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A Volcanic Occurrence: Eruptive Melanocytic Nevi

Case History

An 18-year-old male developed multiple pigmented lesions of the right upper eyelid and conjunctiva over an 18 month to two year period starting at age 16.

His medical/ocular history was positive for severe toxic epidermal necrolysis at the age of five. There was severe ocular involvement of the right eye at the time with extensive corneal scarring and recalcitrant symblepharon requiring permanent tarsorrhaphy. There was good recovery of vision in the left eye. He also had a history of severe atopic dermatitis with almost incapacitating pruritus that failed numerous treatments including narrowband and broadband UVB and broadband UVA. At age 16 pigmented lesions were noted on the right plical conjunctiva and mid right upper eyelid and these were biopsied. He subsequently developed three more lesions and the plical lesion recurred in the right eye over the next 18 months, and these were biopsied. New pigmentation was noted on the left upper eyelid as well. Histopathology of these lesions showed typical dermal melanocytic nevi of the skin and subepithelial of the conjunctiva. The pathology report included a comment that the localization, temporal development and multiplicity of these lesions raises the question of the spectrum of the left of melanocytic nevi; clinical correlation recommended. No documentation of systemic lesions has been provided.

Discussion

In a large clinical survey of 1643 melanocytic and non-melanocytic conjunctival tumors, melanocytic tumors constituted 53% of cases and of the melanocytic tumors nevi represented 52% of the total (1). Interestingly, there is not much literature on the bilaterality or multifocallity of conjunctival nevi. In a review of 410 consecutive patients with conjunctival nevi, the Shields group from Philadelphia found 6 or 1% of bilateral conjunctival nevi in this population. However there was no comment on multifocallity. In a large review of ~~10,675~~ 2371 melanocytic lesions of the conjunctiva from M. Burnier and his group in Montréal, again there was no mention of bilaterality or multifocality (2,3). In an excellent paper by the Shields group and Ralph Eagle, they documented a multifocal blue nevus of the conjunctiva and to other cases of blue nevi (4). The multiplicity of the subepithelial and thermal nevi in this case therefore has to be exceedingly unusual. And given that these lesions occurred at the site of severe damage due to a history of toxic epidermal necrolysis, it raises the question of the phenomena of eruptive melanocytic nevi (EMN) which are known to occur in the setting.

EMN was first described by Hutchinson in 1868 and has typically been used to describe the abrupt development of multiple melanocytic nevi over weeks to months often in association with an underlying trigger: cases of severe blistering skin diseases (toxic epidermal necrolysis/Stevens-Johnson syndrome, erythema multiforme, epidermolysis bullosa and exposure to sulfur mustard gas); immunocompromised conditions (renal and bone marrow transplantation, malignancy, and AIDS); pharmacologic therapy (both non-biologic and biologic immunosuppressants and chemotherapeutics, alpha melanocyte stimulating hormone treatment); trauma, primary adrenocortical insufficiency, cutaneous mastocytosis, Langerhans cell histiocytosis and rarely idiopathic (5-8). Both eruptive Spitz and eruptive blue nevi have been described as well (9-11).

In the setting of TEN/SJS, the onset of EMN in the cases reported in literature varies from six months to two years after the onset of the bullous disease and characteristically occurs in the most severely affected body sites (12-13). None of these reports mention ocular involvement, and, in follow-up as long as 38 years, there is no development of melanoma.

Pathogenesis of eruptive melanocytic nevi is debated in the literature; in the setting of bullous diseases, changes in local growth factors and cytokines such as stem cell factor are elaborated and secreted during epidermal regeneration leading to the epithelial and melanocyte proliferation (11); in the setting of immunocompromised status and pharmacotherapy, attenuated immune surveillance is postulated to allow melanocyte growth factors to promote proliferation in predisposed individuals (5); and an interesting underlying theory is that of a benign metastatic process of nevogenesis (14). In the latter theory, in melanocytic stem cell residing in the dermis or possibly epidermis undergoes an initiating event that primes the cell to proliferate excessively. This nevus progenitor cell would remain quiescent in the dermis until environmental conditions prompt the cell to either (1) undergo localized proliferation to form a nevus at that site, or (2) enter the systemic circulation through a lymphatic (most likely) or hematogenous route. Upon entering the lymph node, the nevus progenitor cell could either implant and remain quiescent or migrate into the capsule and proliferate into a nevus or it could pass through without being sequestered and continue into the circulation. The cell at this point would undergo limited division. This could take place in the tissue where the initiating event occurred, within the lymph node, or upon entry into the circulation. Eventually these cells would be exposed to a microenvironment that encourages diapedesis and implantation and then depending on signaling molecules present in the extracellular milieu, the implanted cells could immediately begin to proliferate or remain quiescent until recruited by a change in local signaling molecules (14). This theory would nicely explain nodal nevi, epidermotrophic metastatic melanoma, EMN and the recent finding of circulating nevus cells in the peripheral blood (15).

The association of multifocal uniocular subepithelial and dermal nevi in a young man over a two-year period with a history of a severe scarring bullous disease (TENS) as a child occurring in the scarred eyelids and ocular surface has provided the opportunity to look at the rare but ontologically interesting phenomenon of eruptive melanocytic nevi.

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