Hong Kong J. Dermatol. Venereol. (2014) **22**, 30-34

Paediatric Dermatology Column: Case Report

Paediatric melanoma: challenges in diagnosis and management

小兒黑色素瘤：診斷和治療上的挑戰

M Liu, CJA Henderson, M Gupta

Paediatric melanoma, although relatively rare, is the most common cutaneous malignant tumour of childhood. It is often not suspected at initial presentation. It may be misdiagnosed due to poor correlation of conventional ABCDE criteria and ambiguous histopathological features. This younger patient group is more likely to have thicker tumours and positive sentinel lymph node biopsy compared with adult melanoma patients at diagnosis. Despite this, melanoma-specific death rates are lower than those in adults. This suggests different biological behaviour of paediatric compared to adult melanomas. Significant psychosocial issues may exist in the patient and their family. These may delay diagnosis and affect the compliance with management and so should be closely monitored, and intervention arranged if warranted.

小兒黑色素瘤雖然較爲罕見，但卻是兒童最常見的皮膚惡性腫瘤。在發病初期，常不以爲意而被誤診，可能因它與傳統所用的ＡＢＣＤＥ標準相關性較差及其含糊的組織病理學特徵所致。這個較年輕的病人群組在確診時，對比起成人黑色素瘤患者，較常有較厚的腫瘤和前哨淋巴結活檢陽性結果。儘管如此，小兒黑色素瘤的特定性死亡率仍較成人爲低。這意味著小兒和成人的黑色素瘤存在着生物學行爲上的差異。此外，患者和其家人可能會有明顯的心理社交影響，或因此而延誤診斷及影響治療的依從性，故在這方面，實有必要作密切的監測和提供適時的協助。

Keywords: Criteria, diagnosis, management, melanoma, paediatric

關鍵詞：標準、診斷、治療、黑色素瘤、小兒

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Introduction

Cutaneous malignancies are rare in children. Children under the age of 10 account for 0.4% of all melanomas.[1] The incidence of melanoma has been increasing from 1992 to 2004 in paediatric patients in the United States with an annual growth rate of 2.8%.[2] More recent data suggests this increase peaked in children aged 10 to 14 in 2004, and in adolescents aged 15 to 19 in 2002, with the incidence now trending down.[3] Data from the Australian Institute of Health and Welfare on

melanomas in Australia appears to parallel the decrease in the incidence noted in children and adolescents in the United States, but the peak incidence in Australia appears to be in the mid to late 1990s.[4]

Case history

A 10-year-old male of Polynesian-Czech heritage presented with a six-month history of an evolving nodule on the left posterior thigh. A previous dermatology appointment was deferred, and he was reviewed only after the intervention by a staff member at the dermatology clinic who was known to the family, and who arranged an urgent consultation. On examination, an erythematous 5 mm diameter nodule with surface ulceration was noted (Figure 1). There was a history of occasional bleeding from the lesion. A provisional diagnosis of pyogenic granuloma was made, with a differential diagnosis of Spitz naevus. Flecks of pigmentation were noted at the inferior margin of the nodule.

The patient's mother was very anxious that he was able to compete at a swimming carnival the following week, as he was a competitive swimmer. She was keen to defer any procedure. After further explanation and discussion, an informed consent was obtained and a surgical excision with narrow margins was performed. Histopathology revealed a focally ulcerated 3 mm thick Clark Level IV Spitz-like melanoma (Figure 2). Features favouring a diagnosis of malignancy included: numerous and grossly atypical mitoses (Figure 3), marked cellular pleomorphism, nuclear hyperchromasia, asymmetry of the dermal nested component with foci of central necrosis and expansile dissecting growth at the deep aspect of the tumour without features of maturation. Regression and perineural invasion were absent. The tumour cells were positive for S100 (Figure 4), melan-A and HMB45 immunohistochemically.

He was then referred to a specialist melanoma treatment centre, where re-excision was performed. A sentinel lymph node biopsy (SLNB) was positive in the left groin. A CT scan of the brain, chest, abdomen and pelvis showed no evidence of metastatic disease.

The mother felt anxious about her deferring the original dermatology appointment. She asked many questions, based upon research on the

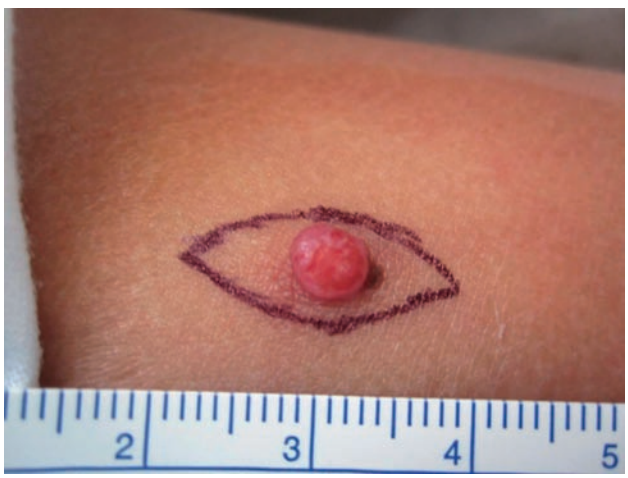

Figure 1. Erythematous nodule on the left posterior thigh.

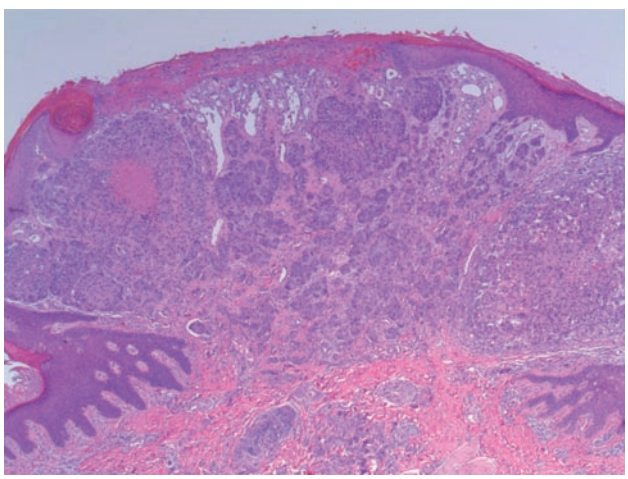

Figure 2. H&E stain showing a polypoid, exophytic tumour with ulceration, an asymmetrical nesting pattern, and marked extension into the reticular dermis (H&E, x20 magnification).

internet, directed to the specialist melanoma team and paediatric oncology unit. Subsequent treatment involved interferon alpha 2b therapy at a tertiary level paediatric oncology unit for stage III melanoma.

He received the standard adult dose of 20 million units intravenously 5 days per week for four weeks, then 10 million units subcutaneously 3 times per week for 48 weeks. During induction therapy, he experienced fever, chills, and decreased appetite, and had a transient urticarial rash, which improved with oral loratidine and topical betamethasone valerate 0.02% ointment. Mild neutropaenia, leucopaenia and slightly elevated liver transaminase enzymes were also noted. Extensive discussions took place with the treating teams to reassure the family that treatment was appropriate and should be continued. Although side effects can be managed with dose modification,[5] the interferon dosage was maintained as he was able to continue to participate in competitive sports such as running and swimming.

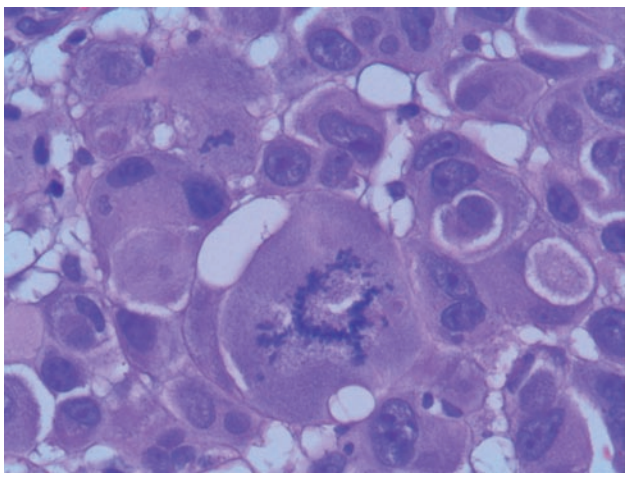

Figure 3. Grossly atypical mitotic figure amongst markedly pleomorphic tumour cells (H&E, x400 magnification).

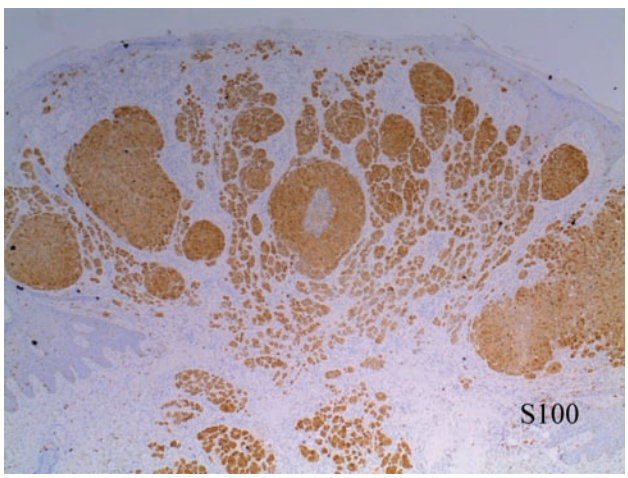

Figure 4. Low power view of positive S100 staining of tumour cells (immunoperoxidase, x20 magnification).

His mother remained very anxious regarding his future, and took the entire family for regular skin examination at a dermatology tertiary referral centre. The patient maintains a positive outlook on life, and remains disease-free two years after initial diagnosis.

Discussion

Paediatric melanoma is often not suspected on initial presentation. This case demonstrates several features, including an initial diagnosis of pyogenic granuloma or Spitz naevus, mixed Polynesian-Caucasian background, relatively thick tumour and positive sentinel lymph node biopsy. It also highlights the distress and parental concerns that should be addressed with this diagnosis.

A recent large cohort study showed that conventional ABCDE criteria will miss 40% of paediatric melanomas in those aged 11 to 19, and 60% of those aged 10 or less. An alternate set of criteria is suggested (Table 1).[1]

Using this modified set of criteria may lead to earlier diagnosis and management. In this case, reference to these criteria may have led to more timely review and earlier excision.

Table 1. Criteria for paediatric melanoma[1]

Conventional ABCDE criteria
Asymmetry
Border irregularity
Colour variegation
Diameter more than 6 mm
Evolution
Suggested additional ABCD criteria for children
Amelanotic
Bleeding, Bump
Colour uniformity
De novo, any diameter

The risk factors associated with poorer disease free survival are: 1) primary tumour features of anatomic site (head/neck and limbs compared with trunk), ulceration, and satellites, and 2) sentinel lymph node features of maximum size, extra-nodal spread, peri-nodal lymphatic invasion and positive completion lymph node dissection.[6] For all melanoma patients, the factors predicting for worse overall survival are older age (over 65 years), male gender, and higher primary tumour (pT) and regional lymph nodes (pN) categories.[7]

Paediatric melanomas have different demographic features compared with adult melanomas. In a single-centre retrospective review, patients pre-pubescent (<age 10 years) compared to adolescent (≥10-18 years), were more often non-White, had thicker tumours, more Spitzoid tumours and more vascular invasion. Younger ages had greater rates of lymph node metastases.[8] Children and adolescents with atypical Spitzoid tumours and positive sentinel lymph nodes have a better prognosis than patients with histologically unambiguous melanoma and positive sentinel lymph nodes.[9] Although the patient in this case study was aged 10, he had features in keeping with pre-pubescent melanoma (those less than 10 years old), with better prognostic features compared to those with adult melanomas.

The most important factors adversely affecting prognosis in primary cutaneous melanomas of all ages are sentinel lymph node status and ulceration.[10] Although SLNB is controversial, it should be discussed with the patient and their family, taking into consideration the Breslow depth.[11] Children and adolescents with melanoma have lower rates of non-sentinel lymph node involvement and melanoma-specific death rates compared to adults.[12]

Higher risk paediatric melanoma patients are those with tumours thicker than 4 mm (stage IIb and IIc), or with sentinel lymph node metastases (stage III), and interferon alpha 2b therapy should be considered in these patients.

An estimated 25-30% of patients and their families find it difficult to cope with the diagnosis and subsequent treatment of melanoma.[13] Issues may include poor academic achievement, decreased social interaction and lowered self-esteem. In some cases, referral for counselling may be indicated.

Conclusion

The incidence of paediatric melanomas may be decreasing, but vigilance and a high index of suspicion should be maintained. Paediatric melanomas appear to have different biology to adult melanomas. Multi-disciplinary care and long term follow-up are essential to improve outcomes and treat early tumour recurrence. Counselling should be carefully considered in all cases of paediatric melanoma patients.

Acknowledgement

We would like to acknowledge the helpful comments provided by Professor Wolfgang Weninger and Dr John de Launey in the preparation of this manuscript.

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