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Simultaneous metastasis of melanoma and lung adenocarcinoma to hilar lymph nodes and pleural effusion after renal transplantation

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The simultaneous involvement of two different primary tumours metastatic to one anatomic site is exceptionally rare. The diagnosis of two malignancies on fine needle aspiration (FNA) cytology is also exceptionally uncommon and typically involves metastasis to a lymph node involved by lymphoma.¹⁻⁵ We describe a case of the simultaneous metastasis of melanoma and lung adenocarcinoma in a hilar lymph node diagnosed by FNA, and subsequent simultaneous metastasis in pleural effusion.

A 79-year-old man, with a history of a renal transplantation for Goodpasture syndrome and chronic immunosuppression with tacrolimus, presented 4 years post-transplant with a 1-cm right posterior auricular skin melanoma. Wide local excision with sentinel lymph node biopsy revealed a superficial spreading melanoma with a Breslow thickness of 5.75 mm (Clark level IV) and metastatic melanoma to one of two sentinel lymph nodes. A positron emission tomography-computed tomography (PET-CT) scan and brain magnetic resonance imaging (MRI) at that time showed no further evidence of metastatic disease. He underwent extended modified radical neck dissection, which demonstrated melanoma *in situ* distinct from the initial lesion (completely excised). None of the 23 lymph nodes were involved.

Six months later, the patient presented with dyspnoea. Chest CT revealed a 3.5-cm spiculated mass at the apex of the left lung, bilateral small hilar lymph nodes and a small left pleural effusion. The patient underwent a therapeutic and diagnostic thoracocentesis. Cytopathologic examination of the pleural fluid revealed a hypocellular specimen with rare small clusters of atypical cells, suspicious for adenocarcinoma.

Endobronchial ultrasound-guided FNA and core biopsy of an enlarged left hilar lymph node showed a mixed population of malignant cells within the same smear (Figure 1). The first population was cohesive with papillary architecture, smaller, convoluted nuclei and small but conspicuous nucleoli (Figure 1a). Immunohistochemistry (IHC) showed that this

population was positive for TTF-1 (nuclear) and Ber-EP4 (membranous) (Figure 1a, inset). The cytomorphology and immunohistochemical profile were consistent with metastatic adenocarcinoma of a lung primary. The second population was discohesive with a predominance of single cells in the background of the aforementioned papillary groups. The cells had enlarged nuclei, prominent nucleoli, nuclear pseudo-inclusions, double mirror-image nuclei and fine brown cytoplasmic pigment (Figure 1b). By IHC, the cells were positive for S-100 and HMB-45 (Figure 1b, inset). The second population was consistent with metastatic melanoma.

The diagnosis of two advanced malignancies – stage IV melanoma and clinical stage IIIA non-small cell lung cancer – in the setting of multiple comorbidities, including renal transplant with immunosuppression, suggested a poor prognosis, and prognostic/treatment decisions focused on melanoma treatment. The initial tumour was negative for BRAF V600E, excluding BRAF-inhibitor vemurafenib. In the setting of renal transplantation, immunomodulatory therapy with ipilimumab was contraindicated. The patient's immunosuppression (tacrolimus) was reduced, but not discontinued. The patient declined chemotherapy, opting to pursue best supportive care.

Six weeks later, the patient underwent palliative thoracocentesis of a large left-sided pleural effusion. The cytology of the pleural fluid revealed metastatic adenocarcinoma and melanoma. Dual chromogen IHC performed on a cell block preparation showed a population of malignant single cells with cytoplasmic positivity for HMB-45 and a distinct second population of cell clusters with nuclear positivity for TTF-1 (Figure 2). The patient's condition continued to deteriorate and he died 1 month later.

We report the first case of two distinct sites of simultaneous metastasis in the same patient – melanoma and lung adenocarcinoma to both a hilar lymph node and pleural effusion. By cytology, the diagnosis of simultaneous tumours has only been reported rarely. Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) has been identified by cytology involving the same lymph node as metastatic Merkel cell carcinoma,¹ squamous cell carcinoma²⁻⁵ and adenocarcinoma.⁵

This case is also of clinical importance as patients with solid organ transplant-associated immunosuppression are at increased risk of a number of malignancies, including lung carcinoma and melanoma.⁶ Our patient was 4.5 years post-renal transplantation for Goodpasture syndrome. As a growing number of solid organ transplants with immunosuppression continue to prolong patient survival, these patients will be at increased risk for multiple malignancies, and collision metastasis may become a more common phenomenon in this population.

We present a case of simultaneous metastasis of melanoma and pulmonary adenocarcinoma diagnosed on FNA of lymph nodes and also pleural fluid. Although exceptionally rare, patients with solid organ transplantation are at risk of secondary malignancies. With the growing use of FNA biopsy, the cytopathologist should be aware of the possibility of simultaneous metastasis on cytology samples, which can be identified and diagnosed, especially with the use of ancillary studies.

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Figure 1.

Fine needle aspirate of hilar lymph node. (a) Direct smears showing cohesive papillary fragments and numerous single cells in the background (haematoxylin and eosin $\times 100$). Inset: cell block showing strong, diffuse nuclear TTF-1 positivity (immunohistochemistry $\times 400$). (b) Direct smears showing single malignant, epithelioid to plasmacytoid cells, double mirror-image nuclei, prominent nucleoli, cytoplasmic pigmentation (haematoxylin and eosin $\times 400$). Inset: cell block preparation showing fragment of metastatic melanoma with strong, cytoplasmic HMB-45 positivity. Note small fragment of papillary adenocarcinoma negative for HMB-45 (immunohistochemistry $\times 100$).

Figure 2. Pleural fluid cytology. Cell block preparation dual staining with TTF-1 and HMB-45 (red). Note distinct cohesive population of metastatic adenocarcinoma positive for nuclear TTF-1 and single cells and small clusters with cytoplasmic staining with HMB-45 (immunohistochemistry $\times 100$).