Blue Nevi and Related Tumors

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KEYWORDS

• Blue nevus • Cellular blue nevus • Atypical blue nevus • Malignant blue nevus

KEY POINTS

- The family of blue nevi and related dermal dendritic melanocytic proliferations includes common blue nevus, cellular blue nevus, atypical blue nevus, and malignant blue nevus.
- Genetically, as uveal and leptomeningeal melanoma, blue nevi harbor mutations in G-protein–coupled receptors subunits GNAQ and GNA11.
- Malignant blue nevi acquire additional mutations including in BAP1 on chromosome 3 and multiple losses or gains of chromosomal material involving multiple chromosomes.
- Molecular techniques, such as mutational analysis, fluorescence in situ hybridization, and array-based comparative genomic hybridization, are emerging diagnostic adjuncts.
- BAP1 mutations and loss of BAP1 locus are associated with more aggressive behavior of malignant blue nevus.

OVERVIEW

Blue nevi (BN) and related dermal dendritic melanocytic neoplasms are considered together as a group because of common clinical and histologic features. They present as pigmented papules, plaques, or nodules with dark-bluish or blue-black coloration. Under the microscope, they contain pigmented dendritic dermal melanocytes combined with other types of melanocytic cells. BN are derived from neural crest cells migrating ventrally along the developing nerves during embryogenesis, which also give rise to glial and Schwann cells.[1] The bluish color of BNs is caused by preferential scatter of the short wavelength component of visible light by melanin

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particles, so-called Tyndall effect. Diagnostic entities in the BN family include the following:

- Common BN
- Cellular blue nevus (CBN)
- Malignant blue nevus (MBN)

The term atypical BN is applied to cellular BN, which show some but not all features associated with MBN. BN are also related to developmental hamartomas/dermal melanocytoses such as Mongolian spot, nevus of Ota, and nevus of Ito. These entities are congenital macular deep dermal proliferations of dendritic melanocytes confined to areas supplied by different cutaneous nerves. Common and cellular BN are benign. MBN is a variant of malignant melanoma. Atypical BN is a borderline diagnostic category including lesions of uncertain biological potential.

Common Blue Nevus (Jadasson-Tieche-Type)

BN was described by Jadasson-Tieche in 1906.[2] It is most common in children and young adults, especially girls, but can occur at any age or as a congenital lesion.[3,4] The most typical sites are the dorsal aspects of extremities, scalp, and buttocks.[5–7] BNs have been also reported in the oral and nasal mucosa, female genital tract, prostate, and lymph nodes.[8–12]

BN presents as a small (<5 mm) dark blue or blue-black macule or papule. Most BN can be diagnosed easily by clinical observation or with help of dermoscopy.[13] Clinical variants of BN include the following:

- Eruptive[14–16]
- Plaquelike[17–19]
- Agminate[20,21]
- Linear[22]
- Satellite[23]
- Disseminated[14,24]
- Familial[25]
- Targetoid[26]

Microscopically, BN are usually symmetric mid and/or upper dermal proliferations of pigmented dermal melanocytes with an inverted wedge-shaped configuration. The base of the lesion is parallel to the surface of the epidermis, and the apex points to deep reticular dermis or subcutaneous tissue (**Fig. 1**A). BN can extend deep into reticular dermis along adnexal structures and/or neurovascular bundles. In most cases, tumor-associated stroma is dense and fibrotic. BN are dermal tumors and lack junctional component. BN contain dendritic spindle-shaped pigmented dendritic cells with slender branching network of dendritic processes (see **Fig. 1**B). Their nuclei are small, elongated, and hyperchromatic. A variable number of spindle or epithelioid melanocytes, some resembling type A and B cells of common nevi, are also present in many BN (see **Fig. 1**C). Nuclear pleomorphism and mitotic activity are exceptionally rare. Rarely, pigmented BN may include melanophages. Immunohistochemically, dendritic melanocytes of BN stain positively with S100, Sox10, HMB-45, and MART-1.[27,28] BN can be a component of a combined nevus.[29,30]

Cellular Blue Nevus

Cellular blue nevus (CBN) was established as a distinct entity by Allen and Spitz,[31,32] who realized that CBN is a benign neoplasm related to BN. CBN can present at all ages, although adults less than the age of 40 are the most commonly affected. The