# 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 MM has rarely been reported in the literature and may result in a misdiagnosis of a histiocytic tumor. Malignant neoplasms containing OGCs are rare and the origin of these cells is often disputed. Molecular studies of OGCs 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 OGCs 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 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 axillary lymph node dissection (T4a, N0, M0, stage IIB). Past medical history included a sarcoma of the back, status post resection in 2005; bladder cancer, status post cauterization; 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 blistering sunburns.

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 noticed a mass in the soft tissue around the angle of the right mandible **(Figure 1)**. A CT scan of the neck confirmed a 3.5 cm mass within the parotid.

The patient was scheduled for a near total right parotidectomy and neck dissection. Intraoperatively, 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 **(Figure 2)**. Microscopic examination showed a malignant tumor composed mostly of large mononuclear epithelioid non-pigmented cells intermixed with numerous OGCs **(Figure 3 & 4)**. The tumor cells were S100 and Melan A positive, and negative for HMB45, AE1/AE3, SMA, and Desmin. The OGCs were negative for all the previously mentioned markers **(Figure 5)**. The findings were consistent with metastatic melanoma involving a parotid lymph node, infiltrating the parotid gland and extraparotid soft tissues, and demonstrating vascular and perineural invasion. Twenty-nine lymph nodes were identified in the neck dissection specimen, all of which were negative for metastatic melanoma.

A staging PET scan in May 2011 revealed an avid nodule 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 tissues 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 presumed to be metastatic tumor nodules. The patient's treatment options included: observation; ipilimumab at 3 mg/kg; and enrollment in an ECOG 1608 clinical trial with 10 mg/kg of ipilimumab with or without GM-CSF. As of October 2011, he had undergone a total of four induction doses of ipilimumab at 3 mg/kg. Most recent scans revealed that his thyroid, lung, and adrenal lesions remain stable and unchanged.

## CLINICAL PRESENTATION AND HISTOPATHOLOGIC FEATURES

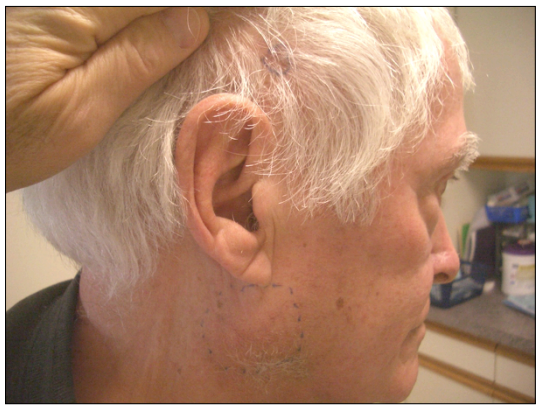

**Figure 1:** A 4 cm firm mass at the angle of the mandible that was not attached to the overlying skin and freely mobile. Scalp lesion shows a previously excised basal cell carcinoma.

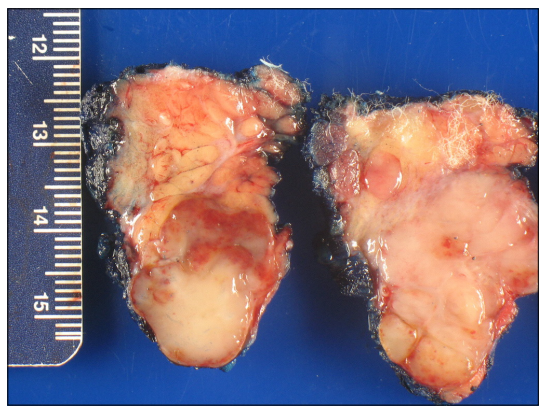


**Figure 2:** The parotid tumor showed a well-circumscribed tan white mass with satellite nodules, many of which infiltrated surrounding soft tissues. At the periphery, residual brown nodal tissue is appreciated within unremarkable parotid gland.

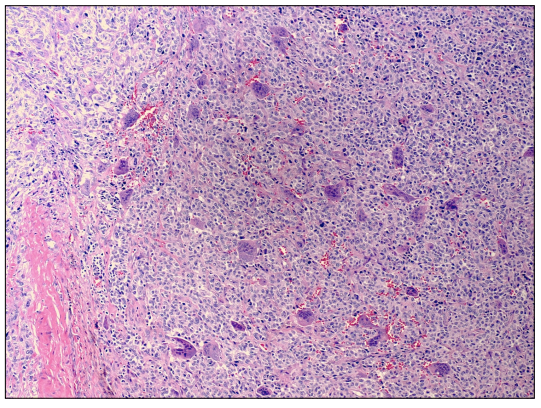

**Figure 3:** The tumor was composed mostly of large mononuclear epithelioid non-pigmented cells intermixed with numerous osteoclast-like giant cells.

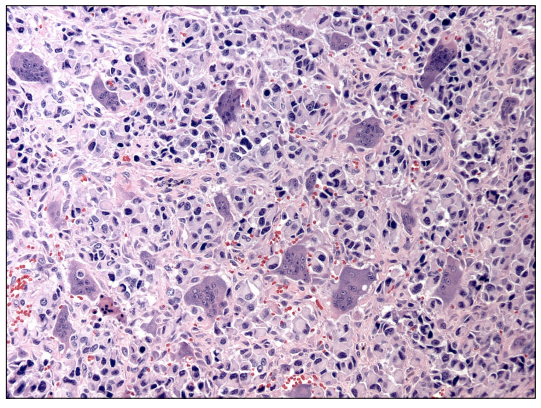

**Figure 4:** Higher power image of osteoclast-like giant cells displaying multiple bland central nuclei.

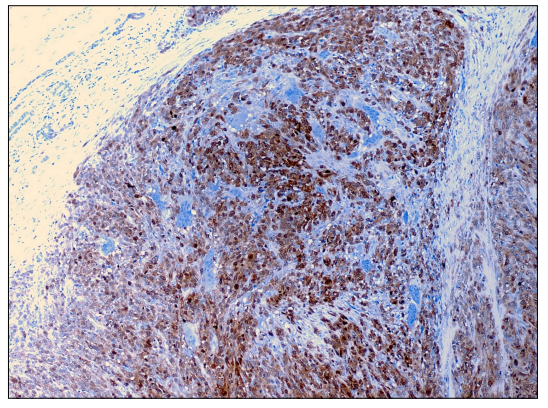

**Figure 5:** S100 immunostain heavily marks tumor cells, while sparing the osteoclast-like giant cells.

## SUMMARY

Malignant neoplasms containing OGCs are rare. The giant cell variant of undifferentiated 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 spindle-shaped cells forming the background for uniformly scattered, osteoclast-like multinucleated giant cells. Mitoses are not uncommon and average 2–3 per 10 high power fields. This tumor is now regarded as a distinct entity: giant cell tumor of soft tissues.[2] The immunophenotype of giant cell tumor of soft tissues display immunoreactivity for vimentin, CD68, and smooth muscle actin. CD68 strongly marks the multinucleated giant cells; the mononuclear cells show only focal staining. Smooth muscle actin stains a few mononuclear cells and does not mark the multinucleated giant cells. Rarely, tumors react focally with antibodies against keratin and S100 protein.[3] The giant cell tumor of soft tissues should be differentiated from other giant-cell–rich neoplasms, namely, giant-cell–rich carcinomas (e.g., pancreas, thyroid, breast, kidney), extraskeletal osteosarcomas, giant-cell–rich leiomyosarcomas, and giant-cell–rich malignant mesenchymomas.

There are two theories regarding the origin of the OGCs in malignant tumors. One suggests that they may represent primary transformed tumor cells. This was supported by studies of OGC 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 mononuclear tumor 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.[4]

The significance of OGCs in melanomas is unknown since only a few cases have been reported. Denton et al[5] reported lymph node metastasis 6 months after the first surgical excision. A case report by Daroca et al[6] described metastasis to the femoral head, simulating a giant cell tumor of bone. Al-Brahim[7] et al reported three 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.

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