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443 paediatric cases of malignant melanoma registered with the German Central Malignant Melanoma Registry between 1983 and 2011

Ines B. Brecht [a,*], Claus Garbe [b], Olaf Gefeller [c], Annette Pfahlberg [c], Jürgen Bauer [b], Thomas K. Eigentler [b], Sonja Offenmueller [a], Dominik T. Schneider [d], Ulrike Leiter [b]

[a] *Pediatric Hematology and Oncology, University Children's Hospital Erlangen, Germany*
[b] *Center for Dermatooncology, Department of Dermatology, Central Malignant Melanoma Registry of the German Dermatological Society, University Hospital Tuebingen, Germany*
[c] *Institute for Biometrics, Erlangen, Germany*
[d] *Clinic of Paediatrics, Dortmund, Germany*

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Abstract ***Background:*** Malignant melanoma is a very rare paediatric tumour. This study was performed in order to understand clinical features and prognosis of malignant melanoma in children and adolescents.

Methods: 443 patients ⩽18 years of age with malignant melanoma were prospectively registered with the German Central Malignant Melanoma Registry between 1983 and 2011. Cases were collected from 58 participating centres. 276 paediatric cases with a follow-up >3 months were evaluated for survival probabilities and prognostic factors by Kaplan–Meier method.

Results: Age of diagnosis ranged from 3 months to 18 years (median age 16 years). The male to female ratio was 0.8 (202 male, 240 female). Most melanoma were located at the trunk ($n = 195$) and the lower extremity ($n = 114$). Patients with >3 months of follow-up (median 55 months) showed an overall survival (OS) of 94.8% in 5 years. Survival according to tumour stage was 98.5% for stage I ($n = 190$), 91.1% for stage II ($n = 39$) and 53.0% for stage III/IV tumours ($n = 11$). Worse outcome was seen in patients with nodular melanoma (OS 77.9%, $n = 42$) compared to superficial spread histotype (OS 100%, $n = 138$) or other histotype (OS 96.9%, $n = 88$) ($p < 0.0001$), in case of thicker tumours (Clark level IV or V, OS 87.1%,

* *Corresponding author at:* Pediatric Oncology and Hematology, University Children's Hospital Erlangen, Loschgestrasse 15, 91054 Erlangen, Germany. Tel.: +49 9131 85 33118.
E-mail address: ines.brecht@uk-erlangen.de (I.B. Brecht).

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$n = 84$) compared to thinner tumours (Clark level I, II, III, OS 99.1%, $n = 164$) ($p = 0.0008$) and in case of ulceration (OS 65.6%, $n = 17$) compared to no ulceration (OS 99.2%, $n = 182$).
Conclusion: Patient and tumour characteristics in paediatric melanoma patients show no evident differences to adult melanoma cases. The same clinical approach as in adults should be used.

1. Introduction

Though malignant melanoma is rare in children and adolescents there has been rising attention within the paediatric community about its occurrence. It has been estimated that in the United States (US) approximately 427 new cases of malignant melanoma are diagnosed in patients under the age of 20 each year [1]. In children under 15 years of age the incidence of malignant melanoma is found to be about 0.7–0.8/million [2–5]. Anyway, as melanoma incidence increases dramatically with age, the incidence in individuals aged 15–19 is reported to be more than 10 times higher (>10/million), already [2–5]. In other words, 1–4% of all new melanoma cases occur under the age of 20 years, and only 0.3% in children younger than 15 years [6]. Due to its rarity little is known about the biology and clinical behaviour of paediatric malignant melanoma. Therefore, clinical management is so far the same as in adults, despite of evidence that malignant melanoma may behave differently in young patients [7]. First of all, diagnosis is extremely difficult to establish. The borders between malignant melanoma and more benign lesions as Spitz nevi [8], atypical Spitz tumours, Spitzoid melanoma and melanocytic tumours of uncertain malignant potential (MELTUMP) are not sharply defined. These diagnostic problems may result in under- or overdiagnoses as well as false therapy decisions. Several authors report that prepuberal children present with relatively thick lesions and in advanced stages [9,10]. It is still unclear whether this observation is due to late diagnosis in children or possible differences in biology [7].

The prospective German Central Malignant Melanoma Registry (CMMR) records approximately 35–50% of all melanoma patients in Germany. It has been founded thirty years ago as voluntary network of dermatooncologists and has evolved into the leading resource of clinical data about melanoma cases in Germany. For the first time CMMR data have been screened to extract all paediatric cases in order to report clinical features and prognosis of malignant melanoma in children and adolescents.

2. Patients and methods

The present study includes 443 patients under the age of 19 years who were diagnosed with cutaneous melanoma and ocular melanoma (one patient) and were prospectively registered with the German Central Malignant Melanoma Registry (CMMR) between 1983 and 2011. The CMMR is a hospital based, prospective registry. As in Germany, the majority of melanoma patients are referred to the hospitals, and patients are cooperatively kept under surveillance by the hospitals and dermatologists in private practice, data from the CMMR can be considered as representative and information from approximately 35–50% of all melanoma patients in Germany is received. The incidence of cases observed over the years did not change substantially in the study period.

2.1. Data and patient management

Our study complied with the guidelines of the Declaration of Helsinki. As such, the institutional review board of the University of Tübingen approved the study. All patients had given their written informed consent to have their data on primary tumour and follow-up recorded within the CMMR. The histopathological diagnosis of malignant melanoma was established by the dermatohistopathologists of the cooperating centres. Lesions with atypical or uncertain behaviour were excluded from the analysis. No independent review process of the histopathologic reports was performed; however, there is a continuous medical education of dermatopathologist as organised by the German Dermatologic Society. Information about spitzoid versus non-spitzoid melanomas was only available in 78 patients from the University Hospital Tuebingen. Fifteen of these patients presented with spitzoid melanoma, 65 patients with non-spitzoid melanoma. Fifty-eight cooperating university dermatology departments reported paediatric patients to the registry. Staging investigations at diagnosis included a physical examination, lymph node ultrasound, abdomen ultrasound, chest X-ray and blood examination. Sixty-nine patients underwent sentinel lymph node biopsy. Tumour characteristics and case history were recorded in a standardised manner, and patients were examined regularly every 3–6 months for a period of 10 years. One hundred and twenty nine patients were initially operated in a hospital, 275 patients in an outpatient clinic. The histopathological diagnosis was established by the dermatohistopathologists of the cooperating centres.