Metastatic Melanoma Resembling a Fibrohistiocytic Tumor with Osteoclast-like Giant Cells

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INTRODUCTION
Numerous histopathologic variants of malignant melanoma (MM) exist. The presence of osteoclast-like giant cells (OCG) in melanoma rarely has been reported in the literature and may result in a misdiagnosis of a histiocytic tumor. Malignant neoplasms containing OCGs are rare and the origin of these cells is often difficult to determine. Studies of OCGs in tumors of the pancreas and the liver have demonstrated the same K-ras mutation as dysplastic ductal epithelial cells suggesting that they may represent transformed tumor cells.1 On the other hand, studies of OCGs in tumors of various organs including skin, observed that the giant cells expressed several monocyte/macrophage markers including leukocyte common antigen and CD68, suggesting that these cells are reactive histiocytes rather than neoplastic. Since only few cases have been reported, awareness of this entity is important to avoid misdiagnosis of melanoma as a histiocytic tumor.

CASE REPORT
The patient was a 78-year-old man who initially presented in 2006 with a changing pigmented lesion on his right postural region. This was biopsied and diagnosed as a 4.3 mm malignant melanoma without ulceration. The patient was treated with a wide excision and sentinel lymph node dissection (T4a, N0, M0, stage IB). Past medical history included a serum calcium of the back, status post resection in 2005, bladder cancer, status post cystectomy, and basal cell carcinoma of the right scalp. He had an 80 pack-year smoking history and he reported very little sun exposure while growing up except in young adulthood, during the summers, vacationing in Cape Cod. However, he did not recall any significant blisters, sunburns, or tans.

PET/CT scans were ordered yearly to monitor for recurrence. A PET scan from January 2010 identified focal increased metabolic activity in the area of the right parotid gland, but the patient was asymptomatic. In March of 2011, the patient and his wife noted a mass in the soft tissue of the right pectoral region. This was biopsied and diagnosed as a 4.3 mm malignant melanoma without ulceration. The patient was treated with a wide excision and sentinel lymph node dissection (T4a, N0, M0, stage IB).

A staging PET scan in May 2011 revealed an avid 1.5 cm mass in the right upper lobe, a 1.0 cm nodule in the left lower lobe, a 0.7 cm right adrenal nodule, and multiple 2–3 mm lymph nodes bilaterally. Twenty-nine lymph nodes were negative for metastatic melanoma. A staging PET scan in May 2011 revealed an avid 1.5 cm mass in the right upper lobe, a 1.0 cm nodule in the left lower lobe, a 0.7 cm right adrenal nodule, and multiple 2–3 mm lymph nodes bilaterally. Twenty-nine lymph nodes were negative for metastatic melanoma. PET scans were ordered yearly to monitor for recurrence.

A CT scan of the neck confirmed a 3.0 cm mass within the parotid. The patient was scheduled for a near total right parotidectomy in 2006. The parotid tumor measured approximately 5 x 6 cm. Grossly, sectioning the tumor showed well-defined, 3 cm mass with satellite nodules. The cut surface was tan-white, fleshy, with heterogeneous areas of hemorrhage. Postoperatively, the patient did well and remained stable and unchanged.

CLINICAL PRESENTATION AND HISTOPATHOLOGIC FEATURES

The tumor was composed mostly of large mononuclear epithelioid non-keratinizing cells intermixed with numerous osteoclast-like giant cells. This was supported by evidence that the OGCs in tumors of the pancreas and liver by molecular genetic methods, where the microdissected giant cells showed the same K-ras mutation as the precursor dysplastic ductal epithelial cells. The alternative theory suggests that the OGCs are stromal, presumably reactive components. This was supported by evidence that p53 mutation and proliferating cell nuclear antigen expression were only found in the mononucleated giant cells and not in the OGCs in tumors of the lung and pancreas, as well as the consistent lack of expression of epithelial markers by these giant cells.2

The significance of OGCs in melanomas is unknown since only a few cases have been reported. Denton et al reported lymph node metastasis 6 months after the first surgical excision. A case report by Danzor et al described metastasis to the femoral head, simulating a giant cell tumor of bone. Arthrex et al reported two cases, one of which similarly developed recurrence within 1 year with metastasis into the lymph node. Similarly, we describe a patient with a lymph node metastasis 5 years after the excision of his primary melanoma. Although the presence of OGCs in melanoma might suggest aggressive behavior, more reports are needed to study long-term prognosis of melanoma with this morphology.

REFERENCES

SUMMARY

Malignant neoplasms containing OGCs are rare. The giant cell variant of unifocalized pleomorphic sarcoma contains numerous, benign-looking, osteoclast-like multinucleated giant cells. In some cases, however, these giant cells may show malignant features. Histologically, they are described as having round to spindled-shaped cells forming the background for uniformly scattered, osteoclast-like multinucleated giant cells. Most of these are non-occlusive and average 2–3 per 10 high power fields. This tumor is regarded as a distinct entity: giant cell tumor of soft tissues.3 The immunophenotype of giant cell tumor of soft tissue display immunoreactivity for vimentin, CD68, and smooth muscle actin. CD68 strongly marks the multinucleated giant cells, the mononuclear cells show focal staining. Smooth muscle actin stains a few mononuclear cells but does not mark the multinucleated giant cells. Rarely, tumors react focally with antibodies against keratin and S100 protein.1 The giant cell tumor of soft tissue should be differentiated from other giant-cell-rich neoplasms, namely, giant-cell–rich carcinomas (e.g., pancreas, thyroid, breast), osteoclast–rich osteosarcoma, giant-cell–rich liposarcoma, and giant-cell–rich malignant mesenchymal tumors.

There are two theories regarding the origin of the OGCs in malignant tumors. One suggests that they may represent proliferation of mature osteoclasts within bone nodules in the right lower lobe of lung, enlarged right thyroid with mild increased avidity, diffusely increased uptake in the stomach thought to be secondary to inflammation or infection, and increased uptake in an enlarged right adrenal gland. A restaging CT scan of the chest, abdomen, and pelvis with contrast done at the same time showed an ill-defined right thyroid mass, 0.5 cm nodule in the right lower lung base, 1.4 cm nodule in the subcutaneous tissue anterior to the inferior sternum, and a 2.1 cm right adrenal nodule. An MRI of the brain showed no evidence of metastatic disease.

PET/CT findings were preclusive to be metastatic tumor nodules. The patient’s treatment options included observation: sunitinib at 3 mg/kg, and enrollment in an ECOG 1668 clinical trial with 10 mg/kg of sunitinib with or without GM-CSF. As of December 2011, he had undergone a total of four induction doses of sunitinib at 3 mg/kg. Most recent scans revealed that his thyroid, lung, and adrenal lesions remain stable and unchanged.