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CASE REPORTS / OPISY PRZYPADKÓW

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# RADICALIZATION OF SURGICAL TREATMENT IN PEDIATRIC MELANOMA MALIGNUM

# RADYKALIZACJA LECZENIA CHIRURGICZNEGO W CZERNIAKU ZŁOŚLIWYM U DZIECI

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## Summary

Introduction. Melanoma is one of the most malignant cancers; however, melanoma in children is a very rare disease, accounting for only 1% of all new cases of cancer diagnosed annually. The objective of this paper is to present two cases of pediatric melanoma malignum with respect to model of surgical management related to stage of the disease with surgical approach based on current guidelines of American Joint Committee on Cancer (AJCC).

Case reports. In first case of 4-year old girl, the melanotic lesion was on the right arm and sentinel lymph node in in right axillary region. After sentinel lymph node biopsy (SLNB) of right axillary space and histologic diagnosis of confirmed malignancy, the patient was qualified for regional lymphadenectomy. The final staging was IIIC grade, and further therapy with interferon was continued. In the second case of 17-year old boy, with congenital naevus on the right earlobe, a SLNB of the right axillary lymph node was performed. Histologic examination of the lymph node did not reveal metastasis to the lymph node. The final was grade IIA and no further therapy was required.

Conclusions. Both patients remain in complete clinical remission for 9 and 12 months after the diagnosis, confirmed by imaging and laboratory examinations. Both cases underline proper therapeutic approach based on radicalization of surgical treatment, sentinel lymph node biopsy followed by regional lymphadenectomy and interferon therapy in case of confirmed metastasis or no further therapy in case of negative histology of sentinel lymph node.

## Streszczenie

Wstęp. Czerniak złośliwy skóry to jeden z najbardziej złośliwych nowotworów, jednak jednocześnie bardzo rzadko występujący u dzieci. Jego częstość występowania nie przekracza 1% wszystkich przypadków nowotworów złośliwych u dzieci. Celem tej pracy jest przedstawienie opisu dwóch przypadków czerniaka złośliwego u dzieci z podkreśleniem dwóch modeli postępowania chirurgicznego w zależności od stopnia zaawansowania nowotworu w oparciu o wytyczne American Joint Committee on Cancer (AJCC).

Opisy przypadków. W pierwszym przypadku 4-letniej dziewczynki, zmiana była zlokalizowana na ramieniu, a węzeł chłonny wartowniczy w dole pachowym. Po wykonaniu biopsji chirurgicznej węzła wartowniczego w badaniu histo-patologicznym potwierdzono przerzut, w związku z czym wykonano zabieg limfadenektomii regionalnej. Po ustaleniu stopnia zaawansowania IIIC,

pacjentkę zakwalifikowano do terapii interferonem. W drugim przypadku, chłopca 17-letniego, z pierwotną zmianą na płatku ucha, wykonano biopsję węzła wartowniczego, jednak nie potwierdzono przerzutu do tego węzła. W związku z tym ostateczny stopień zaawansowania klinicznego ustalony jako IIB oznaczał zakończenie terapii.

W n i o s k i . W obydwu przypadkach pacjenci pozostają w całkowitej remisji przez okres odpowiednio 12 i 9 miesięcy, potwierdzonej w badaniach obrazowych i laboratoryjnych. Obydwa przypadki pokazują prawidłowe postępowanie terapeutyczne, oparte na radykalizacji leczenia chirurgicznego, biopsji chirurgicznej węzła wartowniczego i następowej limfadenektomii regionalnej oraz terapii onkologicznej z zastosowaniem interferonu w przypadku potwierdzenia przerzutów do węzła albo zakończeniu terapii w przypadku nieobecności przerzutów.

***Key words:*** melanoma malignum, naevus, children, adolescents, radical surgery
***Słowa kluczowe:*** czerniak złośliwy, znamię barwnikowe, dzieci, młodzież, radykalny zabieg chirurgiczny

## INTRODUCTION

Melanoma in children is a very rare disease. Melanoma accounts for <3% of all cancers seen in children, and the incidence in children and adolescents accounts for only approximately 1% of all new cases of cancer diagnosed annually [1]. The incidence of melanoma increases with the advancing age, and is very rare in patients younger than 15 years of age compared with those between 15-19 years. An overall pediatric melanoma incidence is 4.9 per 1 million individuals. The annual percentage change of 2.8% makes melanoma one of only a few pediatric neoplasms with significantly increased rates during last two decades [2].

The risk factors for melanoma include inherent (intrinsic) and acquired (extrinsic) factors. Examples of inherent risk factors include age, pigmentation, nevi pattern, genetics and family history, and coincident medical conditions [3]. A systematic meta-analysis of observational studies of melanoma risk factors identified an increased melanoma risk for physical attributes such as blue eye color, fair skin color, red hair color, and high density of freckles [4]. Extrinsic factors that contribute to increased melanoma risk include sunburns or exposures to medications, such as psoralens, which can artificially increase damage caused by UV rays. A number of common phototoxic medications, such as tetracycline antibiotics, cetirizine, propranolol, naproxen, and fluoxetine, lead to increased UV damage and sunburns. Also, long-term use of medications that cause immune system suppression can increase melanoma risk among organ transplantation recipients [5]. Chronic systemic antifungal prophylaxis with voriconazole, which causes photosensitivity, can be associated with melanoma [6].

The most important and visible pre-melanotic feature are the nevi. Congenital nevi are traditionally defined as melanocytic nevi that are present at birth, and have historically been classified based on final, adult size [7]. Categorization of cutaneous features of congenital melanocytic nevi include division of medium (M1: 1.5–10 cm, M2: >10–20 cm), large (L1: >20–30 cm, L2: >30–40 cm), and giant (G1: >40–60 cm, G2: >60 cm) sized nevi [7]. Most patients (>80%) present with localized disease at diagnosis; the remainder either have regional lymph node disease (10% to 15%) or distant metastasis (1% to 3%) [1]. This corresponds to staging of melanoma, including stages I and II which are localized melanoma, stage III is regional metastasis, and stage IV is distant metastasis.

In a patient with ‘signature nevus’ pattern, a nevus should be typically evaluated by examination of clinical features, including the classic ‘ABCDE’ criteria (asymmetry, border irregularity, color variegation, diameter >6 mm, and/or evolution), known also as Friedman clinical rating, as well as pediatric-specific melanoma criteria of melanosis, bleeding, ‘bumps’, color uniformity, diameter variability, and de novo development [8].

Melanoma is one of the most malignant cancers. The suspicion is made clinically with dermatoscopy and the final diagnosis is made by the histopathological examination. The management of patients with melanoma is stage-dependent. Proper staging requires a thorough clinical, histopathologic, laboratory, imaging evaluation and the initial surgical evaluation. Pathological changes are classified also according to Breslow thickness [12].

The objective of this paper is to present two cases of pediatric melanoma malignum with respect to a model of surgical management related to stage of the disease. This surgical approach was based on current guidelines of American Joint Committee on Cancer (AJCC) [9].

CASE REPORT 1

A 4 year old girl, with normal development, was admitted to the Department due to naevus on the right arm, with recurrent bleeding and increasing size over the period of previous six months. Family history was without cases of melanoma. The naevus was resected with safety margin within unchanged tissue. The initial histological diagnosis was melanocytic tumor of uncertain malignant potential (MELTUMP) - atypical Spitz tumor. The histologic diagnosis was verified in reference center (The Children's Memorial Health Institute, Warsaw) and the final diagnosis was compound naevus Spitz with focal transformation of melanoma malignum (Spitz-like melanoma). The lymph node in right axilla region was palpable. Ultrasound examination of this area showed enlarged hypoechogenic lymph node of size 12 x 11 mm. PET-CT showed increased metabolism of the lymph node, typical for malignancy. No other suspicious foci were found by PET scan. The child was qualified for radicalization of surgery at the primary site, with respective margin of 3.5-4 cm in normal tissues (skin, subcutaneous tissue and muscular fascia), followed by transplantation of skin from right groin, together with sentinel lymph node biopsy (SLNB) of right axillary space. Histologic diagnosis of the resected specimen confirmed radical excision of the malignant infiltration in the previous scar. Also the lymph node pathologic examination confirmed metastasis of Spitz-like melanoma. According to AJCC guidelines [9], the patient was qualified for further radical surgery i.e. regional lymphadenectomy. The final clinical AJCC staging was grade IIIC, and further conservative therapy with interferon alpha-2b for 48 weeks (EST protocol). The girl remains in complete clinical remission for one year after the diagnosis, confirmed by CT and ultrasound examinations.

CASE REPORT 2

A 17-year old boy, with congenital naevus of 8 mm diameter localized on right earlobe, without oncologic suspicion, was admitted to the Regional Pediatric Surgery Department due to mechanical injury of right auricle. Family history was without cases of melanoma. The initial histological diagnosis of the resected naevus was: melanoma malignum, naevoid melanoma typus epithelioides exulcerans Clark III, Breslow 4 mm. The histologic diagnosis was verified in reference center (The Children's Memorial Health Institute, Warsaw) and the final diagnosis was: nodular malignant melanoma Clark III, Breslow 4 mm. There was no malignant invasion in the epithelium. The small lymph node in right axilla region was palpable. Ultrasound examination of this area showed enlarged hypoechogenic lymph node of size 8 x 5 mm. PET-CT showed neither increased metabolism of the lymph node nor other suspicious foci. The boy was qualified for radicalization of surgical treatment in the area of the primary lesion with concurrent plastic surgery of the right auricle (Figure 1) together with sentinel lymph node biopsy of right axillary space. Histologic examination of the lymph node indicated no metastasis to the sentinel lymph node. The final clinical AJCC staging was grade IIA (T3, N0, M0). The boy remains in complete clinical remission for nine months after the diagnosis, confirmed by ultrasound examinations.

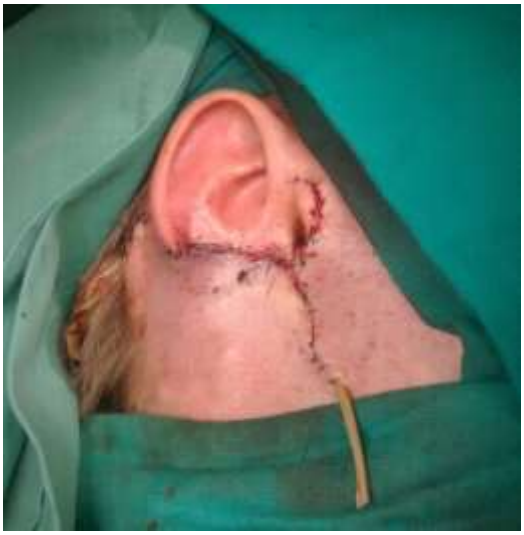

Fig. 1. *Radicalization of the local surgical treatment. Plastic surgery of the right auricle*
Ryc. 1. *Radykalizacja miejscowego leczenia chirurgicznego. Operacja plastyczna prawego płatka usznego*

DISCUSSION

In this report we present two cases of very rare pediatric melanoma. The diagnosis in both cases was confirmed in reference pathology center. In both cases, sentinel lymph node biopsy was clinically present. In first case, of 4-year old girl, the primary melanotic change was oncologically active (increase of naevus diameter and bleeding) and PET scan showed increased metabolic activity of sentinel lymph node. In

second case, of 17-year old boy, the primary melanotic change was oncologically inactive and PET scan did not show increased metabolic activity of sentinel lymph node. In first case radical regional lymphadenectomy was performed, while in the second one it was not required. Further clinical management and follow-up for 9-12 months confirmed proper surgical and oncological approach.

Resection of melanotic change and sentinel lymph node should be performed by a trained surgical oncologist. Lesions should be primarily excised in such a way that the depth of the lesion can be adequately assessed, usually with the margin of 1-3 mm. Exceptions from this rule include lentigo maligna melanoma. Histologic diagnosis of melanoma, with the presence or absence of ulceration, thickness of the lesion, mitotic rate and assessment of the surgical margins will determine the need for further surgery to achieve an adequate surgical margin and the need for nodal staging.

Previous studies have reported that compared with adults, pediatric melanoma patients exhibit higher rates of lymph node metastases ranging from 25 to 40% [10]. Although higher rates of lymph node metastases have been reported in pediatric melanoma patients, the prognostic value of sentinel lymph node biopsy (SLNB) has not been extensively studied in this population. The few studies on SLNB for pediatric melanoma have reported varying results, with some studies reporting no recurrences or deaths in positive SLNB patients while one study showed that the overall survival rate of 94% seen in pediatric melanoma patients dropped to 79 % in positive SLNB patients [10,11]. Currently, there is a common agreement that pediatric patients with clinically localized melanomas >1 mm thickness should be offered SLNB. Also, after clinical diagnosis the melanoma should be resected with one to two centimeter safety margins [12]. Nowadays, it seems that patient and tumor characteristics in pediatric melanoma patients show no evident differences to adult melanoma cases; thus, the literature suggests the same clinical approach as in adults should be used [12].

In conclusion, reported two cases of pediatric patients with clinically localized melanomas who were referred for radicalization of surgery with safety margins together with sentinel lymph node biopsy, followed by an interferon therapy in case of confirmed metastasis or no further therapy in case of negative histology of sentinel lymph node, and confirm optimal oncological management.

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