Revision of immunosuppression in a solid organ transplant recipient leads to complete remission of metastatic undifferentiated carcinoma

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INTRODUCTION

Solid organ transplant recipients (SOTR) suffer an overall 2-fold increased risk of any malignancy compared with the general population. Multiple strategies exist to address this risk in these patients. Revision of immunosuppression is the cornerstone to reducing the risk of skin cancer development. Here we present a patient with a remarkable clinical response to immunosuppression revision.

Case report

A 61-year-old man with a history of a kidney transplantation in 2004 secondary to polycystic kidney disease and a kidney–liver transplant in 2008 for decompensated cryptogenic cirrhosis maintained on tacrolimus, prednisone, and mycophenolate presented to our office with an undifferentiated tumor of the left parotid with distant metastases to the skin. The patient's medical history included multiple cutaneous squamous cell and basal cell carcinomas and a family history of polycystic kidney disease in his father and sister.

Five months prior, he presented to his outside dermatologist with several nodules on the left side of the face. A parotid fine-needle aspiration found atypical cells suspicious for a neoplasm without obvious lineage differentiation. Left superficial parotidectomy found a high-grade malignant tumor with areas of necrosis. The margins were positive, and periparotid lymph nodes were involved. Immunostains were strongly positive for vimentin and focally positive for S100, with absence of staining for a broad panel of epithelial, melanocytic, and hematopoietic markers (Fig 1, *A* and *B*). The final pathologic diagnosis was pleomorphic undifferentiated epithelioid cell neoplasm.

Abbreviations used:

mTOR:	mammalian target of rapamycin
PI3K:	phosphatidylinositol-3 kinase
PET:	positron emission tomography
SCC:	squamous cell carcinoma
SOTR:	solid organ transplant recipient

Postoperative positron emission tomography (PET) scan suggested persistent periparotid and cervical lymph node activity, splenomegaly, and distant metastases to the skin with increased uptake in the left parietal scalp and left anterior chest wall. Core biopsy from the left chest lesion and left scalp found a high-grade undifferentiated epithelioid cell neoplasm identical to the parotid tumor, confirming distant cutaneous metastatic disease (Fig 1, *C* and *D*). These metastases were completely excised, and he underwent a modified neck dissection, which found involvement of multiple cervical lymph nodes.

At the time of presentation to our transplant dermatology clinic, the patient had not undergone treatment. In coordination with the transplant team, recommendations were made to switch from mycophenolate to the mammalian target of rapamycin (mTOR) inhibitor sirolimus while continuing on

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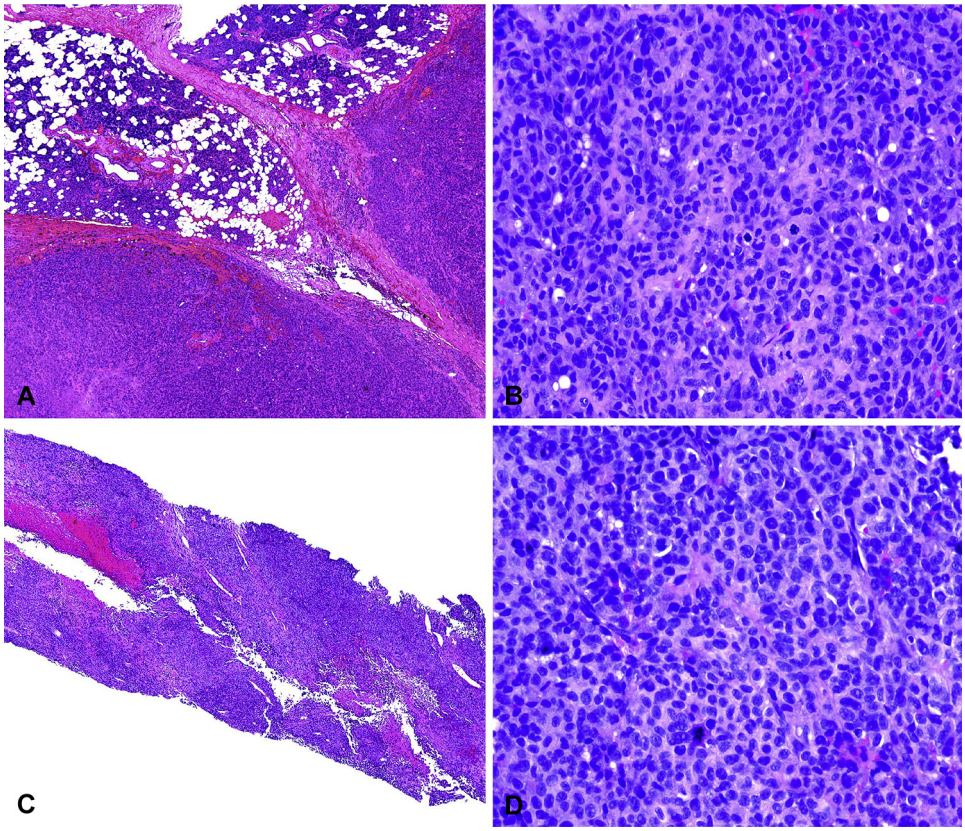

Fig 1. A, Low-power image of tumor nodules (lower portion of Fig 1, *A*) in parotid gland (upper portion of figure), partially surrounded by a fibrous capsule. **B**, Higher magnification shows sheets of pleomorphic undifferentiated epithelioid cells with numerous mitoses. Per report of an outside facility that originally prepared the slides and read the pathology, a panel of immunostains were performed including AE/AE3, EMA, CK5/6, CK7, p40, CK18, 34BE12, p63, calponin, SMA, MITF, MART-1 and HMB-45, GFAP, LCA, CD3, CD20, CD138, CD34, ERG, TTF-1, desmin were negative. Tumor was strongly vimentin positive and focally positive for S100. **C**, Lower power image of needle biopsy from the chest wall shows sheets of pleomorphic cells, focal necrosis, and hemorrhage. **D**, High-power view of undifferentiated pleomorphic epithelioid cells and bizarre mitotic figures, histologically identical to the tumor in the parotid gland. (Hematoxylin-eosin stain; original magnifications: **A** and **C**, ×4; **B** and **D**, ×40.)

tacrolimus and prednisone, 5 mg daily. PET scan at this time found progression of disease with increase in size of the left parotid bed avid nodule from 0.9 × 0.6 cm to 1.3 × 0.8 cm and involvement of new left cervical and left parathyroid lymph nodes (Fig 2). Given the aggressive features of this tumor, the calcineurin inhibitor, tacrolimus, was tapered off. Without any other intervention or change in immunosuppression, repeat PET scan 1 month after discontinuing tacrolimus and 3 months after starting sirolimus found significant improvement with resolution of most periparotid and cervical nodes. Repeat PET scan 4 months off calcineurin inhibitor and 6 months on sirolimus found no evidence of disease (Fig 2). The patient's graft functions remained stable, and his only side effects included nonhealing ulcers of the shin and mild proteinuria.

DISCUSSION

Here we describe a SOTR with an aggressive undifferentiated epithelioid tumor in the parotid gland with skin metastases who had no evidence of disease after converting to an mTOR inhibitor and discontinuing his calcineurin inhibitor and mycophenolate without any other systemic therapy. To date, the benefits of revising immunosuppression regimens have been best studied in the treatment of SOTRs with cutaneous squamous cell carcinoma (SCC); however, there is supporting evidence that decreasing immunosuppression and changing to an mTOR inhibitor may be important in the prevention and treatment of other tumors, including those that are high grade and metastatic as in this case.

SOTRs suffer an overall 2-fold increased risk of any malignancy when compared with the general