# Tracheal squamous cell carcinoma (SCC) metastatic to the skin in a patient on a checkpoint inhibitor

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***Key words:*** antibody-blocking interaction with programmed death ligand 1; checkpoint inhibitor; metastatic squamous cell carcinoma; tracheal squamous cell carcinoma.

Tracheal squamous cell carcinoma (SCC) is an extremely rare cancer, with an incidence of fewer than 10 cases diagnosed in the United States annually.[1] To our knowledge and after extensive literature searching in MEDLINE (PubMed) and Embase databases for published English-language articles, this is the first report of tracheal SCC metastatic to the skin. Our patient was participating in an antibody-blocking interaction with programmed death ligand 1 (anti-PD-L1) checkpoint inhibitor trial, which may or may not have contributed to his metastatic disease.

## CASE REPORT

A 34-year-old man with a known history of tracheal SCC metastatic to bone was enrolled on an institutional review board–approved clinical trial using a checkpoint inhibitor (immunotherapy). He presented with a new and enlarging lesion on the right alar crease for 6 months (Fig 1). Physical examination revealed a 3-mm dome-shaped pink papule with telangiectases, which was removed with shave biopsy. Histopathology showed an essentially normal epidermis with dermal proliferation of epithelioid cells in islands (Fig 2, *A*). The cells were remarkable for marked pleomorphism, hyperchromatic nuclei, numerous atypical mitoses, crowding of nuclei, and displacement of normal cutaneous structures. Examination of the pathology demonstrated a robust lymphocytic infiltration (immune reactivity to the malignancy) and vascular dilatation,

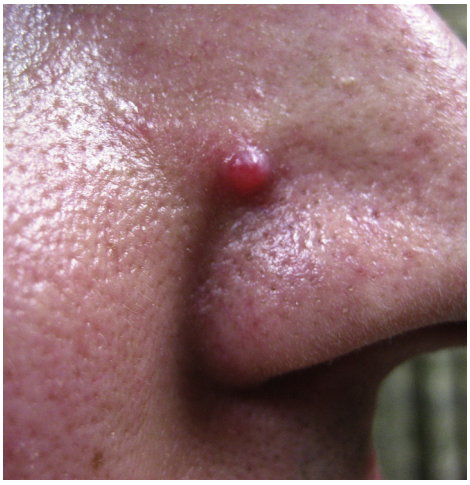

**Fig 1.** Metastatic tracheal squamous cell carcinoma initial presentation.

which is suggestive of neovascularization. The specimen stained positively for cytokeratin 5/6 and 7 (Fig 2, *B*), and stained negatively for cytokeratin 20 and thyroid transcription factor 1. These histopathological and immunohistochemical findings were consistent with metastatic SCC. He had since developed a recurrence at the original site of biopsy, and new similar-appearing lesions on his fingers, which had all responded to radiotherapy (Fig 3). The patient remained on immunotherapy, which was an infusional anti-PD-L1, and had stable disease in all of his sites for 8 months. The patient had stable disease in all of his sites for 8 months. After this time, his tumor

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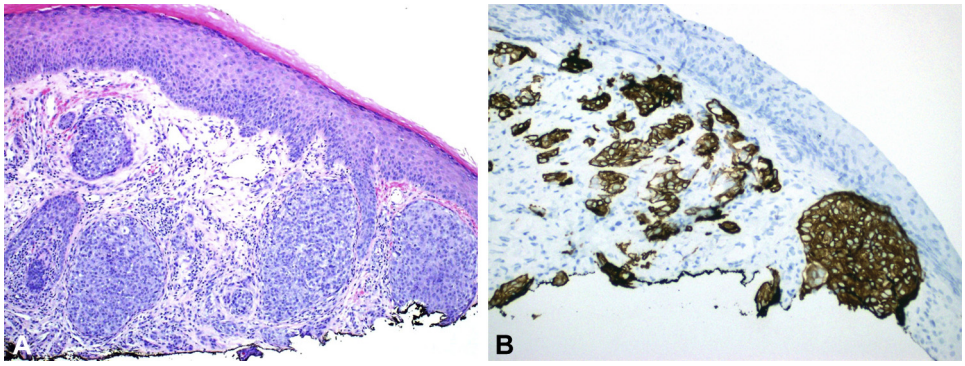


**Fig 2.** **A**, Histopathology of metastatic squamous cell carcinoma, right nasal ala. (Hematoxylin-eosin stain; original magnification: ×10.) **B**, Cytokeratin 7 stain, highlighting neoplastic cells. (Original magnification: ×20.)

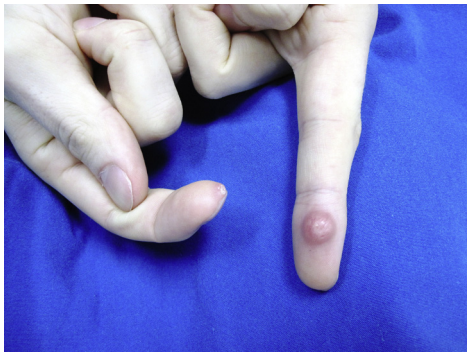

**Fig 3.** Multiple foci of suspected metastatic squamous cell carcinoma.

progressed in all of his known cutaneous sites. Over a period of 2 years, his disease burden increased until he succumbed to his disease.

## DISCUSSION

Advanced tracheal SCC commonly metastasizes to viscera,[2] which was our patient's primary known sites of disease before enrolling on the trial. While on the trial with anti-PD-L1 therapy these sites remained stable, which was documented using contrast computed tomography scans for 8 months. During his treatment, multiple small nontargetable lesions developed within the dermis. The most common side effects currently associated with anti-PD-L1 antibody therapy include fatigue, asthenia, nausea, diarrhea, and rash. Specific cutaneous side effects known to be associated with immunotherapeutics include rash, pruritus, hyperpigmentation, and Sweet syndrome.[3,4] Our patient's cancer progressed while receiving immune checkpoint inhibition in both cutaneous and subcutaneous areas. We are left to postulate that this is either a dynamic of the biology of our patient's tumor, or that it may be in an area where the immune system has a lower recognition of malignant cells secondary to constant exposure to the outside environment. The immune system's inhibitory membrane (checkpoint) ligands have been found to be increased in known immunogenic tumors including nonsmall cell lung cancer, melanoma, and renal cell cancer.[5] Our patient participated in a phase-I, dose-escalation portion of the study, which may also lead to the assumption that not all of his checkpoint inhibitory ligands were inhibited. The patient participated in dose level 2 of 6 dose levels. This is the first reported case to our knowledge of tracheal SCC metastatic to the skin in a patient receiving a checkpoint inhibitor. Although it is too early to draw a conclusion, this may become either a common area to which cutaneous metastasis break through or an unusual correlation.

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