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TITLE: Giant malignant melanoma of the anterior chest wall with widespread metastasis

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ABSTRACT

Introduction:
Giant melanomas are defined as lesions greater than 10 centimeters; independent of their depth of invasion; these entities are rarely encountered in clinical practice and they represent a real treatment challenge as many patients are diagnosed with advanced disease. Here we document our experience with the first reported giant melanoma of the anterior chest wall and the 5th largest melanoma of any anatomic site.

Case Report:
A 63-year-old Caucasian male presented with an irregular, pigmented, non-healing ulcer, measuring 1.5 by 1.5 centimeters on his chest. He was referred for a skin biopsy but was lost to follow up. He returned one year later complaining of fatigue, night sweats, and unintentional weight loss in addition to further growth of the skin lesion. His skin lesion was now a large, fungating mass, fixed to the chest wall and measuring 15 by 13 by 2.5 centimeter. There were multiple satellite lesions on the chest wall and palpable left axillary lymphadenopathy. Skin biopsy confirmed the diagnosis of malignant melanoma. Computerized tomography imaging demonstrated innumerable pulmonary nodules, retroperitoneal and peri-splenic lymphadenopathy with hepatic and bone metastasis. The patient’s clinical course was later complicated by lower extremities arterial and venous thrombosis. Patient expired 15 months after the initial visit.

Conclusion:
Metastatic melanoma portends a long-term survival of less than 10%. Treatment depends on whether the disease is limited or disseminated; the latter is generally managed by systemic therapy or supportive care. Given the rarity of giant melanomas there is not a general consensus regarding the management of this subgroup of patients.

Keywords: Giant melanoma, metastatic melanoma, skin cancer, chest wall tumor.
INTRODUCTION
The incidence of cutaneous melanoma is increasing faster than any other potentially preventable cancer in the United States [1]. In 2015, it is estimated that there will be 73,870 new cases of melanoma in the United States and 9,940 deaths from the disease [2]. Melanoma is the fifth most common cancer in men and seventh in women in the United States. Survival rates tend to decline as the tumor depth of invasion increases. Patients with thin stage I lesions can expect prolonged disease-free survival and even cure, while those with thicker, later stage lesions (e.g. Breslow thickness >2.0 mm) are more likely to die from metastatic disease [3-4].

Giant melanomas are defined as lesions greater than 10 centimeters; independent of their depth of invasion [5]. These lesions are mostly seen in adults with an average age of 57 years (range: 29-88 years) [5]. The most common locations for giant melanomas are the scalp, upper extremities, abdomen and back [6-8]. Here we present the first reported giant melanoma of the anterior chest wall.

CASE REPORT
A 63-year-old Caucasian man with past medical history of hypertension, diabetes mellitus type 2, chronic obstructive pulmonary disease (COPD) and post-traumatic stress disorder, presented to our internal medicine clinic complaining of a left sided anterior chest wall wound “that would not heal”. On examination, he had an irregular, pigmented and non-healing ulcer, measuring 1.5 by 1.5 centimeters (cm). He was referred to the dermatology clinic but was lost to follow up despite multiple attempts to contact him. He returned to the hospital one year later complaining of fatigue, night sweats, lower extremities pain and an unintentional 25 pound weight loss. His skin lesion was now a large, fungating mass, fixed to the left anterior chest wall and measuring 15cm x 13cm x 2.5 cm (Figure 1). The mass was malodorous, necrotic and with evidence of recent bleeding. The surrounding skin was erythematosus with multiple satellite lesions on the chest wall and palpable left axillary lymphadenopathy (Figure 2). A punch biopsy from the lesion revealed a metastatic malignant
melanoma, with perineural and lymphovascular invasion, a mitotic index of 10/mm²,
and negative staining for BRAF v600e mutation. Histological sections showed large
polygonal cells with pleomorphic nuclei that contained prominent nucleoli and
deposits of brown melanin pigment (Figure 3).

Computed tomography (CT) revealed disseminated disease, with brain metastasis,
multiple metastatic foci throughout the subcutaneous tissue, innumerable pulmonary
nodules (Figure 4), retroperitoneal and peri-splenic lymphadenopathy, hepatic
metastases, and a solitary lytic lesion at the L4 vertebral body (Figure 5). The patient
was informed of the poor prognosis of the disease and several treatment options
were discussed, including: cytotoxic therapy with cisplatin or inclusion to clinical
trials. The patient’s clinical course was complicated by arterial and venous
thrombosis in the lower extremities leading to severe ischemic pain. After careful
consideration the patient and family decided for a more conservative management
and he was referred to hospice care. He expired 15 months after the initial visit to the
internal medicine clinic.

DISCUSSION

The term “giant melanoma” is used to describe cases of melanomas with a very
large diameter independent of their depth [6-9]. While no diameter is specified, 10
cm is the usual cutoff. This is in contrast to thick melanomas, which have a Breslow’s
depth greater than 4mm. A total of 16 cases of giant melanomas have been
reported in the English literature in the past 30 years, most of them located on the
lower back and scalp [6, 9]. To our knowledge, our case is the first reported giant
melanoma of the anterior chest wall and the 5th largest melanoma reported of any
anatomic site.

Giant cutaneous melanomas tend to be large fungating lesions, with areas of
necrosis and history of bleeding. Satellite lesions around the tumors are frequently
seen with great percentage of patients having palpable regional lymphadenopathy at
the time of diagnosis. The time of growth of the lesions prior to diagnosis can range
from 6 months to 15 years [9]. The average age at the time of diagnosis is 57 years
(range: 29-88 years). Having an equal distribution between genders, these tumors
are more frequently seen in the scalp, upper extremities, back and abdomen. Their
diameter can range from 4 to 25 cm with most cases having extensive
lymphadenopathy at the time of diagnosis [7].

As part of the initial evaluation most patients undergo a non-invasive staging
process, including full body computed tomography scan, positron emission
tomography (PET) scans and brain magnetic resonance imaging (MRI). In our
patient, the staging process revealed stage IV disease with extensive pulmonary,
 liver and brain metastasis. In cases where local lymphadenopathy is the only finding
of systemic involvement, fine needle aspiration is recommended to confirm the
presence of melanocytic cells in the lymph nodes.

Metastatic melanoma portends a long-term survival of less than 10% [4]. Treatment
depends on whether the disease is limited or disseminated; the latter is generally
managed by systemic therapy and supportive care. Novel systemic therapies
include drugs that inhibit CTLA4-mediated signaling (ipilimumab), BRAF mutants
(vemurafenib, dabrafenib), and MEK1/MEK 2 inhibitors (trametinib). Promising
results have also been demonstrated with the immune-checkpoint inhibitors targeting
PD-1 receptors (nivolumab, MK-2475) and cytotoxic therapy with dacarbazine or
carboplatin based regimens [10]. In our patient, due to his extensive disease and
comorbidities, treatment options were limited.

Malignant melanoma has a good prognosis when diagnosed at an early stage. Most
patients presenting with giant melanomas encountered a delay in diagnosis. Factors
leading to delayed diagnosis in these patients are not clear but could include: pursuit
of alternative medicine, socioeconomic factors or other underlying diseases,
including psychiatric conditions [8].

**CONCLUSION**

Giant malignant melanomas are very rare tumors, usually described as large
fungating, vegetative masses with areas of necrosis and bleeding. Their most
common anatomic locations include: scalp, upper extremities and abdomen. Given
the rarity of giant melanomas, it is difficult to draw any conclusion regarding staging
and management strategies. Therefore, we do not have a validated therapeutic
approach. As most patients present with disseminated disease, systemic therapy is the cornerstone in the treatment of these patients. Given the rapid development of novel, highly-efficacious therapeutic agents, participation in clinical trials should be encouraged as these new therapies could improve survival in patients with giant melanomas.

CONFLICT OF INTEREST

No conflict of interest.

AUTHOR’S CONTRIBUTIONS

Narjust Duma MD
Author was involved in the management of the patient, conception and design, drafting of the article and final approval of the version to be published.

Abdullah M. Khan MD
Author was involved in conception and design, critical revision of the article and final approval of the version to be published.

Basil Kasimis MD
Author was involved in the management of the patient, analysis and interpretation of clinical data, critical revision of the article and final approval of the version to be published.

Victor Chang MD
Author was involved in the conception and design, critical revision of the article and final approval of the version to be published.

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TABLES
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FIGURE LEGENDS

Figure 1: Physical examination revealed a giant, fungating mass on the anterior chest wall.

Figure 2: Multiple satellite lesions and axillary lymphadenopathy.
Figure 3: Hematoxylin and eosin staining demonstrated sheets of cohesive epithelioid malignant cells with abundant cytoplasm and prominent nuclei at a mitotic index of 10/MM2.

Figure 4: Computed tomography of the chest demonstrated multiple pulmonary nodules up to 2.5 cm in size.

Figure 5: Abdominal and pelvic computed tomography scan revealed diffuse lymphadenopathy in addition to hepatic and vertebral metastases.

FIGURES

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Figure 2: Multiple satellite lesions and axillary lymphadenopathy.

Figure 3: Hematoxylin and eosin staining demonstrated sheets of cohesive epithelioid malignant cells with abundant cytoplasm and prominent nuclei at a mitotic index of 10/MM2.
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Figure 5: Abdominal and pelvic computed tomography scan revealed diffuse lymphadenopathy in addition to hepatic and vertebral metastases.