a patient with liver disease, more studies need to be performed to determine whether immunosuppression leads to an increased risk or more aggressive nature of these lesions in this population.

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