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Diagnosis and Management of Nevi and Cutaneous Melanoma in Infants and Children

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The worldwide incidence of cutaneous melanoma is increasing dramatically, at a rate of 3–9% per year during the past several decades. Although childhood melanoma is rare, with only 0.3% of newly diagnosed melanomas occurring in children < 14 years, and with melanoma accounting for only 1% of all pediatric malignancies, it still warrants familiarity on the part of the clinician. As in adults, the most successful treatment of melanoma in children remains prevention and early detection. For the purpose of this chapter, we define children as those younger than 14 years.

Risk Factors

The risk of melanoma is increased in children with giant congenital melanocytic nevi, dysplastic nevi, xeroderma pigmentosum (XP), and immunosuppression. Approximately 20% of patients with xeroderma pigmentosum develop melanoma, though not necessarily in childhood.[1] In patients < 20 years of age with xeroderma pigmentosum, the prevalence of cutaneous melanoma is 1000-fold greater than in the U.S. population at large.[2] Both genetic immunodeficiency states and secondary immunosuppression because of organ transplantation or HIV infection confer modest additional risk of developing cutaneous melanoma, although these malignancies more frequently arise during adulthood. In adults, the risk factors for melanoma have been identified as the following: fair skin, light hair, increased number of melanocytic nevi, inability to tan, blistering sunburns in childhood, or personal or family history of melanoma. The relevance of these risk factors in children is unclear, although Novakovic et al.[3] has reported melanomas in children as young as age 3 in familial melanoma kindreds.

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Congenital Malignant Melanoma

Melanoma may develop in utero in one of three ways: (1) transplacental transmission from a mother with metastatic melanoma to her fetus, (2) primary melanoma arising within a giant congenital melanocytic nevus (GCMN), or, (3) very rarely, as a primary de novo cutaneous congenital melanoma.

Transplacental transmission of melanoma was first reported in 1949,[4] and there have been several case reports since.[5–9] Clinically, neonates with transplacentally acquired melanoma present with multiple small, black macules, papules, or nodules or subcutaneous masses. Multiorgan involvement is common. Although the prognosis is very poor, with fatal outcomes by a few months of age, spontaneous complete regression has been reported.[8,9]

Primary congenital melanoma may very rarely arise within a GCMN. It tends to develop deep in the dermis or in the subcutaneous fat and is difficult to detect clinically, secondary to the irregular surface and complexity of the lesions. Recently, one of us (M. C. Mihm, Jr., et al., unpublished observations, 2000) has reported a pigment-synthesizing melanoma present at birth in a congenital nevus of the scalp of an African-American neonate. GCMNs will be discussed in more detail in the next section.

Finally, congenital melanoma may arise de novo in utero without preexisting maternal melanoma. On presentation, these tend to be between 1 and 3 cm in diameter, grow rapidly, ulcerate, and bleed.[10] It must be emphasized that congenital melanoma is very rare and is often difficult to distinguish from atypical spindle-cell nevi. We strongly urge that consultation be obtained for these very problematic lesions.

Childhood Melanoma

Primary Melanoma Arising Within a GCMN

The incidence of GCMN is approximately 1 in 20,000 newborns.[11] GCMNs are commonly defined as larger than 20 cm at the largest diameter, although definitions

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Figure 1. *A giant congenital nevus. This large congenital nevus covers practically the entire trunk of this child, extending from the neck to the buttocks. Note the raised areas that represent compound nevi. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

may vary; some prefer defining GCMNs as those congenital nevi that would require a graft for closure after surgical removal (Fig 1). They are more frequently seen in girls, and they occur most frequently on the trunk (Fig 2), although they may occur on the extremities or the head. Smaller satellite lesions are often present on the skin or mucous membranes. When located on the extremities, GCMNs have been associated with limb underdevelopment.[1] The concern with GCMNs is that at least one third of prepubertal melanomas arise within them. As mentioned earlier, these melanomas are often difficult to detect because of the underlying complex morphology of the GCMN. Often the melanoma arises from the deep portions of the nevus (Figs 3–5), within

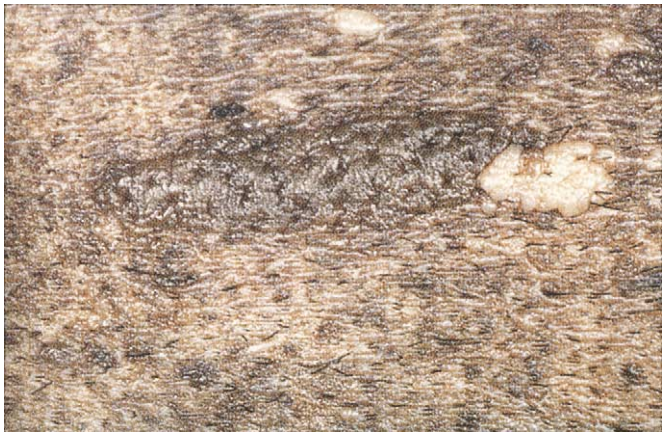

Figure 2. *A giant congenital nevus. These lesions often show strikingly pigmented zones that are usually histologically benign nodules. Areas such as the dark oval, however, must be biopsied. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

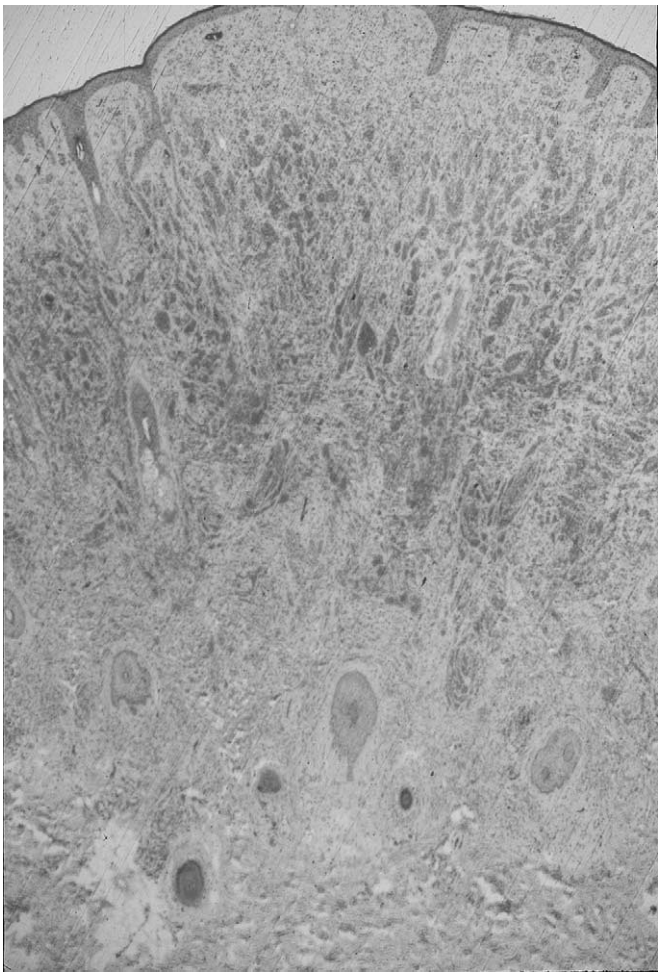

Figure 3. *A giant congenital nevus. Morphologically, the giant congenital nevus characteristically is associated with a proliferation of cells that extend from the dermis into the subcutaneous fat in a very diffuse manner.*

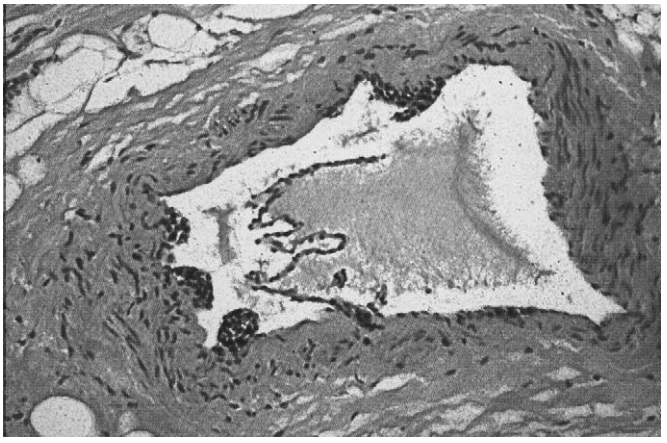

Figure 4. *A giant congenital nevus. Subendothial proliferation of nevus cells is common in congenital nevi. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

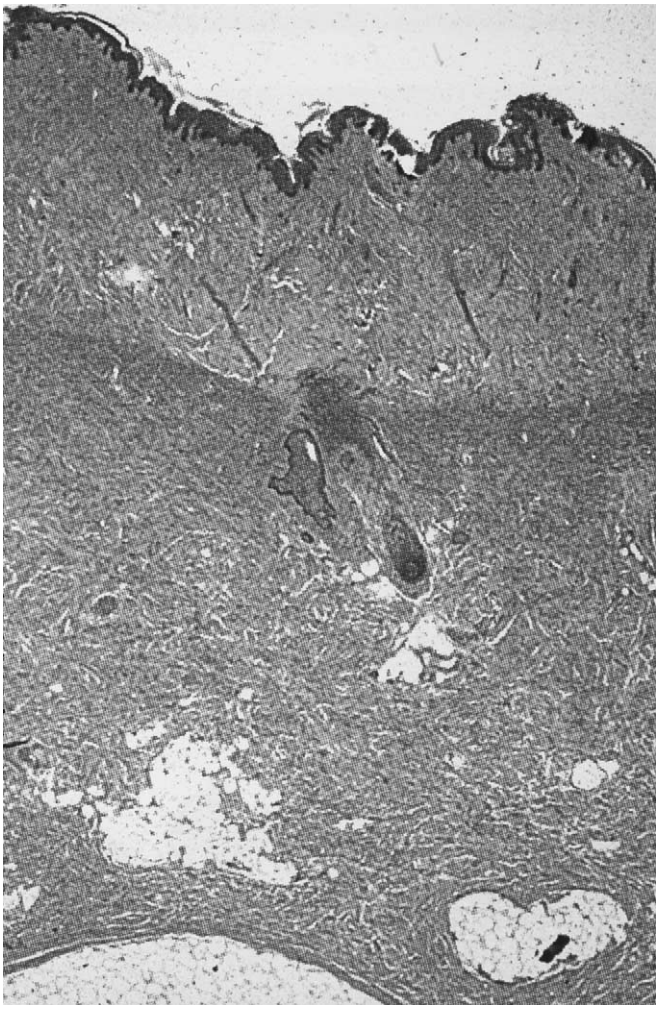

Figure 5. *A giant congenital nevus. This lesion shows a proliferation of nevus cells from the epidermis into the subcutaneous fat, a common finding in congenital nevi. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

the reticular dermis and/or subcutaneous fat, with no visible changes in the epidermal component of the nevus. These deep lesions are usually clinically diagnosed as epidermal cysts. Therefore, the development of any cystlike structure in a GCMN should be biopsied. Furthermore, nests of nevus cells may at times extend into soft tissue such as muscle. When lesions are present on the scalp, especially in the occipital area, the nevus cells may extend into the meninges, into the substance of the brain, including the ventricles and the choroid plexus. A gradual proliferation of these cells can occur with resultant hydrocephalus (Touraine's syndrome).[12] In one case, melanoma developed in a pectoral muscle nest of nevus cells after removal of a truncal GCMN. The lesion had been completely excised with skin grafting, and the melanoma developed under the graft.[13]

The lifetime risk of malignant transformation of GCMN has been estimated at anywhere between 2% and 20%; in a prospectively followed-up series of 80 children, the incidence was 5%.[14] This risk is very high in early childhood; half of the melanomas develop in the first decade of life, particularly in the first 5 years. This early peak is associated with a second peak of incidence in adult life. Thus, there is a bimodal distribution to the pattern of melanoma development in the GCMN. Proliferative nodules occur in GCMNs, especially in the neonatal period. These nodules can be very difficult to differentiate both clinically and histologically from melanoma. An experienced dermatopathologist should always be consulted when such a nodule is atypical and melanoma is considered in the differential diagnosis.

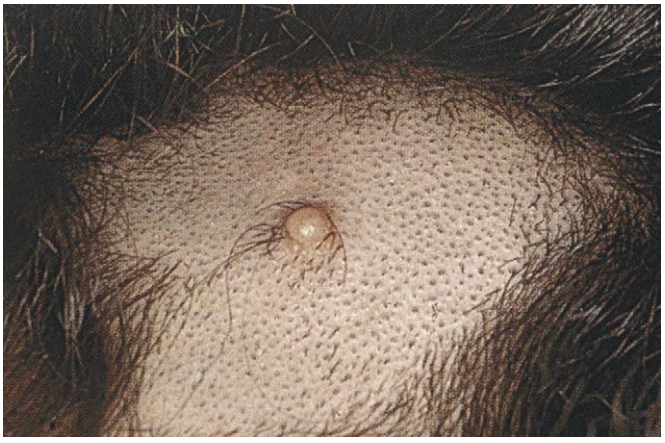

Figure 6. *Small congenital nevus. These lesions can vary in size from a few millimeters to several centimeters. This lesion, on the scalp, was present at birth. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

Management of patients with GCMNs is complex. Some advocate excision of the entire lesion during early

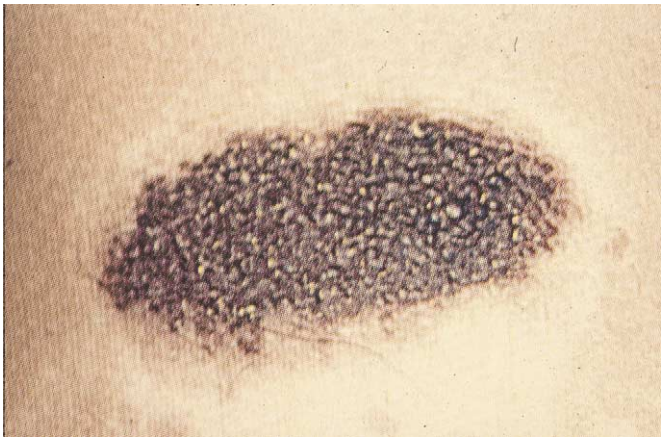

Figure 7. *Small congenital nevus. This lesion shows clinical features of a small congenital nevus. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

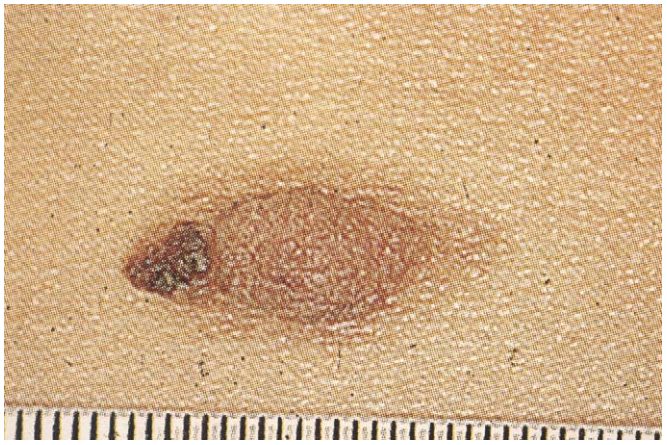

Figure 8. *Cutaneous melanoma arising in a small congenital nevus. The area of darkening represented a superficial spreading melanoma, superficially invasive, arising in a small congenital nevus. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

childhood because of the risk of malignancy. This is usually accomplished with staged surgical resection using tissue expanders. Unfortunately, at times complete excision is not feasible because of the large size of the lesion, its location, or the presence of satellite lesions or even deep placement of nevus cells below the skin. Excision must extend down to the muscle fascia and even include part of the muscle if the nevus nests are seen. Laser treatment of GCMNs is not an appropriate therapy to reduce the risk of melanoma because the tissue ablation does not extend deeply enough into the dermis to effectively obliterate the deeper melanocytes that are part of the lesion. If surgical resection is not feasible, close follow-up is recommended at least once a year. Photographs may be helpful in monitoring a le-

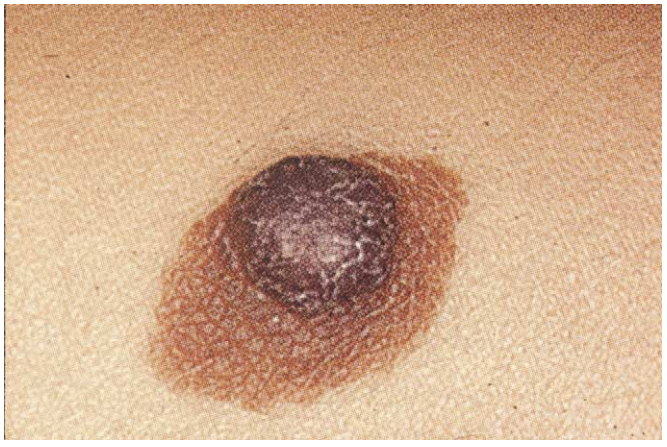

Figure 9. *Congenital combined nevus. This lesion, was clinically suspicious for malignant melanoma. Biopsy showed a combined blue/congenital nevus. From Clemente C, et al. Melanoma E nevi, Effetti Milano, 1997, with the permission of Effetti and Professor N. Cascinelli, Scientific Director of the Istituto Nazionale dei Tumori.*

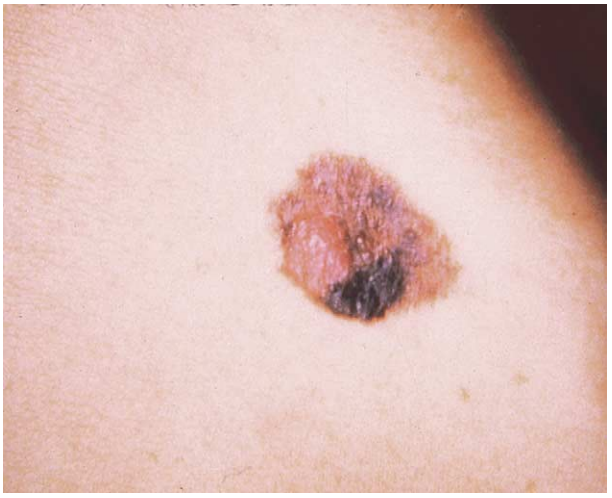

Figure 10. *De novo melanoma. This irregularly colored lesion arose rapidly on the shoulder of a 9-year-old girl. Note the irregularities in color similar to adult melanoma.*

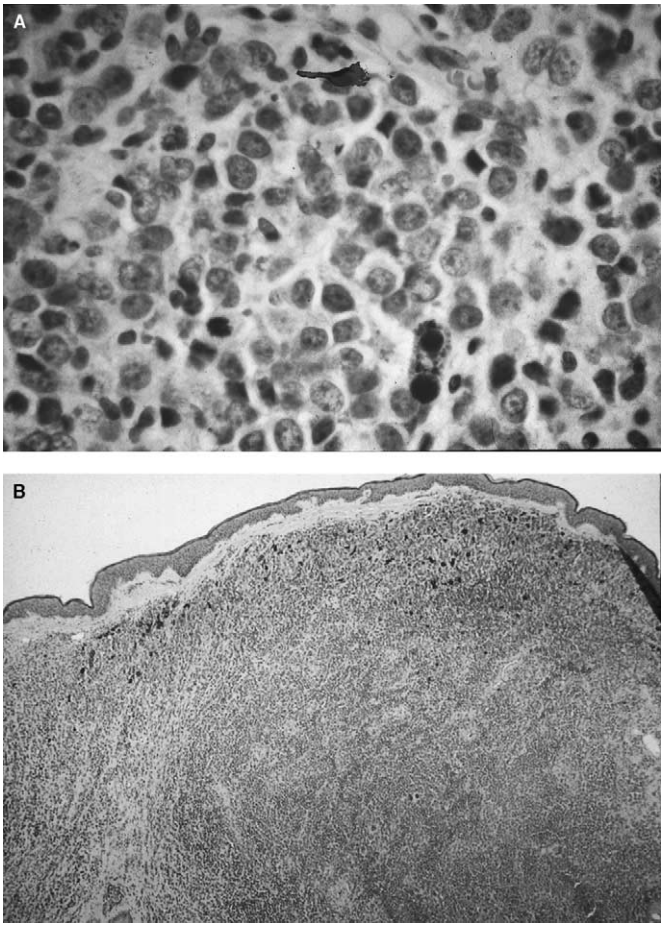

Figure 11A, B. *De novo melanoma. Biopsy of the lesion on the shoulder showed (on low power) (Fig 11A) a nodule of proliferative melanocytes, which on high power (Fig 11B) showed pleomorphic cells with numerous mitoses with a count of approximately 20 per millimeter squared. This patient succumbed to her melanoma.*

sion for change. Some groups think that complete removal of GCMN for melanoma prophylaxis is too mutilating to consider as standard therapy. The policy of our Pigmented Lesion Clinic is to consider each case separately and decide on the course to be taken in discussion with the patient and/or the family.

Primary Melanoma Arising Within Small Congenital Melanocytic Nevi

Small melanocytic congenital nevi (SCMNs) are found in 1% of newborns (Fig 6 and 7). No consensus has been reached on whether these lesions confer an increased risk of developing malignant melanoma. If malignant melanoma does arise within an SCMN (Fig 8), it tends to be in a postpubescent child, unlike a CGMN, wherein the risk of malignant melanoma is quite significant in early childhood. These lesions should be managed on a case-by-case basis (Fig 9). When considered appropriate, prophylactic removal of these lesions is usually done in late childhood or early adolescence, when they can be removed under local anesthesia. For example, lesions in areas such as the lower back, buttocks, or the back of the legs that are difficult for the patient to follow are usually removed. Otherwise, the child can be followed up clinically with photographs at least once a year. Photographs of the lesion may be helpful in monitoring for change.

Primary Melanoma Arising in Association With Dysplastic Nevi

Dysplastic nevi can be precursors of melanoma, and familial cases of dysplastic nevi may occur. The first indication that a child will develop dysplastic nevi is the appearance of a large number of normal-appearing nevi (greater than 20) by age 5 or 6. Many of these lesions, mainly small and uniformly colored, evolve into typical dysplastic nevi as the children mature. The dysplastic nevi tend to be larger than common, acquired nevi, measuring 5–15 mm, and in children often occur first on the scalp.[11] They often have "fuzzy" borders and are variable in color, with shades of brown, tan, and pink. Cutaneous melanoma is more common in patients with familial melanomas and dysplastic nevi; familial melanomas tend to occur at an earlier age, even during the teenage years and early adulthood.[15]

Follow-up of children with dysplastic nevi should focus on preventive measures such as sun avoidance and sunblock use, along with annual skin checks by a dermatologist, and periodic photographs of clinically atypical lesions. Again, because a large number of normal-appearing nevi at ages 5-6 years are often a marker for future development of dysplastic nevi, the child with many nevi should be screened starting no later than age 8–10 years. Prophylactic removal of all dysplastic nevi is not advised.

De Novo Melanoma

Melanomas that do not arise from any preexisting pigmented lesion account for 40–50% of childhood melanomas.[10] The clinical features may include the following: a new pigmented lesion that grows rapidly, bleeds, or changes color (Fig 10). More advanced melanomas may present with a subcutaneous mass or enlargement of regional lymph nodes (Fig 11 A, B). As in adults, the most common subtype of melanoma is superficial spreading.[16] Children are more likely than adults to have a melanoma occurring in the head and neck region (20%).[17]

Diagnosis of Melanoma in Children

The criteria for diagnosis of malignant melanoma in children are identical to those in adults: any suspicious lesion is biopsied, preferably by excisional biopsy, and examined histologically. Excisional biopsy allows the pathologist to look at the entire lesion. In children, however, there are a few diagnostic confounders that are usually less of a problem in adults: the Spitz nevus and the dermal nodules of the GCMNs. Spitz nevi are more common in children than in adults, clinically appearing as $<$ 1-cm, dome-shaped, pink-tan papules, preferentially involving the head and neck. Microscopically, Spitz nevi and melanoma share many features, although clinically, the Spitz nevus is a benign lesion and in most cases, especially in the hands of an experienced dermatopathologist, can be successfully diagnosed. Some lesions defy exact classification, and often unusual clinical features are clues to their nature and behavior, such as large lesions $>$ 1.0 cm, lesions with an irregular shape, and large lesions that ulcerate. In the case of any doubtful lesion, we recommend excision with as close to a 1.0-cm margin as possible, considering location and cosmesis. Some reasonable guidelines have been established to evaluate these unusual or "borderline" lesions.[18]

Therapy of Childhood Melanoma

Once the diagnosis of malignant melanoma has been established, surgical excision should be performed, with 1-cm margins for melanomas $<$ 1 mm in depth and 2-cm margins for thicker melanomas. Dissection of regional lymph nodes in the past has usually been reserved only for clinically apparent lymphadenopathy. Regarding the relatively recent introduction of sentinel nodal biopsy, the same parameters as in adults will probably be used as indications for recommending its use in children. As of this time, however, the sentinel node biopsy is an experimental technique. It serves as one of the easiest, less costly, and efficient methods for staging. Patients with negative sentinel nodes are spared the cost and morbidity of an elective node dissection.

Clinical trials of melanoma therapies for disseminated disease do not usually include children, and there are few pediatric data on stage III and IV melanoma. In a single institutional trial, four children with advanced melanoma responded well to the chemotherapeutic agent dacarbazine.[19] A trial using melphalan limb perfusion on adolescents with both localized and advanced melanoma also showed promising results.[20] Finally, Hayes and Green[21] reported a higher rate of response in children to a triple-chemotherapeutic regimen of cyclophosphamide, vincristine, and dactinomycin than in adults.[21] Other experimental therapies, including interleukin-2, interferon alfa-2b, and vaccine therapies, though sporadically used, have not been studied in children in any randomized, protocol-driven fashion.

Ultimately, as in adults, there is no effective therapy for metastatic melanoma in children. Therefore, the main focus of the parent, the pediatrician, and the dermatologist should be risk reduction and early detection of melanoma. The former consists primarily of avoiding intense sunlight exposure, using protective clothing and broad-spectrum sunblock, and educating children. In Australia, where the incidence of melanoma is very high, a public education campaign about sun protection begins in preschool, with the thought that behaviors learned by children tend to persist throughout adult life. Early detection requires a high index of clinical suspicion, especially on the part of the pediatrician, who sees children with much more regularity than a dermatologist, of any rapidly growing or otherwise atypical pigmented lesion. In addition, the physician should recognize the elevated risk of any child with a family history of melanoma, GCMN, or dysplastic nevi. Again, prevention and early clinical diagnosis are the only current effective cure for cutaneous melanoma. For additional studies on childhood melanoma, see References 22–54.

References

1. Pappo A, Kaste SC, Rao BN, Pratt CB. Childhood melanoma. In: Balch CM, et al., editors. Cutaneous melanoma. 3rd ed. St. Louis: Quality Medical Publishing, 1998; p.175–86.
2. Kraemer KH, Levy DD, Parris CN et al. Xeroderma pigmentosum and related disorders: examining the linkage between defective DNA repair and cancer. J Invest Dermatol 1994;103(5 Suppl):96S–101S.
3. Novakovic B, Clark WH Jr, Fears TR, et al. Melanocytic nevi, and malignant melanoma in children from melanoma-prone families. J Am Acad Dermatol 1995;33:631–6.
4. Holland E. A case of transplacental metastasis of malignant melanoma from mother to fetus. Obstet Gynaecol Br Empire 1949;56:529–36.
5. Freedman W. Placental metastasis: review of the literature and report of a case of metastatic melanoma. Obstet Gynecol 1960;16:550–60.
6. Reynolds A. Placental metastasis from malignant melanoma: report of a case. Obstet Gynecol 1955;6:205–9.
7. Brodsky I, Baren M, Kahn SB, Lewis G Jr, Tellem M. Metastatic malignant melanoma from mother to fetus. Cancer 1965;18:1048–54.
8. Cavell B. Transplacental metastasis of malignant melanoma: report of a case. Acta Paediatr 1963;146(Suppl):37–40.
9. Aronsson S. A case of transplacental tumor metastasis. Acta Paediatr 1963;52:123–4.
10. Ruiz-Maldonado R, Orozco-Covarrubias ML. Malignant melanoma in children: a review [published erratum appears in Arch Dermatol 1997;133:833]. Arch Dermatol 1977;133:363–71.
11. Ceballos PI, Ruiz-Maldonado R, Mihm MC Jr. Melanoma in children. N Engl J Med 1995;332:656–62.
12. Rodriguez-Galindo C, Pappo AS, Kaste SC, et al. Brain metastases in children with melanoma. Cancer 1997;7925: 2440–5.
13. Rhodes AR, Mihm MC Jr, Wood W, Sober AJ. Nonepidermal origin of malignant melanoma associated with a giant congenital nevocellular nevus. Plast Reconstr Surg 1981;67:782–90.
14. Kopf AW, Bart RS, Hennessey P. Congenital nevocytic nevi and malignant melanomas. J Am Acad Dermatol 1979;1:123–30.
15. Tucker MA, Greene MH, Clark WH Jr, et al. Dysplastic nevi on the scalp of prepubertal children from melanoma-prone families. J Pediatr 1983;103:65–9.
16. Lucchina LC, Barnhill RL, Duke DM, Sober AJ. Familial cutaneous melanoma. Melanoma Res 1995;5:413–8.
17. Fisher SR, Reintgen DS, Seigler HF. Juvenile malignant melanoma of the head and neck. Laryngoscope 1988;98: 184–9.
18. Walsh N, Crotty K, Palmer A, McCarthy S. Spitz nevus versus Spitzoid malignant melanoma: an evaluation of the current distinguishing histopathologic criteria. Hum Pathol 1998;29:1105–12.
19. Boddie AW Jr, Cangir A. Adjuvant and neoadjuvant chemotherapy with dacarbazine in high-risk childhood melanoma. Cancer 1987;60:1720–3.
20. Baas PC, Hoekstra HJ, Schraffordt Koops H, et al. Hyperthermic isolated regional perfusion in the treatment of extremity melanoma in children and adolescents. Cancer 1989;63:199–203.
21. Hayes FA, Green AA. Malignant melanoma in childhood: clinical course and response to chemotherapy. J Clin Oncol 1984;2:1229–34.
22. Autier P, Dore JF, Cattaruzza MS, et al. Sunscreen use, wearing clothes, and number of nevi in 6–7-year-old European children: European Organization for Research and Treatment of Cancer Melanoma Cooperative Group. J Natl Cancer Inst 1998;90:1873–80.
23. Barnhill RL, Flotte TJ, Fleischli M, Perez-Atayde A. Cutaneous melanoma and atypical Spitz tumors in childhood. Cancer 1995;76:1833–45.
24. Berg P, Lindelof B. Differences in malignant melanoma between children and adolescents: a 35-year-old epidemiological study. Arch Dermatol 1997;133:295–7.
25. Clark WH Jr, Reimer RR, Greene M, et al. Origin of familial malignant melanomas from heritable melanocytic

lesions. The B-K mole symdrome. Arch Dermatol 1978; 114:732–8.
26. Davidoff AM, Cirrincione C, Seigler HF. Malignant melanoma in children. Ann Surg Oncol 1994;1:278–82.
27. de la Luz Orozco-Covarrubias M, Tamayo-Sanchez L, Duran-McKinster C, Ridaura C, Ruiz-Maldonado R. Malignant cutaneous tumors in children: twenty years of experience at a large pediatric hospital. J Am Acad Dermatol 1994;30:243–9.
28. DeDavid M, Orlow SJ, Provost N, et al. A study of large congenital melanocytic nevi and associated malignant melanomas: review of cases in the New York University Registry and the world literature. J Am Acad Dermatol 1997;36:409–16.
29. Gallagher RP, McLean DI, Yang CP, et al. Suntan, sunburn, and pigmentation factors and the frequency of acquired melanocytic nevi in children: similarities to melanoma: the Vancouver Mole Study. Arch Dermatol 1990; 126:770–6.
30. Gallagher RP, McLean DI, Yang CP, et al. Anatomic distribution of acquired melanocytic nevi in white children: a comparison with melanoma: the Vancouver Mole Study. Arch Dermatol 1990;126:466–71.
31. Goettmann-Bonvallot S, Andre J, Belaich S. Longitudinal melanonychia in children: a clinical and histopathologic study of 40 cases. J Am Acad Dermatol 1999;41:17–22.
32. Goldstein AM, Fraser MC, Clark WH Jr, Tucker MA. Age at diagnosis and transmission of invasive melanoma in 23 families with cutaneous malignant melanoma/dysplastic nevi. J Natl Cancer Inst 1994;86:1385–90.
33. Greene MH, Clark WH Jr, Tucker MA, et al. High risk of malignant melanoma in melanoma-prone families with dysplastic nevi. Ann Intern Med 1985;102:458–65.
34. Karlsson P, Boeryd B, Sander B, et al. Increasing incidence of cutaneous malignant melanoma in children and adolescents 12–19 years of age in Sweden 1973–92. Acta Dermatol Venereol 1998;78:289–92.
35. Kaste SC, Pappo AS, Jenkins JJ 3rd, Pratt CB. Malignant melanoma in children: imaging spectrum. Pediatr Radiol 1996;26:800–5.
36. Kelly JW, Rivers JK, MacLennan R, et al. Sunlight: a major factor associated with the development of melanocytic nevi in Australian schoolchildren. J Am Acad Dermatol 1994;30:40–8.
37. Kopf AW, Hellman LJ, Rogers GS, et al. Familial malignant melanoma. JAMA 1986;256:1915–9.
38. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum: cutaneous, ocular, and neurologic abnormalities in 830 published cases. Arch Dermatol 1987;123:241–50.
39. Kraemer KH, Lee MM, Andrews AD, Lambert WC. The role of sunlight and DNA repair in melanoma and nonmelanoma skin cancer: the xeroderma pigmentosum paradigm. Arch Dermatol 1994;130:1018–21.
40. Lerman RI, Murray D, O'Hara JM, Booher RJ, Foote FW, Jr. Malignant melanoma of childhood: a clinicopathologic study and a report of 12 cases. Cancer 1970;25:436–49.
41. Loescher LJ, Buller MK, Buller DB, et al. Public education projects in skin cancer: the evolution of skin cancer prevention education for children at a comprehensive cancer center. Cancer 1995;75(2 Suppl):651–6.
42. Mehregan AH, Mehregan DA. Malignant melanoma in childhood cancer. Cancer 1993;71:4096–103.
43. Pratt CB, Palmer MK, Thatcher N, Crowther D. Malignant melanoma in children and adolescents. Cancer 1981;47: 392–7.
44. Rao BN, Hayes FA, Pratt CB, et al. Malignant melanoma in children: its management and prognosis. J Pediatr Surg 1990;25:198–203.
45. Ruiz-Maldonado R, Tamayo L, Laterza AM, Duran C. Giant pigmented nevi: clinical, histopathologic, and therapeutic considerations. J Pediatr 1992;120:906–11.
46. Sander B, Karlsson P, Rosdahl I, et al. Cutaneous malignant melanoma in Swedish children and teenagers 1973–1992: a clinico-pathological study of 130 cases. Int J Cancer 1999;80:646–51.
47. Scalzo DA, Hida CA, Toth G, et al. Childhood melanoma: a clinicopathological study of 22 cases. Melanoma Res 1997;7:63–8.
48. Smith CH, McGregor JM, Barker JN, et al. Excess melanocytic nevi in children with renal allografts. J Am Acad Dermatol 1993;28:51–5.
49. Tate PS, Ronan SG, Feucht KA, et al. Melanoma in childhood and adolescence: clinical and pathological features of 48 cases. J Pediatr Surg 1993;28:217–22.
50. Temple WJ, Mulloy RH, Alexander F, et al. Childhood melanoma. J Pediatr Surg 1991;26:135–7.
51. Trozak DJ, Rowland WD, Hu F. Metastatic malignant melanoma in prepubertal children. Pediatrics 1975;55:191–204.
52. Tucker MA, Bale SJ. Clinical aspects of familial cutaneous malignant melanoma. Semin Oncol 1988;15:a524–8.
53. Tucker MA, Fraser MC, Goldstein AM, et al. Risk of melanoma and other cancers in melanoma-prone families. J Invest Dermatol 1993;100:350S–355S.
54. Williams ML, Pennella R. Melanoma, melanocytic nevi and other melanoma risk factors in children. J Pediatr 1994;124:833–45.