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SHORT COMMUNICATION

# Clinical and Pathological Aspects of Melanoma among Children in Finland

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Cutaneous melanoma is one of the most rapidly increasing cancers in fair-skinned populations, but in children melanoma is extremely rare and each case is unique. Melanoma comprises only approximately 1–3% of malignancies in children and adolescents (1). In the entire melanoma patient population, this age group is a minority containing <2% of all cases (1, 2). The incidence of melanoma has been increasing in all age groups during recent decades (3, 4). As in adults, paediatric melanoma occurs in both sex; in adolescents slightly more in girls, but in children, slightly more in boys (1, 2, 5–7).

Childhood melanoma can be challenging to diagnose due to different clinical manifestations from those seen in adults. A particular problem is confusion of Spitz naevi with atypical features with melanoma and lack of specific criteria for their distinction (8).

The aim of this study was to evaluate the incidence, clinical and histopathological features, treatment and survival in paediatric cutaneous melanoma in Finland.

## METHODS

In this retrospective study, the clinical data of children in Finland, aged ≤15 years, with invasive cutaneous melanoma diagnosed during the years 1990–2010 were collected from the Finnish Cancer Registry. Detailed clinical information was obtained directly from the 5 university hospitals where the patients were treated. Only patients with histopathologically confirmed invasive melanoma were included in the study.

Excised and formalin-fixed sentinel nodes were cut and embedded in paraffin, stained with haematoxylin and eosin (HE). If no metastatic melanoma cells were identified in the HE-stained sections, further sections were cut and immunohistochemical staining was performed.

The study protocol was approved by the Institutional Review Board of Turku University Hospital, by the Ethics Committee of the Hospital District of Southwest Finland, and by the National Institute for Health and Welfare including a comment by a Data Protection Officer.

Disease-free survival (DFS) was defined as the time from initial treatment until first recurrence. Melanoma-specific overall survival (OS) was defined as the time from initial melanoma treatment until the disease-specific death due to metastatic melanoma. Survival analyses were performed using SPSS version 21.0 (SPSS; Chicago, IL, USA) software.

## RESULTS

A total of 19 patients were included in the study: 13 boys (68%) and 6 girls (32%). In Finland, the incidence of paediatric melanoma was 0.9 cases per year during the study period. In comparison, during the years 1992–2012 there were, in total, 4,415 cases of cutaneous melanoma in Finland (9). The clinical and histopathological characteristics of the patients are shown in Table I. One example is shown in Fig. 1. This patient is alive and disease-free 4 years after diagnosis.

Table I. *Clinical and histopathological characteristics of the study patients (*n = *19)*

| Characteristics | *n* | Characteristics | *n* |
|---|---|---|---|
| Age, years | | Breslow thickness, mm, median | 2.4 |
| 0–10 | 4 | Range | 0.3–6.0 |
| 11–15 | 15 | Clark level | |
| Total | 19 | II | 2 |
| Anatomical site | | III | 6 |
| Trunk | 6 | IV | 7 |
| Upper extremity | 5 | V | 1 |
| Lower extremity | 5 | Tumour ulceration present | 5 |
| Head and neck | 3 | Sentinel node biopsy: performed | 9 |
| Spitzoid features | 6 | Sentinel node biopsy: positive | 5 |
| Development in pre-existing: | | | |
| Non-Spitzoid naevus | 7 | | |
| Spitzoid naevus | 4 | | |

In each patient, the primary lesion or biopsy scar was excised with 1–3 cm margins, depending on Breslow thickness and anatomical location. Nine patients had metastasis at the time of diagnosis, 5 of them found in sentinel node biopsy (SNB). Four patients had ma-

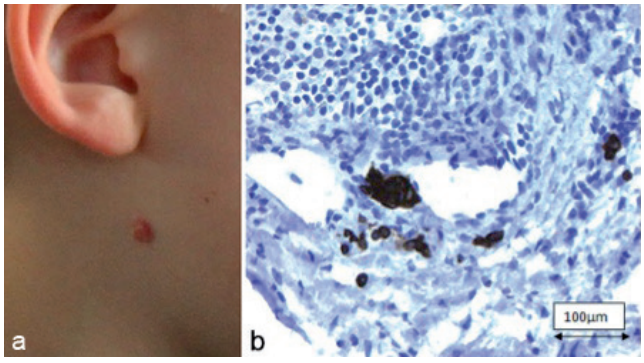


*Fig. 1.* (a) A 5-year-old boy with a nodular skin lesion below the right ear. The lesion was excised at the same time as a hernia operation, and histopathological analysis revealed melanoma. (b) Metastatic melanoma cells found in the sentinel node (Melan-A stain). Primary tumour was Breslow 3.3 mm, Clark IV nodular melanoma with Spitzoid features. In immunohistochemical analysis the melanoma was Pan Melanoma positive, HMB45 negative and Cyclin D1 strong positive. The number of cells positive for Ki-67 proliferation marker was, on average, 5–10%, focally higher.



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croscopic regional lymph node metastases and underwent therapeutic lymph node dissection (TLND). All sentinel-positive patients underwent completion lymph node dissection and all of them had only one metastatic regional lymph node. Interferon adjuvant therapy and/or chemotherapy were used for 7 patients, for one patient for established disease and as adjuvant therapy for others. One patient received palliative radiotherapy.

Median follow-up time was 4.6 years (range 0.6–10.0 years). During follow-up, melanoma recurrence was found in 5 patients (26%) and 4 patients died of systemic stage IV disease (21%). First recurrences were found after a median time of 16 months (range 4–191 months). The first recurrence developed locally in one patient, in regional lymph nodes in 2 patients, and as a distant stage IV disease in 2 patients. Among patients undergoing SNB, recurrent disease was detected in one sentinel-positive patient who soon after died to widely disseminated disease. According to Kaplan–Meier analysis, disease-free survival at 5 years was 81% and melanoma-specific overall survival was 83% (Fig. 2).

## DISCUSSION

This study found the incidence of childhood melanoma in Finland to be, on average, one case per year in the age group ≤15 years or younger. In contrast, the overall incidence of melanoma in all age groups is currently over 1,400 new cases per year in Finland (14.8–15.1/100,000) (10).

The clinical manifestation of paediatric melanoma is not uniform and the heterogeneity is similar to those in adults. The history of the development of the lesion is important as well as its careful inspection. ABCD-criteria apply well for superficial spreading melanoma, but not for the nodular type. In such a situation, melanoma may present a very atypical appearance. In such cases evolution of the lesion is the red flag. Three of our study patients had an amelanotic melanoma; none of the patients with melanomas had any history of giant congenital naevus or even medium-sized congenital naevus.

Surgical treatment of childhood melanoma should be similar to that in adults, although most guidelines are based on studies including only adult melanoma populations (9, 11). Recommended excision margins are based on anatomical dimensions of adult patients and a 1 cm margin, considered narrow in an adult, would be a relatively extensive excision in a small child. SNB is a standard method for nodal staging in adults, but among paediatric patients it has not been studied in prospective randomized trials and its routine use remains under discussion (12, 13).

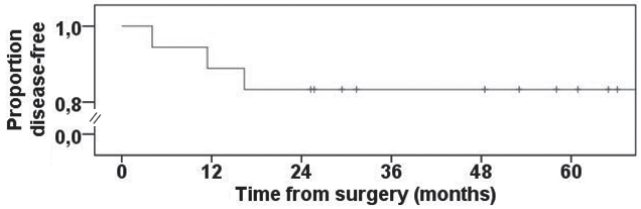


*Fig. 2.* Melanoma-specific overall survival of the study patients ($n = 19$).

Almost half of our patients had regional lymph node metastases at the time of diagnosis. Despite this prognostically unfavourable finding, survival was relatively good, i.e. 5-year DFS was 81% and OS 83%. The same finding has also been described in other studies, but this observation is poorly understood.

This study was limited by its retrospective nature and by the small number of patients. The histopathological specimens were not reviewed, but the original histopathological analyses were performed by experienced skin pathologists. The study would be much stronger if all the specimens had been reanalysed by only one pathologist specialized in paediatric melanoma and Spitz naevi; but it was not possible to obtain all original specimens for re-examination.

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