Blue Nevi and Variants

An Update

Artur Zembowicz, MD, PhD; Pushkar A. Phadke, MD, PhD

● Context.—Blue nevi are a subset of melanocytic proliferations containing cells reminiscent of the embryonal neural crest–derived dendritic melanocytic precursors. They are common specimens in a general pathology practice, but some of their rare variants may pose diagnostic difficulty. Recent molecular studies provide new insights into genetics of blue nevi.

Objective.—To critically review clinical and histologic features of blue nevi with emphasis on diagnostic problems and rare variants, as well as to provide an update on the pathogenesis of blue nevi.

BACKGROUND AND SCOPE

Blue nevi are often grouped together with hamartomatous dermal dendritic melanocytic proliferations such as nevus of Ota, nevus of Ito, and Mongolian spot.2,13 This review focuses only on blue nevi and its variants. We discuss salient clinical and pathologic features of blue nevi, with emphasis on the most diagnostically challenging aspects involving recognition of some rare variants and differential diagnosis between atypical blue nevus and malignant blue nevus. The last section provides an update on the recent advances in understanding the molecular pathogenesis of blue nevi.

JADASSOHN-TIECHE–TYPE BLUE NEVUS

(COMMON BLUE NEVUS)

Blue nevus (BN) is a common specimen in routine pathology practice. It was first described by Jadassohn-Tieche in 1906.3 Blue nevus most commonly arises in children and young adults, commonly females, but can occur at any age or as a congenital lesion.4–6 The most common locations are the dorsal aspects of extremities, scalp, and buttocks.7–9 Extracutaneous presentation is rare but has been reported in the oral and nasal mucosa, female genital tract, prostate, and lymph node.10–15 Clinically, BN presents as a single small (usually 1–5 mm) dark blue or blue-black macule or dome-shaped papule. Multiple BNs may be associated with the LAMB (lentigines, atrial myxomas, mucocutaneous myxomas, and blue nevi) syndrome.16 Numerous clinical variants including eruptive, congenital giant, agminate, and targetoid are described.5,17–24 Satellite nodules of benign BN mimicking metastatic melanoma can also be seen.25 Blue nevi can be associated with nodular mastocytosis.26

Histologically, at low magnification, BN is usually a more or less symmetrical mid and/or upper dermal proliferation of pigmented dermal melanocytes with an inverted wedge-shape configuration, with the base of the lesion parallel to the surface of the epidermis, and the apex pointing to deep reticular dermis or subcutaneous tissue (Figure 1, A and B). Blue nevi have a propensity to extend deep into reticular dermis along adnexal structures and/or neurovascular bundles. Most, if not all, BNs are associated with some degree of stromal fibroplasia. The overlying epidermis lacks a junctional component, except when a BN is part of a combined nevus (see below). The diagnostic cell of BN is a variably pigmented, spindle-shaped dendritic melanocyte that reveals a slender, branching network of dendritic processes (Figure 1, B). Their nuclei are small, elongated, and hyperchromatic. The BN dendritic cells do not display any significant cytologic atypia or mitotic figures. It is important to emphasize that while dendritic cells are the diagnostic cells of BN in most lesions, they are intermixed with elongated, oval to spindle melanocytes reminiscent of intermediate (type B) or neurotized (type C) melanocytes of common nevus (Figure 1, B, D, and E). In many lesions, dendritic cells are only a minor cellular component. Pigmented BN may also contain heavily pigmented melanophages, which feature abundant cyto-

Accepted for publication April 30, 2010.

From the Department of Pathology, Lahey Clinic, Burlington, Massachusetts, www.DermatopathologyConsultations.com, Boston, Massachusetts, the Department of Pathology, Harvard Vanguard Medical Associates, Boston, Massachusetts, and the Department of Pathology, Tufts Medical School, Boston, Massachusetts (Dr Zembowicz); and the Department of Pathology, Duke University Medical Center, Durham, North Carolina (Dr Phadke).

The authors have no relevant financial interest in the products or companies described in this article.

Reprints: Artur Zembowicz, MD, PhD, www.DermatopathologyConsultations.com, Department of Pathology, 6th Floor, 133 Brookline Ave, Boston, MA 02215 (e-mail: dr.z@DermatopathologyConsultations.com).

Reference

1. Durand F, Cazenave C, et al. Blue nevus of Ota, nevus of Ito, and Mongolian spot.1,2 This...
plasm with large melanin granules and round or ovoid vesicular nuclei. Immunohistochemically, the dendritic melanocytes of BN stain positively with S100, HMB-45, and MART-1.2,27

Classic BN is easy to diagnose. However, some rare variants (discussed below) may cause diagnostic dilemmas or be confused with other entities. Nonneoplastic and inflammatory conditions resulting in cellular or extracellular...
lular pigment accumulation can also be mistaken for BN. Posthemorrhagic hemosiderin deposition can sometimes mimic dendritic cells of BN and may require iron stain to distinguish it from Fontana-Masson-positive melanin pigment. Other conditions that can mimic BN are postinflammatory hyperpigmentation and iatrogenic pigmentation by drugs such as minocycline. Pigmented cells in these conditions are fibrohistiocytes or macrophages and not melanocytes. In contrast to BN, postinflammatory pigmentation is usually located around blood vessels and is not associated with stromal fibrosis.

**VARIANTS OF COMMON BLUE NEVI**

**Combined Blue Nevus**

Blue nevus is a frequent component of a combined nevus. It is usually associated with a common compound or dermal nevus, or, much less frequently, Spitz nevus.23,29

**Sclerosing (Desmoplastic) Blue Nevus**

Sclerosing BN, also known as a desmoplastic blue nevus, is an important morphologic variant of BN, which must not be confused with desmoplastic melanoma or a soft tissue tumor.30,31 Clinically, sclerosing BN appears as a firm, solitary, variably pigmented papule or nodule. Histologically, sclerosing BN shows features typical of BN but is associated with exaggerated dermal fibrosis (Figure 1, A through D). Useful architectural clues to the correct diagnosis include an inverted wedge-shape configuration of the lesion, extension into deep dermis along adnexal structures and neurovascular bundles, and lack of epidermal hyperplasia (in contrast to dermatofibroma). The diagnosis can be established by identification of dermal melanocytes. In some paucicellular or hypomelanotic lesions, melanocytic nature of the proliferation may be hard to appreciate. Dendritic cells are usually more abundant and easiest to identify at the periphery of the lesion. Rare cases will require immunohistochemistry (S100, HMB-45, and MART-1) to confirm the diagnosis. Mucinous change within a sclerotic blue nevus has been reported.31 Histologic differential diagnosis of sclerosing BN includes desmoplastic melanoma, dermatofibroma, and other fibroblastic proliferations including scars.

Low-grade desmoplastic melanoma can easily be misdiagnosed as sclerosing BN, especially in a small biopsy specimen interpreted without awareness of the clinical context. Both lesions share the presence of spindled melanocytes and desmoplastic stroma. The most helpful features favoring desmoplastic melanoma include atypical junctional proliferation (observed in 50% of cases), cytologic atypia including nuclear enlargement and hyperchromasia, presence of reactive lymphoid infiltrate at the periphery of the lesion, and mitotic activity (rare in desmoplastic melanoma but unheard of in sclerosing BN).32 In rare cases, which cannot be resolved by examination of routine sections, immunohistochemical studies are invaluable. S100 is usually the only melanocytic marker expressed by desmoplastic melanoma, while expression of HMB-45 is exceptionally rare.33,34 In contrast, strong expression of HMB-45 is an expected feature in all BNs.25,35,36 A BN producing little pigment may be mistaken for dermatofibroma. Features favoring dermatofibroma include overlying epidermal hyperplasia, storiform growth pattern with "collagen trapping" at the periphery of the lesion, and negative immunostaining with S100, HMB-45, and MART-1 and positive staining for Factor XIIIa.

**Hypomelanotic/Amelanotic Blue Nevus**

Rare BNs do not synthesize melanin. Lacking expected pigmentation, amelanotic BN is never suspected clinically.36 Histologically, amelanotic BN shows a dermal proliferation of spindle cells associated with variably desmoplastic stroma. Diagnosis rests on observing architectural features of BN, such as inverted wedge shape and extension into deep reticular dermis along adnexal structures (Figure 1, C and D). Nonpigmented dendritic processes of BN cells cannot be appreciated in routine sections. Yet, they are highlighted by HMB-45 immunohistochemical stain. Other melanocytic markers (S100 and MART-1) are expressed in most but not all cases.37,38 Other entities to be considered in histologic differential diagnosis of hypomelanotic/amelanotic BN are scar, neurofibroma, perineurioma, and desmoplastic melanoma.

**Epithelioid Blue Nevus of Carney Complex/Pigmented Epithelioid Melanocytoma**

Epithelioid blue nevus was first described in patients with Carney complex.40 Histologically indistinguishable lesions occurring in patients without the complex, which frequently metastasize to lymph nodes, have been described and referred to as pigmented epithelioid melanocytoma (PEM).41,42 Further molecular studies demonstrated that most PEMs lose expression of protein kinase A regulatory subunit 1x, a protein that is mutated in 44% of patients with Carney complex.43 This provided additional support for the notion that epithelioid blue nevus and pigmented epithelioid melanocytoma might be considered as the same entity. Perhaps a more appropriate term for the entire group of lesions is pigmented epithelioid melanocytoma as it better reflects the intermediate malignant potential of this tumor (discussed elsewhere in this volume). Importantly, it is not entirely clear that PEM is a member of the blue nevus family at all. Some cases of sporadic and Carney complex–associated PEM show junctional single-cell or nested dendritic component, suggesting that they arise from junctional melanocytes and not dermal dendritic melanocytes like blue nevi.

Histologic features of 3 PEMs from patients with Carney complex are illustrated in Figure 2, A through F. Pigmented epithelioid melanocytoma is typically a darkly pigmented and often symmetrical dermal melanocytic proliferation, with or without (less frequently) epidermal hyperplasia. The dermal proliferation often but not always abuts the epidermis. Rare cases show a grenz zone of uninvolved skin between the tumor and the epidermis. The lesions tend to be more cellular in the center and show an infiltrating margin. Dermal fibrosis is rarely prominent. At higher magnification, PEM is composed of variable proportions of 3 different cell types: dendritic, pigmented polygonal, and large epithelioid. The dendritic cells are reminiscent of dendritic cells of BN but show more abundant cytoplasm and vesicular rather than hyperchromatic nuclei. The pigmented polygonal cells feature coarse cytoplasmic pigmentation, which often obscures centrally located medium-sized vesicular nuclei with prominent nucleoli. Many of these cells are tumor-associated melanophages. The large epithelioid cells are the most characteristic for this entity and their presence is required for definitive diagnosis. They have abundant, finely

---

Arch Pathol Lab Med—Vol 135, March 2011

Blue Nevi and Variants: An Update—Zembowicz & Phadke 329
pigmented cytoplasm and typically show accumulation of the pigment along the cytoplasmic border, sparing areas around the nucleus. The nuclei are moderate in size or large and vesicular with very prominent nucleoli. Multi-nucleated forms are frequent in some cases. The number of large epithelioid cells, their size, and degree of pleomorphism varies from case to case. Examples illustrated in Figure 2 show the spectrum of morphologic

Figure 2. Epithelioid blue nevus/pigmented epithelioid melanocytoma from 3 patients with Carney complex. A, C, and E, Low-power views showing a darkly pigmented, often symmetrical dermal melanocytic proliferation with or without epidermal hyperplasia. B, D, and F, High-power view shows variable proportions of 3 different cell types: dendritic, pigmented polygonal, and large epithelioid. The lesions illustrate the spectrum of cellularity and cytologic atypia encountered in epithelioid blue nevus/pigmented epithelioid melanocytoma, from the least atypical (B) to the most atypical (F) (hematoxylin-eosin, original magnifications ×40 [A and C], ×400 [B, D, and F], and ×20 [E]).
atypia and abundance of large epithelioid cells encountered in epithelioid blue nevus/PEM.

Histologic differential diagnosis between PEM/epithelioid blue nevus of Carney complex and conventional BN is not always easy. As already discussed, in addition to the diagnostic dendritic cells, most BNs contain other types of melanocytes. In many cases these nondendritic BN cells predominate and in some have a variably epithelioid appearance (Figure 1, E and F). It is important to distinguish BN with epithelioid cells from true PEM/epithelioid blue nevus of Carney complex. The former appears to be merely a morphologic variant of BN or cellular BN. The latter represents a distinct clinicopathologic entity. In contrast to epithelioid blue nevus of Carney complex/pigmented epithelioid melanocytoma, BN with epithelioid cells lacks the diagnostic large epithelioid cells, and dendritic cells do not feature vesicular nuclei. The epithelioid cells are reminiscent of cells forming cellular areas in cellular blue nevus. There is no evidence from the literature or our experience that immunohistochemical studies can help in distinguishing between PEM and blue nevus with epithelioid cells. However, molecular studies can be valuable in rare cases in which the diagnosis cannot be unequivocally rendered using routine sections.

Pigmented epithelioid melanocytoma (and cellular blue nevus) also has to be differentiated from deep-penetrating nevus. First described by Seab et al., this entity causes significant confusion owing to its resemblance to a pigmented Spitz nevus, BN, malignant melanoma, and cellular blue nevus. Clinically, it affects young men and women (age range, 10–30 years) with equal incidence and presents mostly as a darkly pigmented, solitary lesion on the face, neck, and shoulder. Histologically, it shows an inverted wedge shape and is composed of nests or fascicles of epithelioid cells with variable pigmentation and numerous pigment-laden macrophages. They tend to associate with adnexal structures and may even involve the subcutaneous fat. The cells are classically described as having some pleomorphism, nuclear pseudoinclusions, and vacuolated nuclei with smudged nuclear contours. In contrast to variants of BN, deep-penetrating nevus does not show mutations in Gnaq and Gna11 proteins.

CELLULAR BLUE NEVUS

Cellular blue nevus (CBN) was established as a distinct entity by Allen and Ackerman. They realized that CBN is a benign neoplasm related to BN and not melanoma (it was a widely held belief at the time of their writing that CBN was related to melanoma). Cellular blue nevus can present at all ages, although adults younger than 40 years are most commonly affected. The most common location of the tumor is the buttocks and sacrococcygeal region, followed by the scalp, face, and extremities. Other locations have also been described including male and female genital tract, breast, subungual, intraocular, and conjunctival. Clinically, CBN is a firm bluish black to bluish gray dome-shaped nodule. While most lesions are small (1–2 cm), larger lesions, including giant tumors measuring more than 10 cm, were documented. Most CBNs are painless, but large, long-standing lesions can degenerate, ulcerate, and become painful.

Representative examples of cellular CBN are illustrated in Figure 3. It is best to think about CBN as a usually pigmented biphasic tumor with a component of classic BN and distinct cellular areas composed of spindled to oval melanocytes with clear or finely pigmented cytoplasm. Rarely, only cellular areas are present in a biopsy. The overlying epidermis is usually unremarkable. Most lesions appear well circumscribed. Depending on the location and the size of the cellular areas in relationship to the BN component, CBNs have different architectural outlines. In some lesions, the cellular areas are entirely surrounded by the BN component or form most of the lesion (Figure 3, A and B). In most cases, the cellular areas emerge from the deep portion of BN and extend vertically into deep reticular dermis and subcutaneous tissue, following adnexal structures or neurovascular bundles forming a dumbbell-shaped outline (Figure 3, C and D). In many cases, the cellular areas are sharply demarcated from the common BN component and form distinct nests or nodules. Multiple nests can form an alveolar pattern and be surrounded by collagen and dense fibrous septae. In less common examples, the cellular component shows fascicular arrangement and blends with the adjacent BN. Myxoid degeneration, hemorrhage, and stromal hyalinization can occur (Figure 3, E through H). These features have to be distinguished from tumor necrosis, which can lead to diagnostic confusion with malignant blue nevus. Cytologic features of melanocytes forming the cellular areas of CBN are quite characteristic. These cells tend to be oval to spindle. They have moderate amounts of clear or lightly pigmented cytoplasm. The nuclei are usually vesicular with finely stippled chromatin and inconspicuous nucleoli. Sometimes multinucleated wreathlike giant cells may be seen. In most cases no or a minimal degree of nuclear pleomorphism or hyperchromasia is observed. Although mitotic activity in cellular blue nevi can be found, it is usually less than 1/mm². Also, the location of mitoses within the lesion may be helpful in evaluating these lesions. Immunohistochemically, the cells stain positively for S100, MART-1, and HMB-45. CD34 expression was reported in a subset of CBNs.

AMELANOTIC CELLULAR BLUE NEVUS

Rare CBN can be unexpectedly amelanotic or hypomelanotic during the initial evaluation, rests on architectural features. Typical amelanotic CBN shows the classic biphasic appearance of a typical CBN, with a variably sclerotic amelanotic BN component and distinct cellular areas. Histologic features of amelanotic BN were discussed above. Cellular component is essentially indistinguishable from that of conventional CBN but lacks pigmentation. Obviously, immunohistochemical studies can be used to confirm the melanocytic nature of the tumor and to highlight dendritic morphology of dendritic cells in the BN component.

Atypical Cellular Blue Nevus

The term atypical cellular blue nevus has been applied to rare CBNs that show atypical histologic features and raise histologic differential diagnosis of malignant blue nevus. There are no established consensus criteria regarding this diagnostic category and there is poor consensus among experienced dermatopathologists and experts regarding classification of individual lesions along
Figure 3. Cellular blue nevus. A and B, Cellular blue nevus. The lesion is composed of blue nevus with small cellular nodules of epithelioid cells. C and D, Large cellular blue nevus showing dumbbell-shaped configuration. At high magnification, cellular blue nevus areas show uniform oval cells with inconspicuous nucleoli and clear cytoplasm. E and F, Atypical cellular blue nevus with area of cystic degeneration. Such changes must not be confused with tumor necrosis. G and H, Large atypical amelanotic cellular blue nevus showing areas of hemorrhage and hemosiderin deposition associated with hot spots of cytologic atypia and increased mitotic activity (hematoxylin-eosin, original magnifications ×20 [A, C, and E], ×400 [B, D, and H], ×200 [F], and ×100 [G]).
the CBN/atypical CBN/malignant blue nevus (melanoma arising in BN) diagnostic spectrum.54 Yet, this term is useful to identify histologically ambiguous lesions and to convey some uncertainty about the biologic potential of a lesion without overinterpreting the tumor as an outright melanoma. Most experts consider CBNs as atypical when they are large, (>5–10 cm), ulcerated, show marked nuclear pleomorphism, and have more than 3 to 4 mitotic figures per mm², and either pushing or infiltrating margins.5 Unfortunately, the above features are not discriminatory and can also be found in conventional CBN as well as in malignant BN.

Atypical mitotic activity and tumor necrosis have emerged as the features most specific for malignant blue nevus.55 Yet, they are not always present in malignant BN; and when present, they have to be interpreted in the context of other features. Pathologists considering diagnosis of atypical CBN have to be aware of potential diagnostic pitfalls. The most critical are the presence of degenerative changes and hemorrhage in large atypical CBN, which can be misinterpreted as tumor necrosis (Figure 3, E through H). Follow-up data available on atypical CBN suggest a favorable outcome, although local recurrence has been reported.56,57 Lymph node deposits were reported in lesions interpreted histologically as atypical CBN.58 Since long-term follow-up in these cases was not reported, it is not clear if presence of lymph node metastases in atypical CBN indicates malignancy or, as in the case of pigmented epithelioid melanocytoma40 or atypical Spitz nevus, is merely an indication of intermediate malignant potential.

Immunohistochemistry has been used in histologic differential diagnosis between cellular blue nevus, atypical cellular blue nevus, and malignant melanoma. It is pertinent to note that our experience, in particular with Ki-67, as a way to differentiate cellular, atypical, and malignant blue nevus is limited. Several studies56–60 have shown that melanomas arising in blue nevus (so-called malignant blue nevus) may lose HMB-45 labeling and show increased Ki-67 expression when compared to blue nevus. These studies indicate that immunohistochemistry may be an important adjunct in the differential diagnosis of these lesions.

Key histologic features helpful in differentiating between cellular blue nevus, atypical cellular blue nevus, malignant blue nevus, and PEM are summarized in the Table.

### MALIGNANT BLUE NEVUS

Malignant blue nevus (MBN) is a rare form of aggressive melanoma first described by Allen and Spitz.44 They described tumors that histologically resembled blue nevi but resulted in metastasis and death. Most MBNs arise in association with a preexisting benign BN or CBN. Therefore, MBN can also be defined as melanoma (any type) arising in BN or at the site of prior biopsy or excision of a BN.45–46 Some authors47 have suggested using the term blue nevus–like melanoma instead of MBN. This term may be too restrictive, as some melanomas arising in blue nevus show high-grade epithelioid or spindle cells atypia and do not resemble blue nevus. Malignant blue nevus occurs in the same anatomic locations as BN, including the face, scalp, and buttocks. Most patients with MBN tend to be older and, in contrast to BN, there is a slight male preponderance. Lesions present as pigmented bluish black nodules or plaques that may ulcerate. The edge of the tumor may contain a bluish zone of discoloration consistent with a precursor BN.

Histologic features of MBN are illustrated in Figure 4, A through F. Malignant blue nevus usually has biphasic architecture similar to that of BN. Adequately sampled lesions often reveal the presence of a precursor BN or CBN (Figure 4, A). However, some MBNs arise de novo (Figure 4, E and F). Histologic diagnosis of MBN relies on the identification of severely atypical cytologic features indicating malignancy, such as pleomorphic (in size, shape, and staining) nuclei, large eosinophilic nucleoli, brisk (usually more than 3–4/mm², although they may sometimes have low [2/mm²] mitotic rates) mitotic activity, or atypical mitotic figures. Other features, especially tumor necrosis and frank invasion of the tumor with destruction of anatomic structures, can also be helpful. Clinicopathologic correlation studies suggested that the presence of atypical mitotic figures and tumor necrosis correlate best with malignancy. Histologic differential diagnosis between MBN and atypical CBN was addressed above.

Earlier studies2,46,61 suggested that MBN has a more aggressive course than conventional melanoma. However, this may not be true and may simply reflect the fact that most MBNs are deeply invasive tumors. A recent study from Australia62 examined the largest series of 23 patients with MBN and found no difference in clinical outcome in comparison to conventional melanoma when the patients’ lesions were matched for Breslow thickness, Clark level, and ulceration.

### PATHOGENESIS OF BLUE NEVUS

The pathogenesis of blue nevi is unclear. The most prevailing notion is that they arise from latent dendritic...
melanocytes remaining in the dermis from the embryologic migration of melanocytes from the neural crest to the epidermis. In the fetal life, melanocytes in the dermis first appear in the head and neck area at 10 weeks of gestation and then gradually populate the dermis of the entire body. By the end of gestation nearly all the dermal melanocytes disappear, except for head and neck region, presacral area, and the dorsal aspects of distal extremities. Coincidentally, these are the most common sites of occurrence of blue nevi. Proliferation of these putative

Figure 4. Malignant blue nevus. A through D, Malignant blue nevus arising in a blue nevus. The large cellular lesion shows tumor necrosis, high-grade epithelioid cell atypia, and brisk mitotic activity. E and F, Another example of malignant blue nevus–like melanoma. This lesion arose de novo. It shows a highly infiltrating growth pattern deep into subcutaneous tissue, marked cytologic atypia, and mitotic activity (hematoxylin-eosin, original magnifications ×20 [A and E], ×40 [B], ×400 [C and F], and ×200 [D]).
latent dendritic melanocytoses is also invoked to explain acquired dermal melanocytoses, which may be induced by inflammation or other insults. Another theory of the origin of blue nevi postulates that they arise from a mutated precursor stem cell in the dermis capable of differentiating into blue nevi. This theory is poorly speculative and is only weakly supported by the fact that CD34, a stem cell marker, can be expressed by some cellular blue nevi. Arguments have also been made that cellular blue nevi arise partly or wholly from nonblue nevi. The female predominance has prompted some authors to suggest that female hormones may play a role in the pathogenesis of BN.

Recent studies shed new light on the molecular basis that governs dermal melanocytic migration and genetics of blue nevi. Two members of the Gnaq class of G-protein α subunits, Gnaq and Gna11, proteins involved in signaling by G-protein–coupled receptors, emerged as the most important molecules controlling early melanoblast proliferation in the dermis. Activating mutations in Gnaq and Gna11 result in a permanent increase in dermal melanoblast numbers. Somatic mutations in the GNAQ gene have also been identified in 83% of cases of human blue nevi, 50% of malignant blue nevi, and 46% of uveal melanoma. This may perhaps explain why patients with nevus of Ota are at a higher risk of developing uveal melanoma. The mutations occur in the ras-like domain of the protein, leading to a constitutively activated GNAQ protein, essentially converting the GNAQ protein into an activated oncogene product.

Overexpression of hepatocyte growth factor or Hras1 causes an increase in dermal melanocytes in transgenic mice. Whether these factors play a role in the pathogenesis of human BN has not been confirmed.

Blue nevi and their variants do not harbor mutations of genes implicated in the pathogenesis of human nevi or malignant melanomas such as BRAF, NRAS, or c-kit. These data further confirm that blue nevi and variants represent a distinct type of melanocytic neoplasms.

References

1. Murali R, McCarthy SW, Scolyer RA. Blue nevi and related lesions: a review highlighting atypical and newly described variants, distinguishing features and malignant melanomas, such as nevi. The female predominance has prompted some authors to suggest that female hormones may play a role in the pathogenesis of BN.

Recent studies shed new light on the molecular basis that governs dermal melanocytic migration and genetics of blue nevi. Two members of the Gnaq class of G-protein α subunits, Gnaq and Gna11, proteins involved in signaling by G-protein–coupled receptors, emerged as the most important molecules controlling early melanoblast proliferation in the dermis. Activating mutations in Gnaq and Gna11 result in a permanent increase in dermal melanoblast numbers. Somatic mutations in the GNAQ gene have also been identified in 83% of cases of human blue nevi, 50% of malignant blue nevi, and 46% of uveal melanoma. This may perhaps explain why patients with nevus of Ota are at a higher risk of developing uveal melanoma. The mutations occur in the ras-like domain of the protein, leading to a constitutively activated GNAQ protein, essentially converting the GNAQ protein into an activated oncogene product.

Overexpression of hepatocyte growth factor or Hras1 causes an increase in dermal melanocytes in transgenic mice. Whether these factors play a role in the pathogenesis of human BN has not been confirmed.

Blue nevi and their variants do not harbor mutations of genes implicated in the pathogenesis of human nevi or malignant melanomas such as BRAF, NRAS, or c-kit. These data further confirm that blue nevi and variants represent a distinct type of melanocytic neoplasms.

References

1. Murali R, McCarthy SW, Scolyer RA. Blue nevi and related lesions: a review highlighting atypical and newly described variants, distinguishing features and malignant melanomas, such as nevi. The female predominance has prompted some authors to suggest that female hormones may play a role in the pathogenesis of BN.

Recent studies shed new light on the molecular basis that governs dermal melanocytic migration and genetics of blue nevi. Two members of the Gnaq class of G-protein α subunits, Gnaq and Gna11, proteins involved in signaling by G-protein–coupled receptors, emerged as the most important molecules controlling early melanoblast proliferation in the dermis. Activating mutations in Gnaq and Gna11 result in a permanent increase in dermal melanoblast numbers. Somatic mutations in the GNAQ gene have also been identified in 83% of cases of human blue nevi, 50% of malignant blue nevi, and 46% of uveal melanoma. This may perhaps explain why patients with nevus of Ota are at a higher risk of developing uveal melanoma. The mutations occur in the ras-like domain of the protein, leading to a constitutively activated GNAQ protein, essentially converting the GNAQ protein into an activated oncogene product.

Overexpression of hepatocyte growth factor or Hras1 causes an increase in dermal melanocytes in transgenic mice. Whether these factors play a role in the pathogenesis of human BN has not been confirmed.

Blue nevi and their variants do not harbor mutations of genes implicated in the pathogenesis of human nevi or malignant melanomas such as BRAF, NRAS, or c-kit. These data further confirm that blue nevi and variants represent a distinct type of melanocytic neoplasms.

Submissions Now Accepted for CAP ‘11 Abstract Program

Abstracts and case studies are now being accepted for the College of American Pathologists (CAP) 2011 meeting, which will be held September 11th through the 14th in Grapevine, Texas. Submissions for the CAP ‘11 Abstract Program will be accepted through Friday, April 1, 2011.