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5

6 **AUTHORS:**

7 Narjust Duma¹, Abdullah M. Khan², Basil Kasimis³, Victor Chang⁴

8

9 **AFFILIATIONS:**

10 ¹Internal Medicine Resident, Internal Medicine Department, Rutgers New Jersey
11 Medical School, Newark, New Jersey, United States. Email ID:
12 perezfna@njms.rutgers.edu

13 ²Internal Medicine Resident, Internal Medicine Department, Rutgers New Jersey
14 Medical School, Newark, New Jersey, United States. Email ID:
15 amokhan1980@gmail.com

16 ³Medical Oncologist, Hematology/Oncology Department, Veterans Affairs, East
17 Orange VA Hospital, New Jersey, United States. Email ID: posidon007@aol.com

18 ⁴Medical Oncologist, Hematology/Oncology Department, Veterans Affairs, East
19 Orange VA Hospital, New Jersey, United States. Email ID: victor.chang@va.gov

20

21 **CORRESPONDING AUTHOR DETAILS**

22 Narjust Duma, MD,

23 59 Maier Street, Belleville, New Jersey, United States 07109.

24 Phone Number: 01-206-841-0615, Fax Number: 973-972-3129

25 Email ID: narjustperezmd@gmail.com

26

27 **Short Running Title:** Giant Melanoma of the Anterior Chest Wall.

28

29 **Guarantor of Submission:** The corresponding author is the guarantor of the
30 submission.

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

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34 **ABSTRACT**35 **Introduction:**

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

42

43 **Case Report:**

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

56

57 **Conclusion:**

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

63

64 **Keywords:** Giant melanoma, metastatic melanoma, skin cancer, chest wall tumor.

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

67

68 INTRODUCTION

69 The incidence of cutaneous melanoma is increasing faster than any other potentially
70 preventable cancer in the United States [1]. In 2015, it is estimated that there will be
71 73,870 new cases of melanoma in the United States and 9,940 deaths from the
72 disease [2]. Melanoma is the fifth most common cancer in men and seventh in
73 women in the United States. Survival rates tend to decline as the tumor depth of
74 invasion increases. Patients with thin stage I lesions can expect prolonged disease-
75 free survival and even cure, while those with thicker, later stage lesions (e.g. Breslow
76 thickness >2.0 mm) are more likely to die from metastatic disease [3-4].

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

82

83 CASE REPORT

84 A 63-year-old Caucasian man with past medical history of hypertension, diabetes
85 mellitus type 2, chronic obstructive pulmonary disease (COPD) and post-traumatic
86 stress disorder, presented to our internal medicine clinic complaining of a left sided
87 anterior chest wall wound "that would not heal". On examination, he had an irregular,
88 pigmented and non-healing ulcer, measuring 1.5 by 1.5 centimeters (cm). He was
89 referred to the dermatology clinic but was lost to follow up despite multiple attempts
90 to contact him. He returned to the hospital one year later complaining of fatigue,
91 night sweats, lower extremities pain and an unintentional 25 pound weight loss. His
92 skin lesion was now a large, fungating mass, fixed to the left anterior chest wall and
93 measuring 15cm x 13cm x 2.5 cm (Figure 1). The mass was malodorous, necrotic
94 and with evidence of recent bleeding. The surrounding skin was erythematous with
95 multiple satellite lesions on the chest wall and palpable left axillary lymphadenopathy
96 (Figure 2). A punch biopsy from the lesion revealed a metastatic malignant

97 melanoma, with perineural and lymphovascular invasion, a mitotic index of 10/mm²,
98 and negative staining for BRAF v600e mutation. Histological sections showed large
99 polygonal cells with pleomorphic nuclei that contained prominent nucleoli and
100 deposits of brown melanin pigment (Figure 3).

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

112

113 DISCUSSION

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

122

123 Giant cutaneous melanomas tend to be large fungating lesions, with areas of
124 necrosis and history of bleeding. Satellite lesions around the tumors are frequently
125 seen with great percentage of patients having palpable regional lymphadenopathy at
126 the time of diagnosis. The time of growth of the lesions prior to diagnosis can range
127 from 6 months to 15 years [9]. The average age at the time of diagnosis is 57 years
128 (range: 29-88 years). Having an equal distribution between genders, these tumors

129 are more frequently seen in the scalp, upper extremities, back and abdomen. Their
130 diameter can range from 4 to 25 cm with most cases having extensive
131 lymphadenopathy at the time of diagnosis [7].

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

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

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

153
154

155 **CONCLUSION**

156 Giant malignant melanomas are very rare tumors, usually described as large
157 fungating, vegetative masses with areas of necrosis and bleeding. Their most
158 common anatomic locations include: scalp, upper extremities and abdomen. Given
159 the rarity of giant melanomas, it is difficult to draw any conclusion regarding staging
160 and management strategies. Therefore, we do not have a validated therapeutic

161 approach. As most patients present with disseminated disease, systemic therapy is
162 the cornerstone in the treatment of these patients. Given the rapid development of
163 novel, highly-efficacious therapeutic agents, participation in clinical trials should be
164 encouraged as these new therapies could improve survival in patients with giant
165 melanomas.

166

167 CONFLICT OF INTEREST

168 No conflict of interest.

169

170 AUTHOR'S CONTRIBUTIONS

171 Narjust Duma MD

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

174 Abdullah M. Khan MD

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

177 Basil Kasimis MD

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

181

182 Victor Chang MD

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

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189

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TABLES

NIL

FIGURE LEGENDS

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

223 Figure 2: Multiple satellite lesions and axillary lymphadenopathy.

224 Figure 3: Hematoxylin and eosin staining demonstrated sheets of cohesive
225 epithelioid malignant cells with abundant cytoplasm and prominent nuclei at a mitotic
226 index of 10/MM2.

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

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

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FIGURES



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

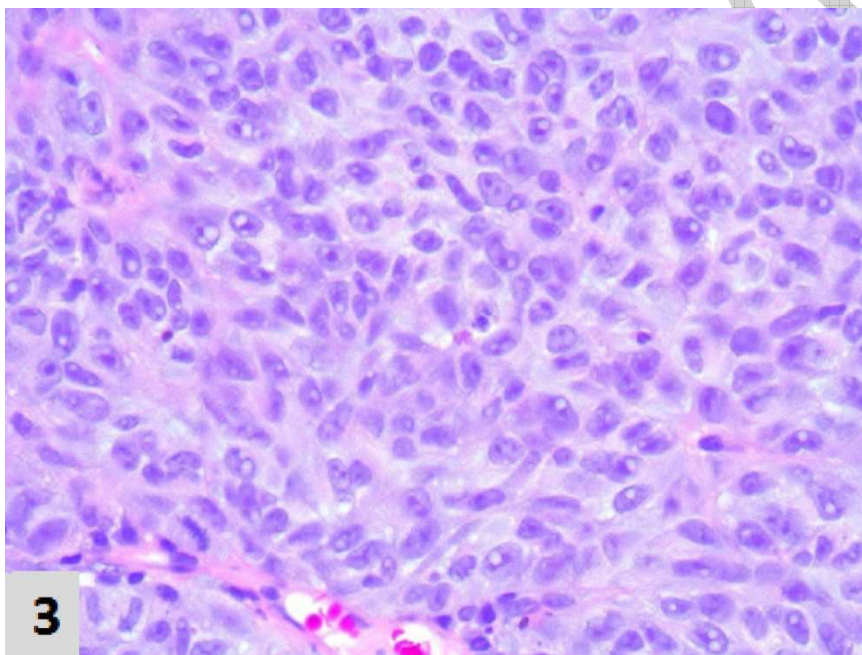
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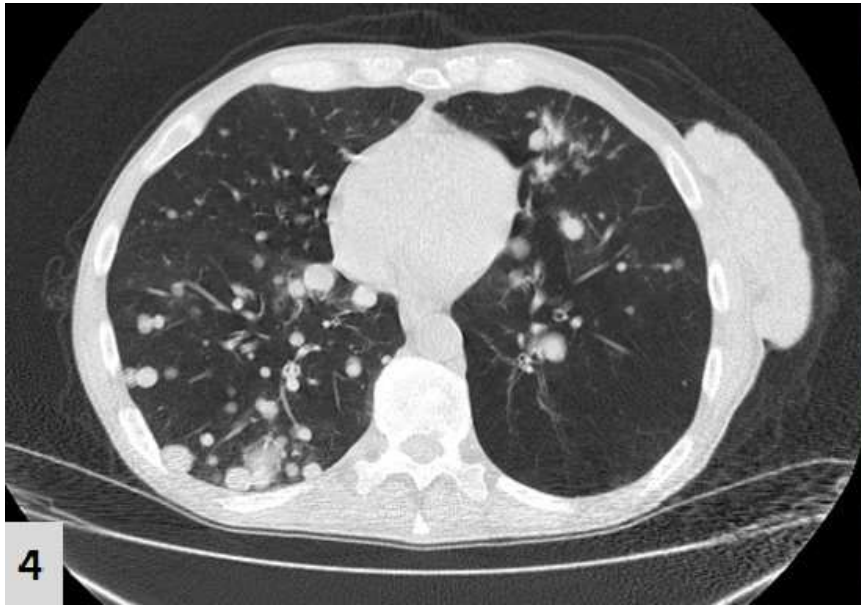
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251 nodules up to 2.5 cm in size.



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254 lymphadenopathy in addition to hepatic and vertebral metastases.

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