

# Giant primary melanoma of the skin arising on the left foot

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## ABSTRACT

Melanoma of the skin usually does not reach a greater dimension. The authors describe unique case of the patient with a huge (giant) primary cutaneous melanoma. 56-year-old man was diagnosed to have melanoma arising on the left foot. Partial surgical amputation with a complete tumor removal was done. Melanoma measured 8 x 4 cm and exhibited massive ulceration, Breslow's thickness 15 mm, Clark's level V, high mitotic and proliferative activity. A patient was classified as stage III B. After surgery, he was relegated to the oncological dispensary health care and took part additional clinical investigations. Finally, PET/CT scan revealed pulmonary and regional lymph node metastases. Therefore, paliative chemotherapy was started. Huge skin melanomas like this are very rarely diagnosed in clinical practice and they are almost always the result of long-term neglect of growing lesion. Currently, it is not answered, whether certain specific factors predispose some melanomas to grow such enormously.

**Key words:** Malignant melanoma; Biological behaviour; Foot

## INTRODUCTION

Melanoma of the skin is one of the most aggressive and prognostically the most unfavorable malignancies in humans. Currently, it is extensively studied oncological entity, mostly due to its dramatically increasing incidence all over the world [1,2]. Cutaneous melanoma usually does not reach a greater dimension. In recent analysis, Seidenari et al. [3] found a mean (microscopically verified) horizontal diameter 1.06 cm. In contrast to skin carcinomas, pathological TNM (Tumor, Nodes, Metastasis) classification of cutaneous melanoma [4] does not include horizontal, but vertical dimension (Breslow's thickness), which is prognostically much more important. Considering an aggressive biological behaviour and high metastatic potential of melanoma there is a small chance, it could grow to the greater size. Moreover, some melanomas may also completely regress, what is usually accompanied by metastases [5]. Therefore, a presence of metastasis of malignant melanoma with unknown primary origo is not unique finding in clinical practice [6,7]. Anyway,

medical literature has sporadically documented case reports of huge (so-called giant) melanomas, although their cut-off limit has not been consensually defined. Some papers [8,9] have considered giant melanomas those, diameter of which exceed 10 cm. However, several authors [10-15] have described cases of giant melanomas not reaching this size. Herein, we present a patient with a huge (giant) cutaneous melanoma arising on the foot.

## CASE REPORT

A 56-year-old man presented with a huge solid tumor involving the toes and instep of the left foot. He admitted the lesion was long standing and originally started to arise on the skin between the fourth and fifth toe almost 3 years ago. Initially, it was asymptomatic and painless. During the last months, however, tumor has began to grow rapidly, progressively increased in size and was accompanied by extensive ulceration, intermittent bleeding and pain. Therefore, he had to see a medical attention and visit an ambulatory surgeon

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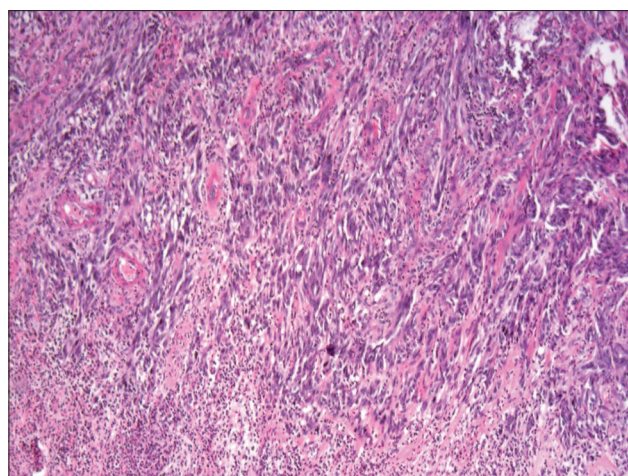
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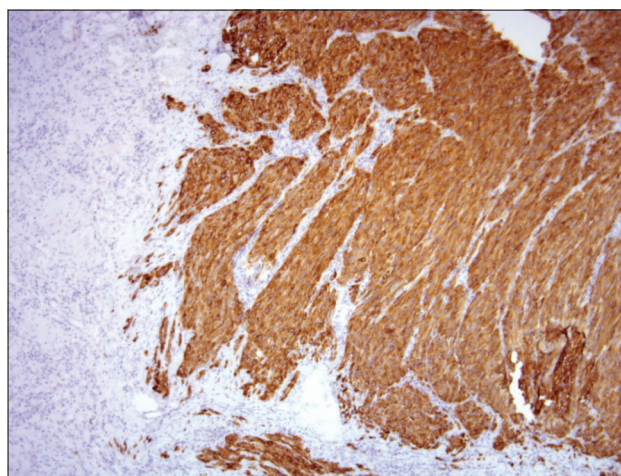
(March, 2015), who performed a probatory incision. After getting a histologically proven diagnosis, he referred him to the hospital. Subsequently, a patient was admitted to the Department of Surgery, where a partial amputation of the foot was preferentially planned. Routine preoperative clinical investigations were done. Among them, none revealed an evidence of distant metastases. X-ray imaging of affected leg did not confirm a tumor infiltration of the bone tissue. A chest X-ray showed no obvious pathology in the pulmonary parenchyma. The standard laboratory parameters were (except slightly elevated serum glucose) within normal limits.

A partial surgical amputation and exarticulation of the foot was done, biopsy specimen was immediately fixed in formalin and sent for definitive histopathological examination. A received biopsy sample consisted of a part of the foot with three toes. On macroscopic examination, the toes, interdigital and metatarsal regions were massively infiltrated by gray-brownish tumor mass. The fourth toe was affected most severely, it was twisted and deformed. A tumor measured 8 x 4 cm in greatest dimension, it was irregularly shaped, protuberant and ulcerated. All nails were intact without tumor changes. There were four colored surgical stitches fixed on the basis of the sample to better indicate resection margins.

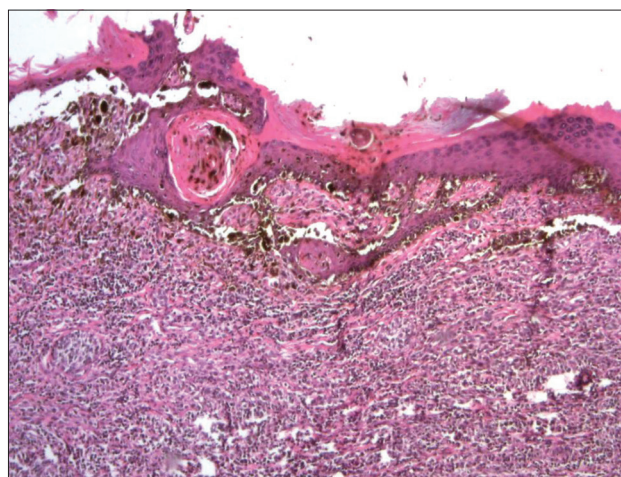
Histopathology revealed a primary malignant melanoma predominantly composed of atypical spindle-shaped cells (Figure 1). It was markedly ulcerated with a purulent detritus on the ulcer basis. Breslow's thickness was at least 15 mm and Clark's level V. Immunohistochemically, it was strongly positive for melan A (Figure 2), HMB-45, S-100 protein and negative for polyclonal cytokeratins. Disseminated deposits of melanin pigment were present in the entire sections. Mitotic activity reached 25 mitoses per 1 mm<sup>2</sup>. Proliferative activity (Ki-67 index) was also high (cca 40%). Neither lymphovascular nor perineural tumor invasion was found in excised sections. In one region, small tumor satellite occurred 8 mm from the main tumor mass. There was scattered intratumorous lymphocyte infiltration (TIL +). Because of advanced stage of the lesion, it was not possible to clearly determine an original histological type of melanoma. However, in one histological section, a small focus of residual atypical lentiginous melanocyte proliferation was detected (Figure 3), which might suggest (even in the context with anatomical site) an acral lentiginous



**Figure 1:** Melanoma predominantly composed of atypical spindle-shaped cells accompanied by secondary desmoplastic reaction and leukocyte infiltration (hematoxylin & eosin staining, original magnification, 100x).



**Figure 2:** Strong immunopositivity for melan A. (monoclonal mouse antibody against melan A, clone A 103, DAKO, original magnification, 100x).



**Figure 3:** A focus of atypical lentiginous melanocytic proliferation at the periphery of melanoma. (hematoxylin & eosin staining, original magnification, 100x).

type. According to the UICC (Union for International Cancer Control) TNM staging system [4], the patient was classified as stage III B (pT4b,N2c,MX). All resection margins marked with surgical stitches were free of tumor and a minimum of 15-mm clearance was achieved. Surrounding skin tissue did not exhibit a solar damage.

Shortly after surgery, CT (computed tomography) scan of thoracic cavity and mediastinum was realized. It confirmed multiple intraparenchymatous nodular lesions in both lungs, some of which unsharply demarcated. The largest one measured 13 x 11 mm and grew out the pleural surface. Thus, melanoma metastases or mycotic infection were considered in differential diagnosis. Furthermore, enlarged lymph node (15 x 11 mm) in the right pulmonary hilus was visible. CT imaging of the abdomen and pelvic cavity did not reveal obvious pathological changes in the visceral organs, either intraabdominal lymphadenopathy. Similarly, both groins were without evident enlargement of the lymph nodes. A postoperative course was uneventful, the patient left the hospital and consequently, he was relegated to the oncologic dispensary health care. An oncologist recommended further examinations to elucidate the origin of pathologic nodules in the lungs. Bronchoscopy did not confirm persuasive pathological changes within the bronchial tree. An aspiration lavage was done and sent for cytological analysis, but no tumor cells nor mycotic microorganisms were found in the fluid. Therefore, the patient underwent PET/CT (positron emission tomography – computed

tomography) examination, that showed an increased glucose metabolism (FDG, 2-fluoro-2-deoxy-D-glucose) within the nodules in both lungs, as well as in the left groin. Based on clinically very suspicious evidence of metastases, a palliative chemotherapy was started. At the time this report was written, our patient had underwent monochemotherapy with dacarbazine. Additionally, there was not detected BRAF gene mutation in tumor tissue.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

## DISCUSSION

Huge skin melanomas like this are very rarely diagnosed in routine clinical practice, mainly because the patients tend to come for treatment early before the tumor enlarges. Therefore, they are almost always the result of long-term neglect of growing lesion. An overview of the cases that have been published until now, including our present case report are summarized in Table 1. As may be seen, they usually occur in the middle or elderly age with approximately equal sex distribution. However, sometimes have been observed in young people up to 35 years of age. In the most documented cases they were localized on the trunk [8,10,13,16-18], but involved also other sites, such as scalp [9,19], arm [20,21], shoulder [22], thumb [11,12], and eyelid [14]. To the best of our knowledge, there has been published only one paper describing giant cutaneous melanoma involving the

**Table 1:** Summary of giant cutaneous melanomas, that have been published until now, including our present case report

Literature	Age	Sex	Location	The largest dimension	Breslow's depth	MTS
Ching & Gould [9]	70	Male	Scalp	14.5 cm	18 mm	+
Tseng et al. [20]	88	Male	Left arm	10 cm	31 mm	+
Tseng et al. [20]	63	Male	Right arm	23 cm	75 mm	+
Kim et al. [11]	56	Female	Left thumb	7 cm	> 4 mm	+
Eisen et al. [13]	47	Male	Back	9 cm	40 mm	+
Grisham [8]	45	Female	Back	13 cm	55 mm	+
Harting et al. [16]	29	Male	Back	25 cm	54 mm	+
Kruijff et al. [10]	56	Female	Back	8 cm	48 mm	+
Panajovic et al. [19]	57	Male	Scalp	12 cm	100 mm	a/n
Del Boz et al. [21]	29	Female	Left arm	20 cm	70 mm	+
Zeebregst et al. [12]	74	Female	Left thumb	7 cm	No mention	+
Pai et al. [14]	53	Male	Left eyelid	5 cm	45 mm	+
Di Meo et al. [17]	60	Female	Abdomen	18 cm	40 mm	+
De Giorgi et al. [18]	45	Female	Abdomen	16 cm	0.45 mm	a/n
Zou & Lam [15]	35	Female	Left leg	8 cm	No mention	a/n
Zou & Lam [15]	72	Male	Right leg	8 cm	No mention	+
Liu et al. [12]	60	Female	Left shoulder	15 cm	> 100 mm	+
Our case	56	Male	Left leg	8 cm	15 mm	+

MTS: Metastases in regional lymph nodes or distant organs, confirmed either clinically or histologically. +: Present. a/n: Absent or not mentioned



foot. Zou and Lam [15] briefly introduced two patients with nodular malignant melanoma located on the sole, both reaching the largest diameter of 8 cm.

According to the literature data [17], a majority of giant melanomas of the skin grew up primarily (*de novo*) without association with precursor melanocytic lesion. Occasionally, there have been described the cases arising from congenital [16] or acquired pigmented melanocytic nevus [14,21]. In our case, it was likely to develop *de novo*, because a patient did not state a previous pigmented skin lesion on the incriminated region. In advanced melanomas, it is very difficult (and usually impossible) to determine an original histological type. Therefore, several case reports of giant melanomas have not precisely classified an histological type. We suppose that our patient could originally have acral lentiginous melanoma, which is the most typical for this anatomical site. In addition, microscopic features of atypical junctional lentiginous melanocytic proliferation were detected at the periphery of the tumor mass. Anyway, in such advanced stages, an exact histological typing does not play a prognostical significance. It is not surprising, a majority of reported giant melanomas were accompanied by metastases in regional lymph nodes or distant organs, whether detected within primary tumor diagnosis, or during further investigations. Except two case reports [18,19], all others corresponded to the clinical stage III or IV and the patients were usually subsequently treated with paliative modalities (i.e. chemotherapy or  $\alpha$ -interferon immunotherapy). However, in such cases, cure effect, as well as disease outcome and survival are hardly predictable.

In conclusion, it is not clear, whether melanomas, which are capable to progress in such large dimension exhibit different biological phenotype from that of "usual" melanoma of equivalent thickness. Further, we have insufficient knowledge, whether certain specific factors predispose some melanomas to grow such enormously. Some melanoma patients with much more smaller primary lesions behave poorly with early distant metastasis, while others develop very extensive primary tumors without or with only late metastases. In addition, some melanomas may fully regress and this phenomenon is usually accompanied by metastatic spread. More light remains to be shed on the pathobiology, malignant progression and pathways of metastasis in this neoplasia, as they are still only partially understood.

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## CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles.

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