 Conjunctival Melanoma in Children: A Clinicopathologic Study of 2 Cases

Conjunctival melanoma is a disease of middle-aged and elderly persons, with very few cases reported in children. In children, pigmented conjunctival lesions are predominantly nevi, and in rare cases, malignant transformation may occur. We report 2 cases of conjunctival melanoma in children younger than 10 years.

Report of Cases. Case 1. A 9-year-old white girl underwent excision of a small, rapidly growing, black pigmented lesion of the inferior palpebral conjunctiva and the adjacent margin of the right lower eyelid. The original histopathologic diagnosis was an active junctional nevus of the conjunctiva and eyelid margin. The lesion recurred 3 years later and was excised by a dermatologist who did not send the specimen for histopathologic examination. Two years later, the pigmented lesion again recurred and was treated by a large-wedge eyelid resection, with an initial histopathologic diagnosis of active compound nevus.

One year later, the pigmented lesion recurred in the same location, progressively enlarged to 9 mm in width, had a nodular appearance, and extended to the inferior fornix (Figure 1). The histopathologic diagnosis of the excised tumor was melanoma. After 12 years of follow-up, there was no evidence of recurrence or metastatic disease.

Histopathologic findings of the first specimen (taken at age 9 years) showed a small fragment of mucocutaneous tissue with some clusters of melanin-containing cells in the junctional region and with pagetoid invasion of the epithelium by epithelioid cells with involvement of 1 lateral margin (Figure 2). The diagnosis was revised from active junctional nevus to in situ melanoma of the conjunctiva and eyelid margin.

The second specimen (obtained at age 14 years) disclosed a melanocytic tumor containing some melanin pigment in the junctional region with pagetoid invasion into the overlying epithelium. Clusters of plump cells showing cellular atypia with nuclear pleomorphism, prominent nucleoli, and occasional atypical mitoses extended into the subepithelial connective tissue with involvement of 1 lateral margin. A lymphocytic infiltrate was noted mainly at the edge of the lesion. The maximum tumor thickness was 0.7 mm (as measured by the Breslow method). The diagnosis was re-
vised from active compound nevus to invasive melanoma.

The third specimen (obtained at age 16 years) showed features similar to those noted in the second specimen except for a greater degree of atypia of the neoplastic cells (Figure 3). There was no appreciable radial growth phase and all of the margins were free of tumor. The tumor thickness was 1.2 mm. The diagnosis was invasive melanoma.

Case 2. A 4-year-old Mexican boy had a yellowish-pink nodule in the bulbar conjunctiva of his left eye near the limbus at the 6-o’clock position. The lesion remained stationary for 5 years, after which it started to grow and became ulcerated. An excisional biopsy was diagnosed histopathologically as conjunctival melanoma. Four years postoperatively, the patient was in good health with no evidence of recurrence or metastatic disease.

The conjunctival epithelium showed extensive ulceration over a hypercellular nodule. The underlying stroma showed infiltrating cords of tumor cells that exhibited moderate nuclear pleomorphism, prominent nuclei, multinucleated forms, and abundant eosinophilic cytoplasm (Figure 4 and Figure 5). Moderate mitotic activity with occasional atypical mitoses was noted. A moderate lymphoplasmacytic infiltrate was intermixed with lobules of the tumor. The tumor thickness was 2.9 mm (as measured by the Breslow method). All of the margins were free of tumor. Occasional tumor cells contained intracellular melanin granules. The conjunctiva adjacent to the nodule showed lightly pigmented, uniform nests of nevus cells with occasional atypical cells including multinucleated melanocytic cells located in the junctional region and in the superficial stroma, which contained a lymphocytic infiltrate. The latter lesion was interpreted as an active compound nevus with moderate melanocytic atypia (Figure 6).

Comment. We identified in the reviewed English literature only a few well-documented cases of conjunctival melanoma in children, with none of the children younger than 10 years. On the other hand, conjunctival nevi in children are relatively common, indicating that the vast majority of conjunctival nevi do not progress to melanoma.

The proposed histogenesis of conjunctival melanoma includes the following: (1) primary acquired melanosis with atypia (71% of cases); (2) malignant transformation of a preexisting nevus (17% of cases); and (3) de novo (12% of cases). The first biopsy specimen from case 1 in our study was initially diagnosed as an active junctional nevus, but this subsequently was revised to in situ
melanoma, which is consistent with primary acquired melanosis with severe atypia or a de novo origin of the neoplasm, in accordance with the unitary theory of melanoma.5,6,8 Although the initial biopsy specimen showed pagetoid invasion of the epithelium by atypical melanocytes, the biopsy specimens obtained from 2 subsequent recurrences disclosed predominantly invasive vertical growth; hence, we preferred in situ melanoma rather than primary acquired melanosis with severe atypia for the diagnosis of the initial biopsy specimen.5,6 In our second case, the biopsy specimen disclosed a compound nevus containing some atypical melanocytic cells adjacent to the melanoma, suggesting that the nevus was the precursor lesion that underwent malignant transformation.1,3,4 The clinical history of the lesion that was stationary for 5 years prior to excision supports this hypothesis.

There is no single criterion for the histopathologic diagnosis of early melanoma of the conjunctiva. We believe, however, that the combined findings of atypical melanocytic cells involving various epithelial levels, invasion of the conjunctival stroma without maturation, and atypical mitoses are the major histologic features that strongly favor a diagnosis of melanoma.1,3 Both the clinician and the pathologist should avoid the pitfall of being influenced by the patient’s youth, as occurred with our first patient.

Although the mortality rate from conjunctival melanoma in adults is approximately 30%,1,8,9 we are aware of only 2 reports of metastases from conjunctival melanoma in children.2,3 The first was in an 11-year-old child who underwent excision of a limbal pigmented melanoma and subsequently developed recurrent tumor and extensive systemic metastases.2 The second was in a 12-year-old child who underwent excision of a limbal pigmented melanoma that subsequently metastasized to the ipsilateral parotid lymph node, but the child appeared to be disease free after 8 months of systemic chemotherapy and for 15 months following the positive lymph node biopsy results.2 Both of our patients were diagnosed as having conjunctival melanoma when they were younger than 10 years. Despite the presence of undesirable clinical and histopathologic prognostic features including tumor thickness greater than 1 mm in both cases and involvement of the palpebral conjunctiva and the initial tissue margins in our first patient,8-10 both the first and second patients were disease free 12 and 4 years, respectively, after the histopathologic diagnosis of conjunctival melanoma was established.

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Langerhans cell histiocytosis (LCH) is a rare disease of the mesenchymal dendritic cell system caused by a clonal proliferation of dendritic cells with Langerhans cell characteristics that may affect any organ, often with multisystem involvement and predominantly in children. Langerhans cell histiocytosis exhibits the characteristics of chronic inflammation, with typical granulomas consisting of CD1a-positive Langerhans cells, macrophages, T lymphocytes, and multinucleated giant cells and eosinophils. The most common central nervous system manifestation in LCH is involvement of the hypothalamic-pituitary region. Cerebral parenchymal involvement outside of the hypothalamic-pituitary axis by LCH is rare and may occur in the setting of multifocal systemic disease. Solitary unifocal LCH involving cerebral parenchyma is exceptionally rare. Ocular involvement in LCH is well recognized, but it normally manifests as eyelid or orbital infiltration and may involve multiple ophthalmic sites as part of a multisystem disseminated disorder. Choroidal involvement in LCH is rare. We report a case of an adult previously diagnosed with a solitary left frontal LCH lesion who developed a solitary choroidal mass in his left eye believed to represent another LCH lesion 4 years later. We describe the clinical features of the lesion and the rapid response to external beam radiotherapy with resolution of visual symptoms.

Report of a Case. A 29-year-old man came to the emergency department with a 4-day history of sudden onset of metamorphopsia in his left eye and a reduction in subjective visual acuity. His right eye was asymptomatic. He had no previous ophthalmic history of note and was eunotrop. Four years previously, he had a grand mal seizure. Neuroimaging (magnetic resonance imaging) detected a solitary 1.5-cm lesion at the gray matter–white matter interface of the postero medial region of the left frontal lobe that had a pattern of ring enhancement following gadolinium administration (Figure 1). No other lesions were identified. Complete excision had been achieved via a left frontal craniotomy. Histopathologic analysis revealed a polymorphous cellular infiltrate (Figure 2) with marked perivascular sclerosis. Immunocytochemistry revealed that the cellular population was CD1a and S100 protein positive. Ultrastructural evaluation confirmed a population of cells with irregular, notched, and eccentrically placed nuclei, relatively abundant cytoplasm, and well-formed endoplasmic reticulum. A small number of Birbeck granules were identified in this population of cells (Figure 3), and a diagnosis of solitary cerebral LCH was made. Throughout the following 4-year period, repeat magnetic resonance imaging...