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CASE REPORT

Malignant melanoma in an 8-year-old Caribbean girl: diagnostic criteria and utility of sentinel lymph node biopsy

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Summary The incidence of malignant melanoma (MM) is continuing to rise, although childhood MM remains rare. We describe an 8-year-old Afro-Caribbean girl who developed a non pigmented lesion on the tip of her left thumb, which persisted despite treatment in primary care with cryotherapy. At biopsy she was found to have an acquired acral MM. She underwent amputation of the distal phalanx of her thumb, together with positive sentinel lymph node (SLN) biopsy and subsequent axillary lymph node clearance and adjuvant chemotherapy. MMs are very rare in this age and skin-type group, therefore requiring strict diagnostic criteria. These criteria include the distinction from MM mimics, especially Spitz tumours, and an appropriate use of staging techniques such as SLN biopsy to influence management.

Key words: childhood, malignant melanoma, sentinel lymph node biopsy, Spitz naevus

We describe an 8-year-old girl born in the U.K. of Afro-Caribbean descent, who presented with a non healing lesion on the tip of her left thumb, which proved to be an adult-type acral malignant melanoma (MM). The lesion had been treated as a 'wart' for 10 months prior to referral. This case emphasizes the point that, although childhood melanoma is rare, it can occur in an individual with type V skin before puberty and should be included in the clinical differential diagnosis of lesions which have not responded to conventional therapy. Positive sentinel lymph node (SLN) biopsy led to a subsequent axillary node dissection, and the patient is currently well after 18 months of follow-up, with no evidence of residual malignancy.

Case report

An 8-year-old girl of Afro-Caribbean origin was referred by her general practitioner with a 10-month history of an ulcerated 'wart' on the radial tip of her left thumb. There was no history of any pre-existing naevus. The lesion had bled intermittently and had been treated with cryotherapy on two occasions. The child was healthy, with no family history of melanoma, but with a strong maternal family history of polydactyly, which had resulted in the child undergoing surgical excision of extra digits. The lesion on her thumb was subsequently curetted and the tissue was routinely processed for histological study.

Histology revealed a 10-mm ulcerated polypoid tumour with a nested growth pattern. Pleomorphic and hyperchromatic cells, some containing coarse melanin granules, predominated in the tumour; they did not reveal any evidence of deep maturation. Numerous widespread mitotic figures (7·4 per mm^2) were observed in the lesion, extending to the deepest dermal margin of the tumour. The tumour invaded down to the limit between the papillary and reticular dermis (Clark III) and showed nested and lentiginous junctional activity. Breslow depth was not possible to assess because of the superficial nature and orientation of the specimen. All these features were diagnostic of adult-like MM.

Examination following referral to the plastic surgery/dermatology multidisciplinary clinic revealed a depigmented, irregular area with a halo of brown

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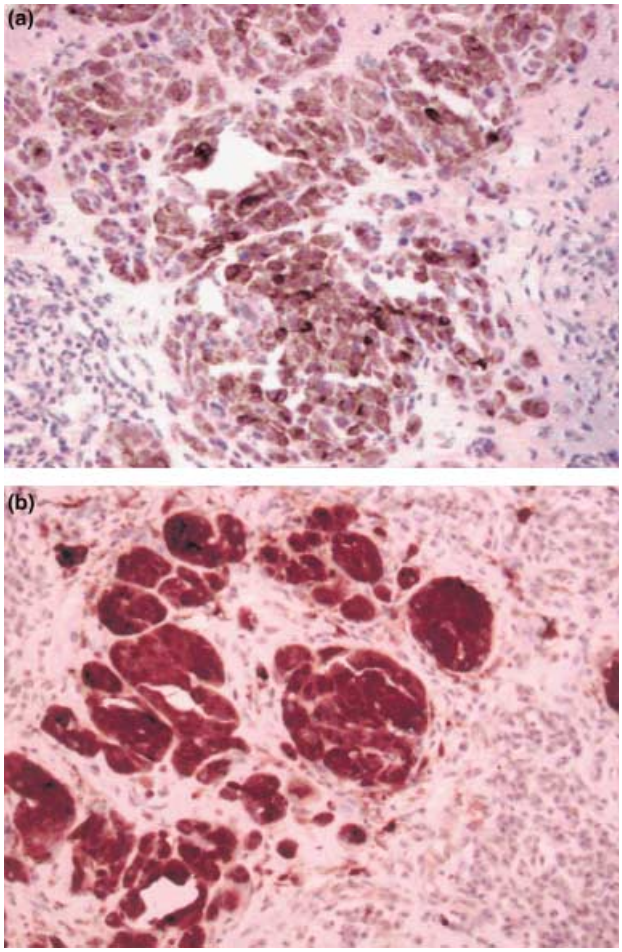

Figure 1. Histological examination of the lesion excised with the distal phalanx of the thumb following referral from primary care. The skin lesion reveals aggregates of atypical melanocytes with cytoplasmic immunostaining for (a) HMB-45 (original magnification × 100), and (b) S-100 protein (original magnification × 200).

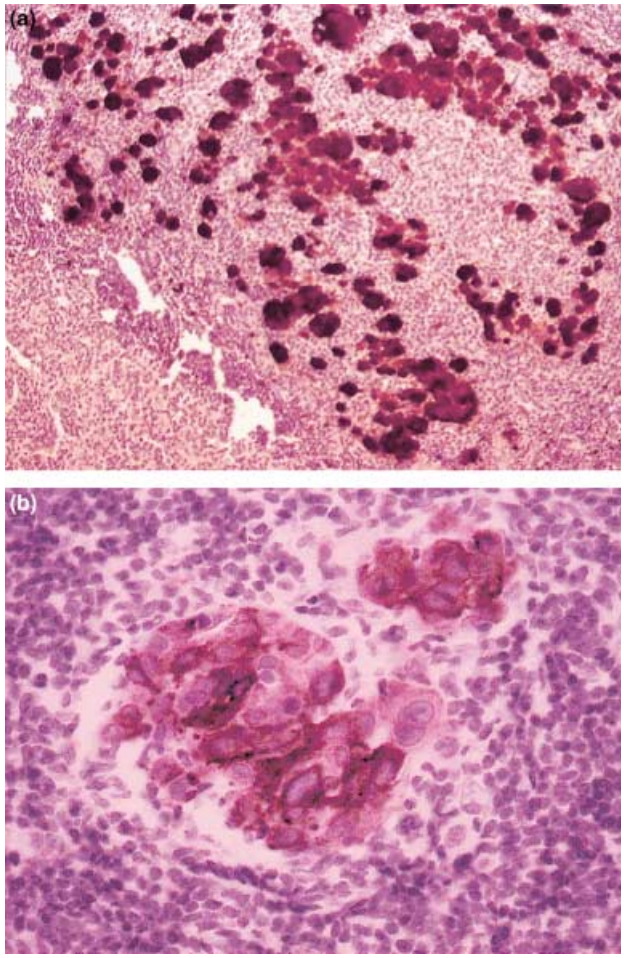

Figure 2. Histological examination of the sentinel lymph node. The sentinel lymph node contains paracortical collections of atypical melanocytes expressing (a) S-100 protein (original magnification × 100), and (b) Melan-A (original magnification × 650).

pigment at the radial tip of the left thumb. Some soft left axillary lymph nodes were noted, but no cervical lymphadenopathy or hepatosplenomegaly. In view of the results of the curettage, urgent excision of the thumb tip was performed. Under general anaesthesia the child underwent amputation of the distal phalanx of the left thumb, together with axillary SLN biopsy.

Histological examination of the thumb demonstrated complete excision of the melanoma, with scar tissue only following the previous curettage, and resection margins free of tumour. The sentinel node showed preserved architecture with irregular reactive follicles and extensive sinus histiocytosis. Microscopic foci of MM were seen within the lymph node cortex. The tumour cells stained intensely positive for S-100, and focally for HMB-45 and Melan-A, but negative for CD68. Irregular channels lined by CD31-positive endothelial cells were seen in and around tumour nests (Fig. 1a,b indicates the histological features seen in the residual lesion excised as part of the excision of the distal phalanx of the thumb and Fig. 2a,b shows the histological features seen in the sentinel node). There was no subcapsular spread. Further axillary clearance and histological examination showed all other nodes to be free of tumour involvement. Following the histology results she was also referred for adjuvant chemotherapy and to date has remained well with no evidence of residual malignancy (18 months of follow-up).

Discussion

This case illustrates an acquired MM with lymph node metastases in a prepubertal girl. These neoplasms are very rare, especially in this age group and in Caribbean patients (skin type V). Therefore, highly specific diagnostic criteria need to be applied to both skin and lymph node lesions to avoid overdiagnosis of malignancy. A proper evaluation requires consideration of aspects such as MM mimics and the use of additional techniques to improve diagnostic accuracy and staging.

Clinical and histological melanoma mimics are difficult to discriminate from MM, particularly a subset of Spitz tumours with atypical features. MM presenting before the age of 10 years is very unusual,[1] and therefore requires the application of strict diagnostic criteria.

Several features have been proposed to help in differentiating atypical Spitz tumours from MM, including the preservation of some cell maturity at the base, an absence of atypical mitoses, no significant upward epidermal spread and the nuclear chromatin pattern.[2] However, the lack of objective criteria for the distinction of Spitz tumours from MM and for gauging their malignant potential has resulted in substantial diagnostic difficulties, even among experts, especially for those with atypical features.[3] It is likely that these lesions represent a broad histological continuum extending from benign to malignant tumours.

A categorization of Spitz tumours into low-, intermediate- or high-risk categories based on the accumulation of abnormal features has been proposed. Features including diagnosis at age greater than 10 years, diameter of the lesion greater than 10 mm, presence of ulceration, involvement of the subcutaneous fat (level V), and a dermal mitotic rate exceeding 6 per mm^2 carried a likelihood ratio greater than 1·50 and were therefore used for the grading system.[4]

In this case, the lesion fulfilled two of the above criteria, with a diameter of 10 mm and mitotic index > 6 per mm^2. It was not possible to assess for ulceration, because of previous treatments. Additional histological features favouring malignancy were present, including mitoses within 0·25 mm of the dermal margin of the lesion, surface exudate, large pigment granules, and absence of spindle cell predominance (especially in association with clear cell differentiation).[5] All these features support the diagnosis of MM (adult-like) rather than Spitz tumour.

The diagnostic problems in differentiating MMs from atypical Spitz tumours explain why many paediatric MMs present at a more advanced stage than those in the adult population. When dealing with a childhood MM, the clinician is likely to be faced with a thick lesion, and one in which the actual diagnosis may even be in doubt. Although some ancillary techniques such as dermatoscopy do not help in making that distinction,[6] the novel use of SLN biopsy in paediatric melanoma patients has helped to confirm the diagnosis of malignancy,[7] and has improved the staging system. The presence of lymph node micrometastasis is recognized as a separate category in the staging system of MM,[8,9] although the significance of identifying very small groups of tumour cells is still unknown.

Clinically, the proportion of patients with MM of more than 0·75 mm depth who suffer a relapse is about 30%, whereas the incidence of positive SLN by reverse transcription–polymerase chain reaction (RT–PCR) of tyrosinase is approximately 50%.[10,11] This finding highlights the need for validation and, eventually, quantification of molecular techniques that must be carried out under morphological control. This morphological control helps in the identification of nodal naevus cells, a potential cause of RT–PCR false-positive results. Biologically, the meaning of these solitary melanoma cells is also questionable. As the definition of metastasis includes the capacity for angiogenesis and autonomous growth, the detection of tumour cells alone is unsatisfactory. The term 'disseminated tumour cells', instead of 'micrometastasis', should be preferred until the biology of melanoma cells becomes clearer.

It appears too early to make therapeutic decisions (i.e. radical lymphadenectomy of the entire basin) based on RT–PCR findings alone. However, this experimental tool can significantly contribute to improve the knowledge and understanding of the metastatic cascade. Preliminary evidence also supports the prognostic value of tumour volume in the evaluation of a positive SLN.

Potential pitfalls in the diagnosis of positive SLN need to be excluded. The main diagnostic problem in the interpretation of SLNs is the distinction of MM micrometastases from hyperplastic interdigitating dendritic cells, melanin-laden macrophages and naevus cells.

1 Interdigitating dendritic cells are located in the paracortical area and do not reveal melanocyte-specific markers. These cells are S-100 positive and become hyperplastic in immunosuppressed patients. The location and the absence of nuclear atypia help in the distinction.

2 Melanin-laden macrophages are located in subcapsular and medullary sinuses, show coarse melanin granules and mild nuclear atypia, and express CD68 instead of melanocytic markers.

3 Melanocytic naevi are a potential source for false-positive results in the examination of SLN for metastatic melanoma. The presence of melanocytes has been reported in the capsule of lymph nodes, especially axillary lymph nodes, and the incidence varies from 0·3% (lymph node examination in patients with breast carcinoma) to 22% (nodes in MM patients), probably reflecting methodological differences.[12] Nodal naevi are located in the peripheral capsule (90%) and in the internal trabeculae (10%), do not show cytological atypia, grow in small nests, and do not induce stromal reaction. These lesions can also show features of blue naevi (pigmented spindle and dendritic cells).

Thus, it is important to be aware of the appearance and morphology of nodal naevi to avoid misinterpreting them as melanoma metastases in SLNs. These features and their location allow a reliable distinction from Spitz tumours with atypical histological features that have been reported metastatic to regional lymph nodes, but with no further metastases. This variant has been called malignant Spitz tumour and is not associated with further aggressive disease despite treatment by surgical excision alone.[13,14] The indolent behaviour of these lesions does not mean that they are benign, especially considering that cytogenetic analysis of metastatic lesions has revealed clonal chromosomal abnormalities, such as add(6)(q12–13), previously noted in cases of MM.[15] Therefore, it would seem sensible to record these cases as Spitz-like MMs, assuming that both lesions share the same clonal origin.

Handfield-Jones and Smith[16] reported a series of 24 cases of MM in children. They noted that clinical and histopathological features suggestive of MM in an adult should override the apparent reluctance of clinicians to diagnose MM in children. The difficulties in distinguishing Spitz naevi from MMs were also highlighted.

This case illustrates an acquired MM with lymph node metastases in a prepubertal Afro-Caribbean girl (skin type V). MMs are very rare in this age and skin-type group, therefore requiring highly specific diagnostic criteria to avoid overdiagnosis of malignancy. These criteria include making a distinction from MM mimics, especially Spitz tumours, and an appropriate use of staging techniques such as SLN biopsy.

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