Delayed Diagnosis of Epidermal Nevus Syndrome Associated With Substantial Brain Malformations: A Case Report and Review of the Literature

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Epidermal nevus syndrome (ENS) often describes a spectrum of different clinical and histologic subtypes of epidermal nevi as well as their genetic and systemic associations. Although the true incidence of ENS is unknown, it is estimated that 8% to 18% of patients with epidermal nevi have systemic disorders. We report a case of ENS in adulthood; on further workup, our patient was found to have substantial central nervous system (CNS) abnormalities. This case highlights the necessity of appropriate workup in patients presenting with epidermal nevi at any age.

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Case Report

An 18-year-old black man presented for removal of congenital lesions. His prior medical history included dysplastic pulmonary valve and atrial septal defect, both repaired at 17 months of age. The patient had never been evaluated for his cutaneous findings prior to his presentation to us. Examination of the skin revealed diffuse, bilateral, brown verrucous plaques in a whorl-like pattern on the neck, trunk, and all extremities (Figure 1). The skin biopsy specimen showed papillated epidermal hyperplasia with overlying orthokeratosis consistent with epidermal nevus. There was no evidence of epidermolytic hyperkeratosis in the biopsy.

Further workup, which included magnetic resonance imaging of the brain, revealed low-lying cerebellar tonsils, projecting 6 mm below the level of the foramen magnum, consistent with a mild Chiari I malformation (Figure 2A). Magnetic resonance angiography of the brain showed a 3-mm aneurism in the right internal carotid artery at the level of the posterior communicating artery (Figure 2B).

Comment

Epidermal nevi are hamartomas that are thought to arise from mutations in ectodermal pluripotent cells during early embryonic development. On histology, these hamartomas typically present with keratinocytic hypertrophy, along with other features resembling structures of skin, such as presence of hair, sebaceous glands, and eccrine and/or apocrine glands.[1] Epidermal nevi subclassifications according to the predominant histologic structure include the following: keratinocytic or verrucous nevi, sebaceous nevi, follicular (including comedo) nevi, apocrine nevi, and eccrine nevi.[1-3]

Epidermal nevi typically present at birth or within the first few months of life and are estimated to affect about 1 in 1000 live newborns.[1,3] In rare cases, epidermal nevi have been reported to appear during puberty.[3] Epidermal nevi develop along the lines of Blaschko and can be associated with underlying neurologic, vascular, and musculoskeletal defects.[1] The presence of epidermolytic hyperkeratosis within the nevi has been linked to increased risk for having an offspring with bullous congenital ichthyosiform erythroderma in affected individuals.[4]

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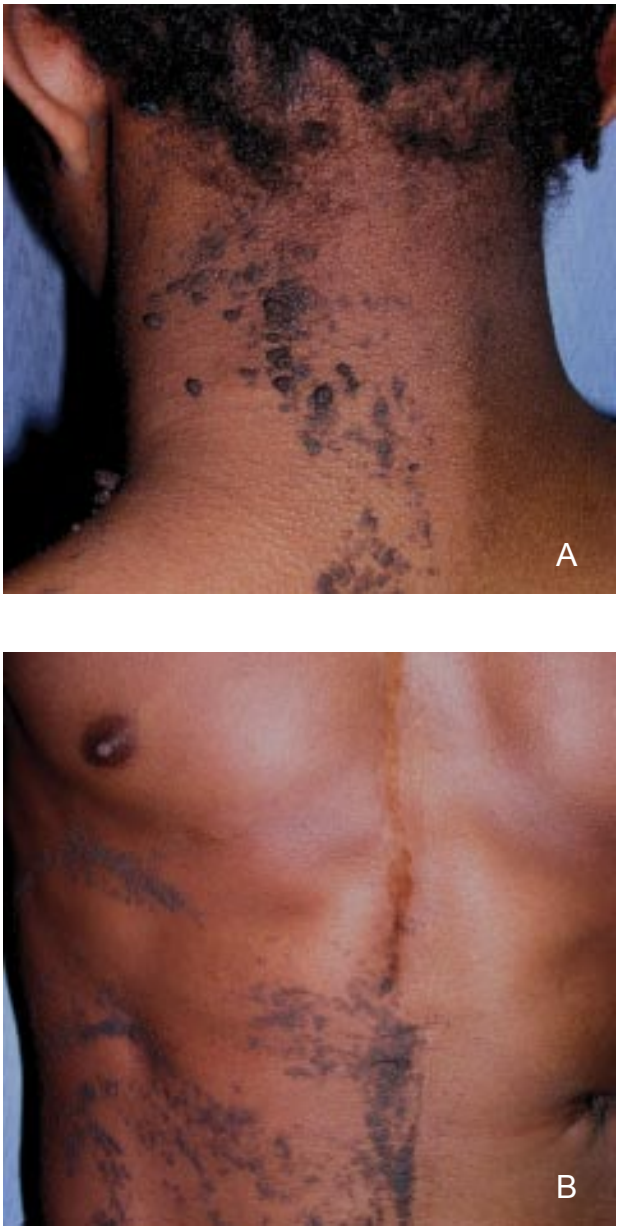

Figure 1. Brown verrucous plaques in a whorl-like pattern on the neck (A) and trunk (B).

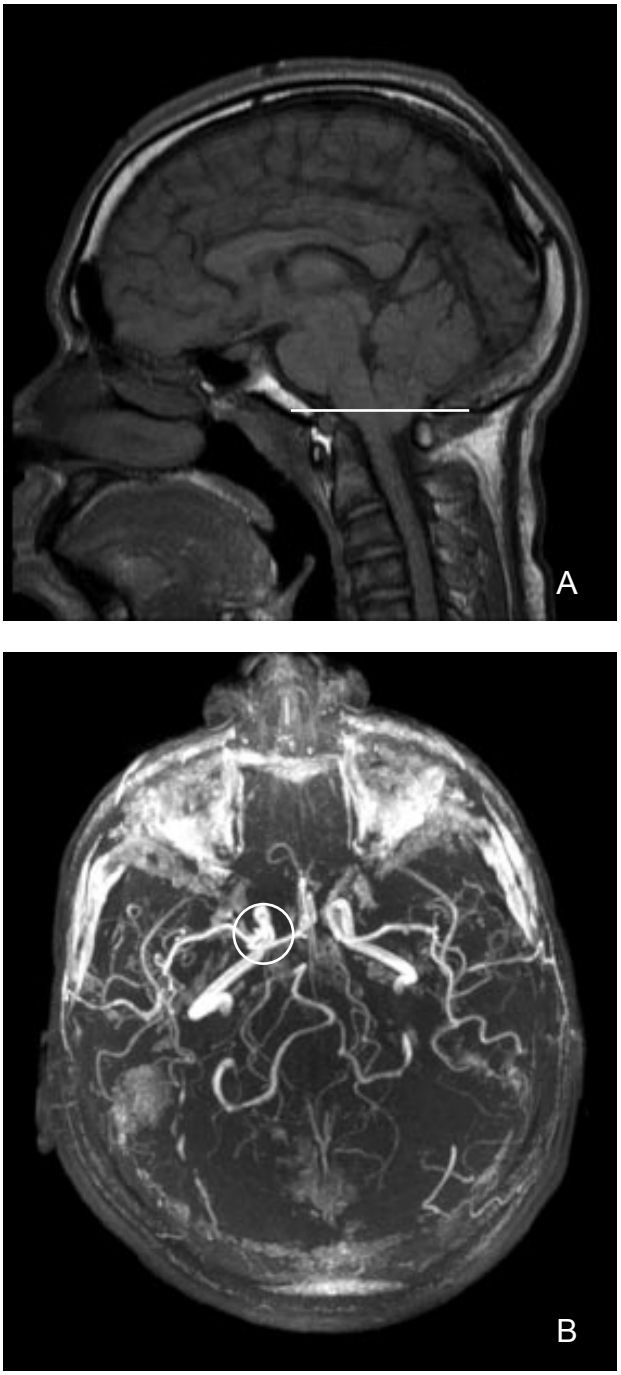

Figure 2. Magnetic resonance imaging of the brain showed low-lying cerebellar tonsils projecting below the level of the foramen magnum (line)(A). Magnetic resonance angiography of the cerebral vasculature showed an aneurism in the right internal carotid artery (circle)(B).

Epidermal nevus syndrome (ENS) often describes a spectrum of different clinical and histologic subtypes of epidermal nevi as well as their genetic and systemic associations.[1,5] Often included in this category are nevus comedonicus syndrome, Becker nevus syndrome, congenital hemidysplasia with ichthyosiform erythroderma and limb defects, Proteus syndrome, phacomatosis pigmentokeratotica, Schimmelpenning syndrome, and keratinocytic nevus syndrome.[2,6] Although the true incidence of ENS is unknown, it is estimated that 8% to 18% of patients with epidermal nevi have systemic disorders.[6]

Among the systemic manifestations of ENS are central nervous system (CNS) abnormalities, which may affect as many as 50% of patients with ENS.[1] Some researchers suggest that the rate of CNS

involvement may be even higher depending on the ENS subtype, with Proteus syndrome having 88% involvement compared to 66% with sebaceous nevus syndrome and 43% to 66% with keratinocytic nevus syndrome, depending on the gender (higher rate in females).[6] CNS abnormalities can range from mental retardation, estimated to be present in up to 40% of patients, to seizures to structural brain malformations.[1,3,6] Among structural brain malformations, brain dysgenesis, cortical atrophy, microcephaly, hemimegalencephaly, ventriculomegaly, intracranial vascular malformations, hydrocephalus, and cranial nerve (CN) abnormalities (especially in CN VI, VII, VIII) have all been described.[1,3,5,7-9] Some studies suggest that there may be a correlation between epidermal nevi overlying the head and the likelihood of CNS involvement.[7,9,10] Although there does appear to be an association between epidermal nevus location and CNS involvement, as our case demonstrates, anyone with extensive epidermal nevi should be screened for CNS abnormalities, regardless of the nevi location.

Conclusion

In summary, we report a case of ENS in adulthood. Our patient had extensive bilateral verrucous epidermal nevi that did not involve the head and, on further workup, was found to have CNS abnormalities on magnetic resonance imaging and magnetic resonance angiography. This case highlights the necessity of appropriate workup in patients presenting with epidermal nevi at any age.

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