Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report DOI: 10.6003/jtad.16102c2

Malignant Melanoma with Unknown Primary; Case Study

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Published:
J Turk Acad Dermatol 2016; **10 (2)**: 16102c2
This article is available from: http://www.jtad.org/2016/2/jtad16102c2.pdf
Keywords: Malignant melanoma, unknown primary, prognosis

Abstract

Observation: Malignant melanoma is a cutaneous cancer which has been seen more frequently in the recent years with increasing mortality. Primary focus cannot be detected in some patients. This delays the diagnosis and the patient is noticed in the later stage. In this study, a case whose primary focus is not known, whose treatment is continuing, who was noticed in later stage was presented. Malignant melanomas which their primary focus is not known originate from usually regressed primary focus. Therefore, we recommend people particularly having predisposing characteristics to undergo medical screening more frequently.

Introduction

Malignant melanoma is a tumor with aggressive course originating from skin, eye, mucous membranes and central nerve system [1]. Although it constitutes 4% of all cutaneous cancers, it is the most frequent cause of mortality among the cutaneous cancer [2]. Its incidence is gradually increasing. It is usually seen in ages between thirty and sixty years. In males, it is observed most commonly on the trunk and on the head and neck secondarily [3]. The known risk factors in the development of melanoma development are as follows; the history of congenital nevus, melanoma covering more than five percent (>5%) of the body surface, family history, dysplastic nevus syndrome, those having five nevi in dimensions of five millimeters or greater than five millimeters or fifty nevi greater than two millimeters, red hairs, blue eyes, living in equatorial regions [4]. Malignant melanoma has radial and vertical growth pattern. Many primary cutaneous lesions have a radial growth pattern lasting for months-years and this enables the physicians, the family or the patient himself or herself to note the lesion in early phase, before progressing to the vertical growth phase and to perform effective surgical treatment. The ten-year survival rates of the melanomas having a depth less than 0.76 millimeters is greater than 95%. To notice the lesion before progressing to the vertical growth phase is important is important in terms of the long-term survival [5]. As a result of the studies and screening programs based on this fact, some risk factors are identified and the screening programs are focused on the people carrying these factors.

However, it is not possible to catch the melanoma cases with unknown primary and it is difficult to establish the diagnosis. Since the patient does not usually describe the nevoid lesion or any cutaneous lesion which is previously existing, malig-

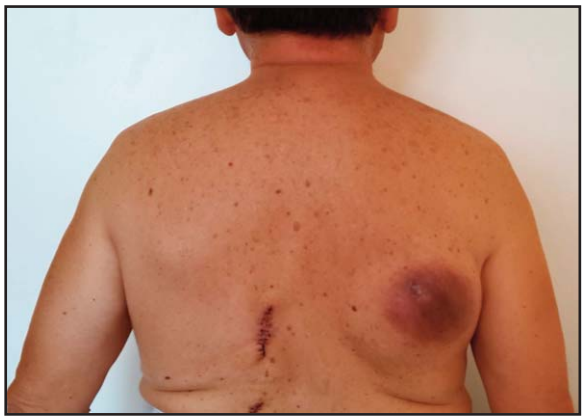

Figure 1. Fixed mass with 5*8*10-centimeter dimensions at the posterolateral dorsum

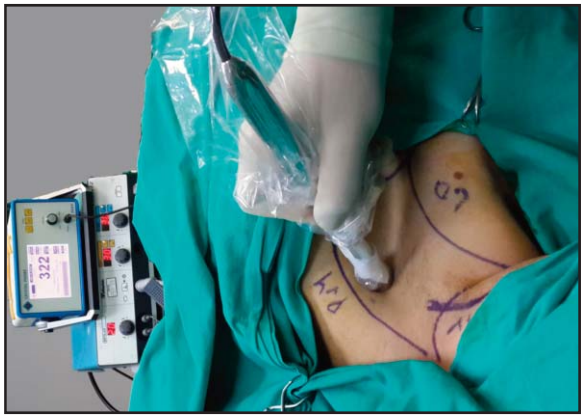

Figure 2. Lymphoscintigraphy with the pre-diagnosis of malignant melanoma

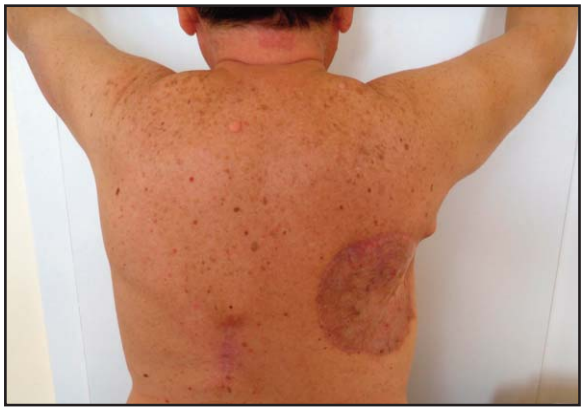

Figure 3. The repair of the mass excision with a skin graft with partial thickness

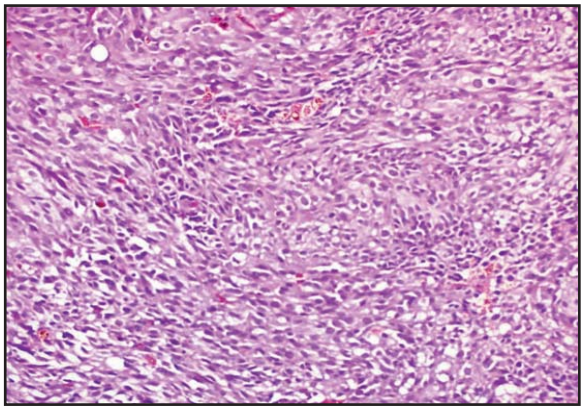

Figure 4. Atypic cells with prominent nucleoli, large vesicular nucleus, eosinophilic cytoplasm and melanin pigment

nant melanoma is in the first rank among the pre-diagnosis. Beside the difficulty of diagnosis and, since they are not noticed by screening differently from other melanomas, complete cure is almost impossible except those being regressed. Malignant melanomas which their primaries are not known are seen rarely; they constitute 4% to 6% of all melanomas. In this study, we aimed to discuss a case which is rarely seen whose diagnosis is established difficultly, that referred us for the purpose of analysis of malignant melanoma cases which could not be detected.

Case Report

A sixty seven-year old male patient referred to our clinic due to the pain caused by a mass existing for one year and growing increasingly. In the physical examination of the patient, there was a hard and fixed mass with 5*8*10-centimeter dimensions at the posterolateral of the dorsum, which expands the skin, which has no alteration in color and, which has no erosion on the surface (**Figure 1**). The patient did not describe any previously existing lesion here. The patient had no characteristic in his medical history. In the acquired Magnetic Resonance Images of the patient a mass lesion in 52*83*94-millimeter dimensions, being localized at the subcutaneous adipose tissue in the right periscapular distance, exhibiting an expansion toward adjacent muscle groups and toward chest wall however, in which a capsule structure that does not exhibit invasion can be distinguished and in which hemorrhage areas are observed was seen. The hematological and biochemical parameters of the patient was within normal limits. Incisional biopsy was done from the current lesion of the patient. As a result of the histopathological examination, it was reported as malignant melanoma metastaz. In the physical examination performed to detect the primary lesion two distinct lesions were found. Excisional biopsy was done from this lesion; however, no malignant melanoma was detected in the histopathologic examination of

these lesions and they were reported as dysplastic nevi. Surgery was planned following the lymphoscintigraphy with the pre-diagnosis of malignant melanoma with unknown primary. Two foci demonstrating Tc99m nanolloid accumulation assessing as centinel lymphatic node in the corresponding to right axillar area was observed in the lymphoscintigraphy (**Figure 2**). So, axillar centinel lymphatic node biopsy was planned for the patient. Incision for biopsy purpose was taken from the region with the highest uptake through gamma counter. However, since the lymphatic nodes with black pigment macroscopically in malignant melanoma view and the uptake was diffuse, axillar dissection was done. After the axillar dissection, the repair of the mass excision and that of open defect was achieved with a skin graft with partial thickness. The case was discharged from the hospital at the post-operative seventh day (**Figure 3**).

While malignant melanoma was reported in one of the six lymphatic nodes taken in the histopathologic examination histiocyte accumulation was reported in other five lymphatic nodes. The patient was taken in follow-up after the pathology report (**Figure 4**). c.1799T>A (p.V600E) mutation was detected in the fifteenth exon of BRAF gene by medical oncology. Peginterferon alpha-2b treatment was continued by the prompted oncologist.

Discussion

Since 93% of the primary malignant melanoma cases are visible, screening programs can be easily applied through cutaneous examination [**6**]. On mucosal surfaces, cases which cannot be seen and which its primary is not known constitute the remaining percent of malignant melanoma.

Commonly seen typical nevi are small pigmented lesions with regular boundaries. Having more than five nevi being larger than five millimeters or more than fifty nevi being larger than two millimeters increases three folds the risk of malignant melanoma risk [**7**]. Atypical nevi are important risk factors in the development of melanoma. According to the study conducted by *Kraemer* et al, if there is atypical nevus in one person in a family, the risk of development of malignant melanoma in people having atypical nevus increases twenty seven folds compared to normal population and, if there is atypical nevus in more than one people with malign melanoma history, risk is increased one hundred forty eight folds [**8**].

While diagnosis of melanoma can be easily established by applying screening programs to the precursor lesions or by following closely the patients with family history, the diagnosis of melanoma cases with unknown primary is extremely difficulty due to the fact that there is no precursor lesion and that it has not been found in the family history. Therefore, the malignant melanoma case with unknown primary can be diagnosed in later period.

To be able to establish the diagnosis in the patients with malignant melanoma with unknown primary, the patients should fulfill the following criteria; [**9**] not to detect any abnormalities in physical examination eyes, rectum and vulva; [**10**] no orbita enucleation or exentration should be done in the medical history of the patient; [**11**] no cauterization or surgery should be applied due to the stork bite, chronic paronychia or skin scars; [**12**] no previous local intervention should be applied in the skin region where lymphatic glands in which metastatic melanoma was detected are drained; [**12**] (Our patient is consistent with these criteria).

Malignant melanomas wit unknown primary are seen commonly in males and in people older fifty years old [**12**]. There are several causes why primary of malignant melanoma cases cannot be found. For example, primary might be regressed after melanoma has made metastasis. In our case, a focus with regression was observed, but no melanocytic cells were found in the pathology specimens. This made us to suggest that either focus is not here or all cells could be migrated.

Primary melanoma can be developed directly from ectopic lymphatic gland or tumor can be in a localization which cannot be reached easily [**13**].

In the patients having malignant melanoma with unknown primary, sentinel lymphatic gland sampling should be done in the current lesion during the diagnosis, excision of the current lesion and sentinel lymphatic node dissection should be done only in patients with regional lymphatic gland. By performing regional lymphatic node dissection, the disease can be taken under the control locally.

In the cases having malignant melanoma with unknown primary, there are different opinions for the prognosis of the patients. The

prognosis of the patients with distant organ metastasis are worst compared to that of the patients having only regional lymphatic gland involvement.

Although malignant melanomas are among the tumors having increasing incidence in the recent years and the patients having malignant melanoma with unknown primary are those whose diagnoses can be established via the metastases in the local late stage, it is likely to obtain long-term survival by means of surgical interventions and adjoin therapies. Therefore, surgical treatment for curative purpose should be applied to the patients in this group and adjuvant therapies should be added to surgery. As known, all of the malignant melanoma cases are not only originated from a primary nevus; but some of them can develop form normal skin [**14**]. Furthermore, since the primary focus is missed in the malignant melanoma cases with unknown primary also, the diagnosis is delayed. Therefore, the screenings of the patients having risk factor in terms of malignant melanoma should be done frequently and in a careful manner. In the screenings, it should not be focused only on nevi but also, the entire cutaneous mucosa (rectum, vagina), the eyes and, cutaneous scars should be also included.

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