

Case report

MULTIPLE PRIMARY MELANOMAS: A CASE REPORT

МУЛТИПЛИ ПРИМАРНИ МЕЛАНОМИ: ПРИКАЗ НА СЛУЧАЈ

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Abstract

Introduction. Patients diagnosed with single primary melanoma of the skin have an increased risk of developing other malignancies, particularly other melanomas and non-melanoma skin cancers. Review of literature shows that most patients with multiple melanoma lesions develop only two melanomas, although patients with 3 or 4 lesions are also not uncommon.

Case report. A case of a 46-year-old woman with diagnosed 10 primary melanomas and 2 basal cell carcinomas (BCC) is presented. The patient came to the University Clinic for Plastic and Reconstructive Surgery in Skopje for a second opinion two months after a nodular melanoma on her left arm had been excised. As part of the regular monitoring schedule, dermoscopy examination recognized 9 other pigmented lesions as melanoma lesions and excisional biopsy was advised. The histopathological result revealed 9 primary melanomas and 2 BCC.

Discussion. Nodular melanoma is most frequently seen as the first described melanoma. The subsequent melanomas are usually thinner in terms of Breslow thickness and Clark's level. The first diagnosed melanoma in this case report was also nodular melanoma and the subsequent melanomas were thinner. There were no signs of lymphovascular invasion with in the initial tumor and brisk and non-brisk presence of tumor infiltrating lymphocytes (TIL) was observed. All of this is in accordance with literature data.

Conclusion. It is important to highlight the significance of the screening programs for early melanoma detection together with regular self-examination and preventive behavior. Early tumor detection is vital for decline in melanoma morbidity and mortality.

Keywords: skin melanoma, multiple primary lesions

Апстракт

Вовед. Пациентите со дијагностициран примарен меланом на кожа имаат зголемен ризик за развој на други малигноми, особено меланоми и не-меланомски кожни карциноми. Прегледот на литература покажува дека повеќето од пациентите со мултипли меланомски лезии имаат по две, три или четири лезии.

Приказ на случај. Прикажан е случај на 46 годишна жена со дијагностицирани 10 примарни меланоми и два базоцелуларни карциноми. Пациентката се јави на Клиниката за Пластична и реконструктивна хирургија во Скопје за второ мислење откако и бил дијагностициран и опериран нодуларен меланом на левата надлактица. Како дел од рутинските иследувања, направена е дермоскопија која посочи 9 други пигментни лезии сомнителни за меланоми. Промените се отстранети, а патохистолошкиот резултат покажа постоење на уште 9 примарни меланоми и два базоцелуларни карциноми.

Дикусија. Нодуларениот меланом најчесто се јавува како примарната лезија, додека следно откриените меланоми се обично потенки земајќи ги во предвид класификациите на Бреслов и Кларк. И во овој приказ на случај, првиот откриен меланом беше нодуларен, додека останатите лезии беа потенки. Не беше забележана лимфоваскуларна инфилтрација, а беше забележана силно и умерено изразена лимфоцитна инфилтрација околу секоја од отстранетите меланомски промени. Сите податоци се во согласност со податоците од литературата.

Заклучок. Раното откривање на меланомот е круцијално за намалувањето на неговиот морталитетот и морбидитет. Затоа е важно е да се потенцира значењето на скринингот во рано откривање на меланомот заедно со свесноста за само-преглед и превентивното однесување.

Клучни зборови: меланом на кожа, мултипли примарни лезии

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Introduction

Melanoma of the skin accounts for about 10% of all skin cancers. It is mainly caused by UV light-induced DNA damage with intense intermittent exposure at an early age, which has a very strong harmful effect. A personal history of dysplastic nevi syndrome is another well-known risk factor [1-2].

Melanoma patients are mainly concentrated in highly developed countries. They have lighter skin and thus greater susceptibility to ultraviolet radiation. The highest incidence has been observed in Australia and New Zealand followed by Western Europe, North America and Northern Europe [3-4].

Patients diagnosed with single primary melanoma of the skin have an increased risk of developing other malignancies during their lifetime. They are especially susceptible for developing multiple primary melanomas and non-melanoma skin cancers (NMSCs) [2,5].

Multiple primary melanomas are defined as more than one synchronous or metachronous melanoma in the same individual. Synchronous melanomas are distinct melanoma lesions discovered within three months after the diagnosis of the first melanoma. Some of them can be detected during a single visit at the doctor's office while others can be detected during the follow-up period. According to different population-based studies, the incidence of multiple primary melanomas in melanoma patients with focus on cutaneous melanomas ranges from 2 to 10%. Synchronous lesions are discovered in 26-40% of the cases while the remainder of the lesions develops as metachronous. Almost half of the subsequent cutaneous melanomas are diagnosed in the first three years after the initial melanoma diagnosis [2,5-6]. However, cases with subsequent melanomas are reported up to 2 to 3 decades after the first lesion.

Etiological factors responsible for developing of a subsequent melanoma can be grouped into host-related, lifestyle factors and environmental influences. These factors include older age, fair skin type, male sex, family and personal history of melanoma, dysplastic nevi syndrome and multiple cherry angiomas [7-9]. The pathogenesis of cherry angiomas and its association with skin tumors is not yet clearly known. The study of Pastor Thomas N *et al.* suggests that cherry angiomas might be a result of actinic skin damage in patients with some degree of genetic susceptibility, but their association with multiple melanomas should further be investigated.

Review of the literature shows that most patients with multiple melanoma lesions develop only two melanomas. Patients with 3 or 4 lesions are also not uncommon. Rare case reports or studies report patients with

multiple primary melanomas. Cleason *et al.* in their study that included 12.152 patients in Western Sweden reported only one patient diagnosed with a total of 16 separate melanomas. However, a case of as many as 48 melanomas in one patient was reported in the literature [10].

Case report

A case of a 46-year-old woman with diagnosed 10 primary melanomas and 2 basal cell carcinomas is presented. The patient came to the University Clinic for Plastic and Reconstructive Surgery in Skopje for a second opinion two months after a melanoma lesion on the outer part of her left arm had been excised in another institution. The first melanoma lesion was seen as nodular melanoma with T4a tumor thickness. The patient had no positive family history of melanoma or history of immunosuppression. She had fair skin and high count of nevi all over her body.

As part of the regular monitoring schedule, she was advised to perform a full skin body check-up at the dermatology unit. Dermoscopy examination recognized 9 pigmented lesions as melanoma lesions and excisional biopsy was advised (Figure 1a-f).



Fig. 1a.

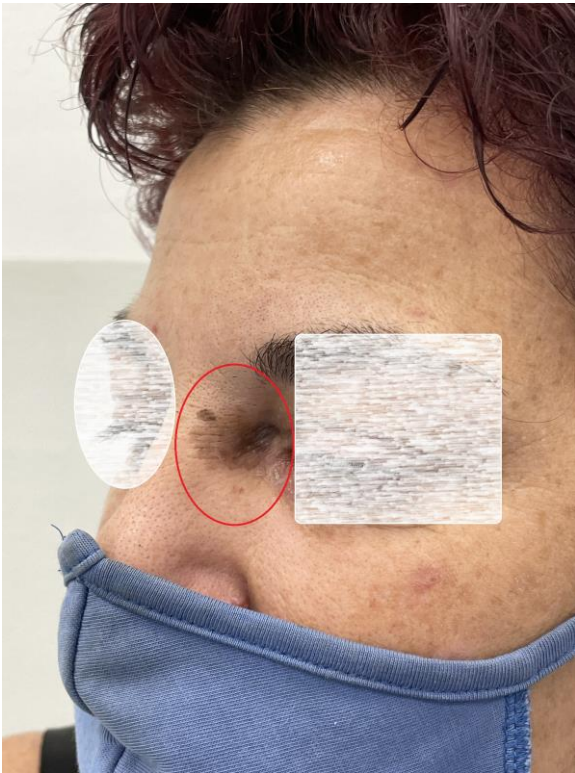


Fig. 1b.



Fig. 1d.



Fig. 1c.



Fig. 1e.



Fig. 1f.
Fig. 1a-f. Multiple primary melanomas in the presented patient



Fig. 2b.



Fig. 2a.



Fig. 2c.



Fig. 2a-c. Some of the defects after excision of melanoma were closed with direct suture while as the others were closed with split thickness skin grafts

The protocol of 2-stage treatment was described to the patient. Considering the need of two operations and having in mind her family obligations, a decision was made to perform a single, more radical operation of all the suspected lesions.

Radical excision of all the suspected melanoma lesions was performed with a safe margin ranging between 10-20 mm depending on the dermatological result, clinical finding and depending on where the lesions were located. The operation was performed in local potentiated anesthesia. Some of the defects were closed with direct suture while the others were closed with split thickness skin grafts [Figure 2a-c]. The postoperative period was uneventful. The patient was released on the 5th postoperative day. All the wounds healed with primary intention.

The histopathological result revealed 9 primary melanomas and 2 basal cell carcinomas. One of the melanoma lesions was described as superficial spreading melanoma (SSM) and another one was described as lentigo maligna melanoma (LMM). The rest of the lesions, seven, were diagnosed as non-otherwise specified melanoma lesions. The thickness of the tumors was varying between 3.2 mm and 0.3 mm. According to the TNM classification of cutaneous melanomas (UICC TNM 8), they were classified between T3a and T1a. No lymphovascular invasion was detected within any of the lesions, moreover brisk and non-brisk tumor infiltrating lymphocytes (TIL) presence around every tumor lesion was established respectively.

With regard to the anatomic side, 3 of the subsequent melanoma lesions were placed on the face; one was set on the neck whereas 3 melanoma lesions were found on the trunk and 2 on the upper extremities.

The performed PET scan showed no pathological accumulation. Afterwards she was treated with biological therapy (Pembrolizumab) at the Institute for Oncology. Eighteen months after the operation, her condition is stable and she is still on biological therapy.

Discussion

The presence of high count of dysplastic nevi is a well-recognized risk factor for developing multiple primary melanomas, which has also been shown in the presented case. Patients with single primary melanoma are prone to developing other malignances, especially multiple melanomas and non-melanoma skin lesions. The presented patient was diagnosed with 10 separate primary melanomas and two basal cell carcinomas.

Nodular melanoma is most frequently seen as the first described melanoma. The subsequent melanomas are usually thinner in terms of Breslow thickness and Clark's level of invasion. SSM together with LMM are the most common histological subtypes with subsequent melanomas. The first diagnosed melanoma in this case report was nodular melanoma as well. The other diagnosed melanomas were thinner. One of them was described as SSM and another one as LMM.

LMM usually occurs on sun damaged skin, hence, it is found more often on the sun exposed body parts. On the other hand, SSM occurs most often on the trunk and lower extremities. In the case presented here, the SSM lesion was set on the body (infraclavicular region) while the LMM lesion was set on the face, a fact which is in accordance with literature data.

Even when invasive, the second and high-order melanomas in MPM patients are usually thinner than the primary ones [11]. It has also been observed that these melanomas have negative sentinel lymph nodes and lack lymphovascular invasion with the initial tumor [5, 12]. This might be a result of both the biological tumor behavior and improved surveillance.

In this case report, no signs of lymphovascular invasion within the initial tumor were noticed and there was no non-brisk and brisk presence of TIL.

Most existing literature suggests that patients with MPMs have enhanced survival compared to patients with single primary melanoma [10,13]. This may be due to the "immunization effect" to common melanoma tumor agents. Namely, it has been suggested that patients who have had a melanoma may develop increased immunity against certain antigens expressed by tumor-associated melanocytes, and thus, the host immune response can result in slower tumor progression [14,15].

Conclusion

SSM together with LMM are the most common histological subtypes with subsequent melanomas. Since LMM is considered to be related with a high degree of cumulative exposure to UV radiation, active preventive measures against chronic sun damage should be stressed in patients with MPMs.

Furthermore, as 26-40% of the melanomas develop as synchronous lesions and might be discovered during a single visit at the attending doctor, it is imperative to underline the importance of a complete skin examina-

tion during the initial examination with a particular attention on chronically sun-exposed areas. On the other hand, the risk of developing subsequent primary melanomas remains increased for at least 20 years after the primary lesion, which leads us to the need of lifetime clinical follow-up.

The cutaneous melanoma incidence may be increasing at an exponential rate worldwide. If 2020 rates continue, the burden from melanoma is estimated to increase to 510,000 new cases (a roughly 50% increase) and to 96,000 deaths (a 68% increase) by 2040 [16]. That is why it is important to highlight the significance of the screening programs for early melanoma detection together with regular self-examination and preventive behavior. Early tumor detection is vital for decline in melanoma morbidity and mortality, thus decreasing the burden to the health system as well.

Conflict of interest statement. None declared.

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