Conjunctival blue nevus

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Abstract

The authors report a case of a conjunctival blue nevus and review the literature pertaining to these pigmented lesions in this location, describing clinical and histological report of a patient with a blue nevus of the palpebral conjunctiva with a literature review. A 64-year-old white female was evaluated for a darkening pigmented lesion of the left lower palpebral conjunctiva. Examination revealed a 3 mm x 6mm blue-black lesion with sharply demarcated edges and an irregular border. Histopathology showed plump spindle-shaped, pigmented melanocytic cells revealing a branching network of dendritic processes with small, elongated, and hyperchromatic nuclei consistent with a common blue nevus. No recurrence was noted at 9-month follow-up. Blue nevi of the conjunctiva are lesions that have a low risk for malignant transformation but can appear clinically similar to primary acquired melanosis or melanoma. Blue nevi of the conjunctiva are rare and represent 0.5%-3.0% of pigmented conjunctival lesions. There was one reported case in a literature search of a malignant melanoma arising from a conjunctival cellular blue nevus. Treatment is complete wide excisional biopsy.

Introduction

Blue nevi are skin lesions containing melanocytic proliferations which can present in a variety of locations, most commonly in the dorsum of the hands and feet, the scalp, and the sacrococcygeal regions.[1] Blue nevi also rarely present in mucosal membranes, such as the mouth, nose, uterus, vagina, endometrium, prostate, bronchus, and esophagus.[2] We present a case of a rare presentation of a common blue nevus in the palpebral conjunctiva.

Case Report

A 64-year-old white female was referred for a darkening pigmented lesion noted on her left lower palpebral conjunctiva. The patient reported that the lesion had been present for more than 10 years and while she had not noticed any growth in the size of the lesion, it had become darker in appearance. She denied any family history of skin malignancies or ocular lesions. She had no history of previous pigmented lesions or history of malignancy, and review of systems was noncontributory.

On slit lamp exam, a flat hyperpigmented lesion with irregular borders was noted in the inferior palpebral conjunctiva on the right eye measuring 3.1 mm vertically and 6.2 mm horizontally (Figure 1). The remainder of the ocular exam was unremarkable. The lesion was fully excised and sent for histopathologic analysis.

Histologically, there was mid to deep dermal proliferation of pigmented dermal melanocytes with no junctional component and no involvement of the epidermal layers (Figure 2). On higher magnification, there were pigmented spindle-shaped dendritic melanocytes revealing a branching network of dendritic processes with small, elongated, and hyperchromatic nuclei (Figure 3). The dendritic cells did not display any cytologic atypia or mitotic figures. A diagnosis of common blue nevus was made. At 9 month follow-up, the patient displayed no evidence of recurrence.

Discussion

Blue nevi were first described by Jadassohn-Tieche in 1906 with a distinction made by Allen and Spitz in 1953 dividing blue nevi into the classically described categories of common blue nevus and cellular blue nevus.[1-3] In current literature, the common blue nevus type has been further subtyped to include common blue nevus, combined blue nevus, sclerosing (desmoplastic) blue nevus, hypomelanotic/amelanotic blue nevus, and epithelioid blue nevus of Carney Complex/pigmented epithelioid melanocytoma. The cellular blue nevus has been further subtyped into cellular blue nevus, amelanotic cellular blue nevus, atypical cellular blue nevus, and malignant blue nevus.[2]

Common blue nevi are distinguished histologically by characteristic variably pigmented spindle-shaped dendritic melanocytes in the mid to deep dermis which do not have a junctional component and which do not display any significant cytologic atypia. Cellular blue nevi are distinguished from common blue nevi in that they usually present as a pigmented biphasic tumor with a classic blue nevus component and a component of distinct cellular areas of spindled to oval melanocytes with clear cytoplasm. Both common and cellular blue nevi can present at any age, although typically present in the third or fourth decade and most commonly are found in the sacrococcygeal region, scalp, face, and dorsal areas of the extremities.[1] A subtype of cellular blue nevus has been described as malignant blue nevus, which has features of cellular blue nevus but can metastasize and result in death. Malignant blue nevi can arise from prior biopsy or excision sites of blue nevi or can arise *de novo*.[2] Histopathologically, malignant blue nevi appear similar to cellular blue nevi with a biphasic architecture but have severely atypical cytologic features.[4] Malignant blue nevi have a poor prognosis, with a high rate of recurrence and metastasis. In a case series of 12 patients with melanoma arising from blue nevus in the skin, 10 of 12 (83%) patients developed metastases over a mean period of 40 months.[5] Some studies have shown that immunohistochemistry may be of benefit, showing that malignant blue nevi show increased Ki-67 expression and may lose HMB-45 labeling.[6] Recently, Zembowicz *et al*. have suggested that the Gnaq and Gna[11] proteins of the G-protein alpha subunits involved in signaling by G-protein coupled receptors are important for controlling early dermal melanoblast proliferation, citing that there is a permanent increase in dermal melanoblast numbers with activating mutations in Gnaq and Gna11, and also that somatic mutations in the GNAQ gene have been identified in 83% of cases of blue nevi, 50% of malignant blue nevi, and 46% of uveal melanoma.[2]

The pathogenesis of blue nevi has not been well established, but most currently, the prevailing theory postulates that dermal melanocytes are arrested during embryologic migration from the neural crest to the epider-

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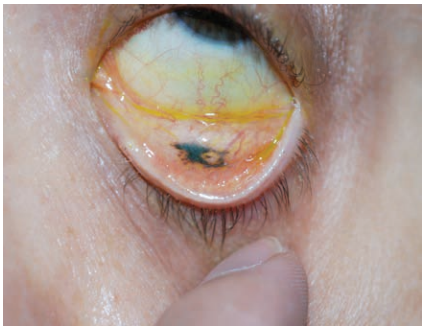

Figure 1. External photograph shows a flat, hyperpigmented blue-black lesion with irregular borders deep in the stroma with no apparent vascularity.

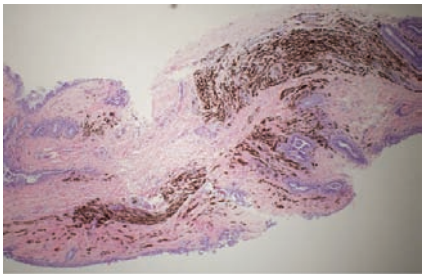

Figure 2. Conjunctival blue nevus. Heavily pigmented dendritic melanocytes located in the substantia propria with normal conjunctival epithelium and no evidence of acquired melanosis (hematoxylin-eosin, original magnification x 40).

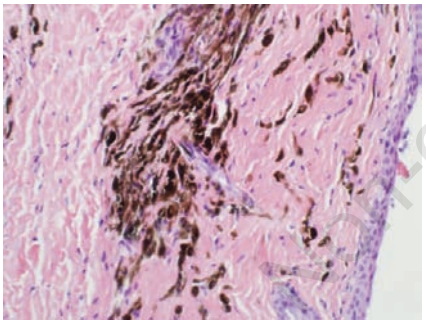

Figure 3. Plump, heavily pigmented spindle-shaped melanocytes with no junctional activity and no involvement of the conjunctival epithelium with small, elongated, and hyperchromatic nuclei (hematoxylin-eosin, original magnification x 200).

mis.[2] This theory is supported by the fact that melanocytes, after population of the dermis from 10 weeks of gestation, will disappear at the end of gestation except in the presacral area, head and neck area, and dorsal areas of the distal extremities, which are also the most common sites of presentation for blue nevi in the skin.[1]

Blue nevi rarely occur in the conjunctiva, with only 22 reported cases of conjunctival blue nevi in the literature to date. There have been four large case series of pigmented conjunctival lesions, which noted blue nevi. In the largest series of 418 conjunctival nevi, Shields, *et al*. reported that 4 of the cases conjunctival nevi were histologically confirmed as blue nevi. Of these 4 cases, 2 were located in the bulbar conjunctiva, one in the tarsal conjunctiva, and one in the fornix. All were brown in color, none had cysts, none had feeder vessels, and one has intrinsic vessels. One of the cases of blue nevus developed malignant melanoma; this case was one of the only 3 patients out of 410 patients in the series who developed malignant melanoma.[7] Grossniklaus, *et al.* reported five out of 317 (1.5%) pigmented conjunctival lesions to be blue nevi in adults.[8] Out of a series of 71 pigmented conjunctival lesions in children reported by McDonnell, *et al*., only one (1.6%) was found to be a blue nevus.[9] Of the conjunctival blue nevi which report histopathologic analysis, there were 6 common blue nevi, including the blue nevus in this report, and 5 cellular blue nevi.[10-12] In addition to the one case from the Shield, *et al*. series in which malignant melanoma developed,[7] there was only one case of malignant transformation of a blue nevus reported, which was described histologically as a cellular blue nevus that appeared on exam as primary acquired melanosis and reported no recurrence after excision at 7 year follow-up.[11] It is uncertain whether these two reports represent the same patient or two different patients, as the two reports are from the same institution and share some authors.

In summary, blue nevi are distinct melanocytic neoplasms that are commonly found in the skin but rarely occur in mucosal membranes, including the conjunctiva. Conjunctival blue nevi, particularly the cellular blue nevus subtype, have a rare potential for malignant transformation and have the potential to recur after excision. Because of this low potential for malignant transformation, treatment is wide local excisional biopsy with surveillance.

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