



Melanoma in Children

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Abstract

Melanoma is a highly malignant skin cancer that begins in melanocytes. Many preexisting conditions increase the risk of development of melanoma during childhood. These include giant congenital melanocytic nevi, the familial dysplastic nevus syndrome, and xeroderma pigmentosum. The signs and symptoms associated with melanoma in children are similar to those in adults, as well as the histopathologic features, biologic behavior, and treatment of this tumor. Treatment is mainly based on surgery at the localized stages. For metastatic melanoma, the therapeutic options are chemotherapy, immunotherapy and targeted therapy. We report a new case of a 6-years-old child with Xeroderma pigmentosum, who was operated several times for face and back tumors, who's morphological and immunohistochemical study confirmed the appearance of a melanoma. We also report recent data from the literature on this subject by describing the features of melanoma in children and the associated problems in order to facilitate an early diagnosis and thus an appropriate therapeutic management.

Keywords: Melanoma; Child; Xeroderma Pigmentosum; Skin

Background

Melanoma is very rare in children. It represents 1 to 4% of the malignant tumors in the pediatric population [1]. There has been a steady increase in the incidence since the 1970s, particularly in the 15-19 age group [2]. It is often diagnosed late because of its atypical form in children [3,4].

Case Report

A 6 years old female child with xeroderma pigmentosum who was operated several times in the plastic surgery department (on the face and back). The last excision was done for of a lesion at the forehead that evolving for 8 months (Figure 1). The macroscopic examination revealed a fusiform cell melanoma with a thickness of 2cm according to Breslow and level IV of Clarck and Mihm (Figure 2 and 3). A surgical resumption was made 3 months later. At the histological examination, it was seat of discrete fibrous rearrangements without tumor residue. Then, the child was sent to the oncology department. The clinical examination did not record any lymphadenopathy. The chest, abdomen and pelvis Computed Tomography (CT) scan was normal. Surveillance was adopted in the absence of indication for adjuvant therapy.

Discussion

The current incidence of childhood melanoma is much less known for the child compared to adult. However, adolescents aged from 15 to 19 years old were the most affected (73.2% of the cases), followed by 10 to 14 year old (17.3% of cases), then 5 to 9 year old (5.7% of cases) and finally 1 to 4 years (3.8%) [5]. Wong JR "et al". [6]. Studied the incidence of melanoma in the United States between 1973 and 2009 using data collected by the Surveillance, Epidemiology and End Results program and showed that 1,230 white-skinned children were diagnosed of melanoma and increasing the incidence of pediatric melanoma by 2% per year. The incidence was significantly higher in girls aged 15 to 19 than in boys and younger children. In boys, the incidence is higher for the face and torso while in girls the incidence is higher for the lower limbs and hips [2]. Another study in the United States carried out between 2000 and 2010 counting 1185 children, found that: the incidence of melanoma increases with age. Girls are more often affected than boys except between 0 and 4 and between 10 and 14 years of age, where both sexes are affected equally. The whites are mostly concerned (96.96%). The tumors are located mainly on the trunk between 15 and 19 years of age, on the trunk, head and neck between 10 and 14 years, at the extremities

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Figure 1: Fronto-parietal melanoma on xeroderma pigmentosum after surgery.

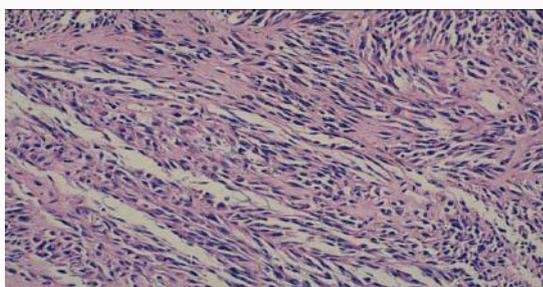


Figure 2: Cross-bundled fusiform cell melanoma (HE × 40).

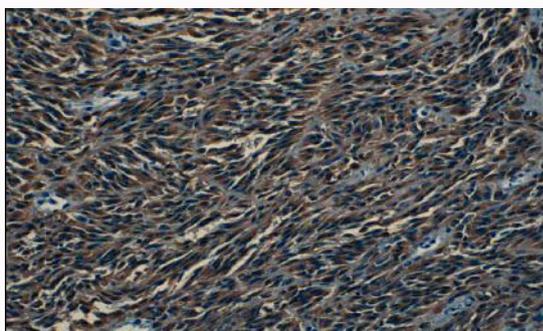


Figure 3: Cytoplasmic expression of tumor cells to anti-HMB45 × 20 antibody in favor of melanoma.

(hands feet) between 5 and 9 years, and on the head and neck for the younger ones [5]. Approximately 60% of melanomas have a BRAF V600 mutation and 20% have an oncogenic NRAS mutation [6], leading to the development of targeted therapies directed against BRAF. However, these mutations alone cannot explain the genesis of tumor, as evidenced by their presence in acquired, congenital or spitzoid naevi [7,8]. The occurrence is possible on a congenital nevus, especially if it is giant, or a dysplastic nevus, in a context of Xeroderma pigmentosum (risk X 2000, average 13 years in boys and 20 years in girls, especially head and neck) Clear photo type or exposure to UV rays. Otherwise, immunosuppression syndromes, whether acquired or not, increase the total number of naevi, a neoplastic history (leukemia, retinoblastoma) or family history in 5% to 10% of infantile cases [9]. All types of melanoma can be seen in children. They are often of rapid growth and their diagnosis proves difficult, given their often atypical appearance. The child's melanomas are often spitzoid, nodular or unclassifiable [3,4,9]. The authors have developed ABCDE

Table 1: Diagnostic criteria for pediatric melanoma according to Cordoro "et al". [10].

	Classic Criteria	Criteria for children
A	Asymmetry	Amelanotic
B	Irregular edges	Bleeding / Nodule
C	Color inhomogeneous	Uniform color
D	Diameter >6 mm	lesion de novo
E	Evolution	Evolution

criteria for children, to be used in addition to those already existing and which should significantly increase sensitivity [10] (Table I). In most studies, especially in prepubertal children, their tumor thickness is significantly higher than that observed in adolescents and adults [9-11]. This is particularly important because, apart from the lymph node status, tumor thickness is the main prognostic factor for melanoma [12]. Therefore, the child's melanoma is of bad prognostic: at the 1-2-year stage at 10 years is 90%, vs. 60.1% at stage 3 and 30% at 5 years if advanced form, age >10 years. At equal thickness, pediatric melanomas often have the same prognosis as those of adults [13-15].

The first stage in the treatment of melanoma, as in adults, is complete and wide excision with margins that vary with depth infiltration. For Stages I and II (absence of metastasis irrespective of the depth of invasion), only a broad lesion of the lesion is consensual. The indication of an adjuvant treatment in localized melanoma is discussed. It can be considered for melanomas with high evolutive risk (thickness according to Breslow >1.5mm, lymph node invasion and histological ulceration of the primary tumor). Treatment of regional lymph node metastases is radical lymph node dissection. For locally advanced and metastatic stages, management involves chemotherapy, biochemotherapy, immunotherapy or targeted therapy [15-20]. The reference treatment among active drugs is dacarbazine. Temozolomide also gives identical response rates to dacarbazine, with the advantage of oral administration. The chemotherapeutic agent compared to dacarbazine monotherapy did not show superiority, but on the other hand a higher toxicity. Interleukin 2 plus interferon plus Polychemotherapy trials have been performed and appear to give a better response rate without overall better survival, but this therapeutic regimen seems to be hard to tolerate by infants [16,17]. For immunotherapy, ipilimumab, a monoclonal antibody to the CTLA4 lymphocyte receptor has been validated in metastatic melanomas, first in the second and then in the first line [19]. The targeted therapy pathway was also opened following the demonstration of the BRAF mutation and the approved molecule was vemurafenib [18]. Systematic prophylactic excision of giant congenital naevi is currently common in many centers due to the risk of degeneration that often appears before 5 years. However, the difficulty lies in the possibility of total lesion removal, in particular at depth [21]. The 5-year survival rate varies from 50% to 76%. The rate of recurrence after initial treatment is higher than in adults (52% versus 40%), but these recurrences are often late (after 10 years) [22,23].

Conclusion

The incidence of melanoma in children is steadily increasing. Careful analysis of histologic features as well as the additional information provided by immunohistochemistry should allow for a correct diagnosis in most cases.

The epidemiology, the clinical and histological aspects are

different from the adult, but the management of these melanomas is similar.

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