CASE REPORT

Blue nevus presenting as umbilicated nodule

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ABSTRACT

The blue nevus is a solitary blue-colored mole that can present at birth or develop later on in life. It can remain unchanged throughout the duration of a person's life. The blue color, or ceruloderma, is caused by the Tyndall effect when light is preferentially scattering shorter wavelengths by melanin found in the dermis of the skin. It is unclear at this time as to whether there is a genetic component associated with a blue nevus. Since it is commonly found in Asian populations and in women more than in men, some suggest a genetic association. In our case, Blue nevus presented as a umbilicated nodule of bluish-black color on the trunk. Histological examination was consistent with cellular blue nevus (CBN); revealed the pigmented spindled and dendritic melanocytes typical of a blue nevus and in addition, more cellular islands of larger spindle-shaped cells with pale to clear cytoplasm containing minimal pigment and large ovoid nuclei.

INTRODUCTION

A 33-year-old man presented with bluish, firm lesion on abdomen since 2 years. It started as a small papule and gradually increased in size. There was no improvement with oral antihistamines and topical therapy including topical steroids, pimecrolimus and emollients. There was no past history of similar lesions or other skin problems. The patient had no systemic complaints and there was no family history of similar lesions.

Cutaneous examination revealed well defined, dome-shaped, soft to firm, darkly pigmented, umbilicated nodular lesion on abdomen measuring 1.2 cm in diameter [Fig. 1, 2]. Hair nails and mucous membranes showed no significant abnormalities. General physical and systemic

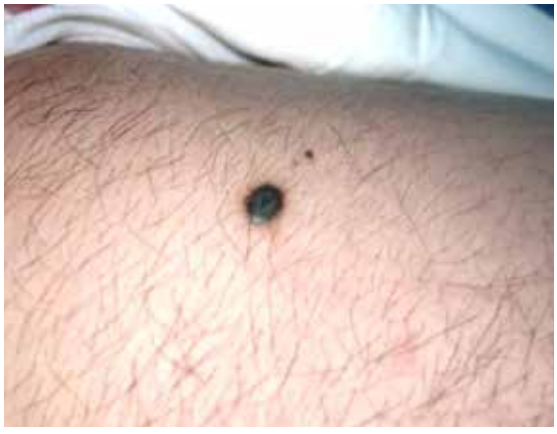

Figure 1: A Solitary, dark pigmented nodule on the abdomen.

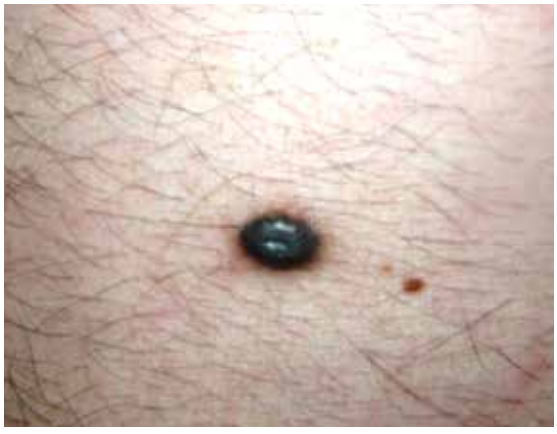

Figure 2: A Solitary, umbilicated, dark pigmented nodule surrounded by brownish pigmentation in the abdomen.

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examinations were within normal limits. Routine laboratory and radiological investigations were all within normal limits.

We performed a total excisional biopsy and microscopic examination showed ill-defined dermal proliferation of spindle shaped melanocytes with abundant pigment and melanophages interspersed in-between dermal collagen bundles. The overlying epidermis showed hyperkeratosis with follicular plugging and an epidermal atrophy [Fig. 3, 4].

FINAL DIAGNOSIS

- Blue nevus

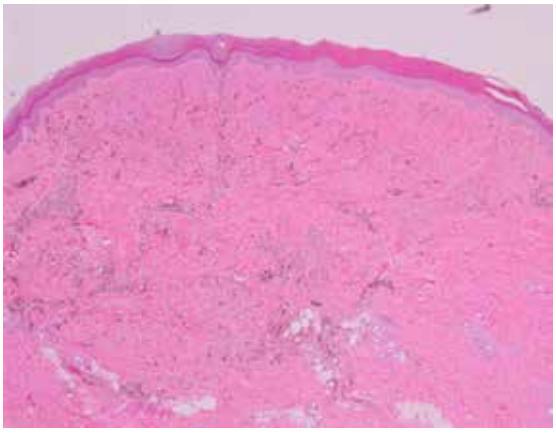

Fig. 3 Dome shaped lesion formed of ill-defined dermal mass containing pigmented cells. The overlying epidermis shows hyperkeratosis with follicular plugging and an epidermal atrophy.

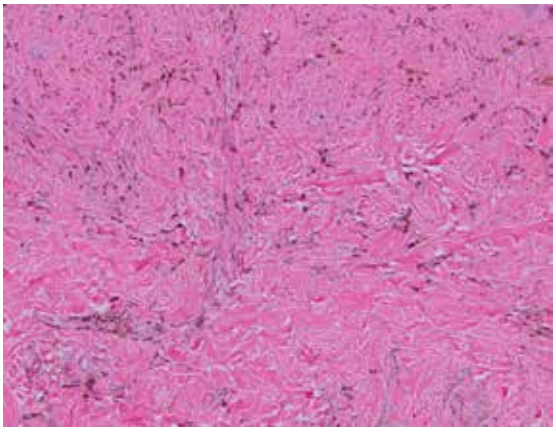

Fig. 4 Spindled shaped melanocytes with abundant pigment and melanophages in-between dermal collagen bundles.

DISCUSSION

According to the original description by Tieche,[1] to which little can be added, blue nevus is a dermal-based, benign melanocytic lesion histopathologically made up by variable proportions of oval/spindle and bipolar, usually heavily pigmented dendritic cells (G. Ferrara *et al*. submitted).[2,3] The aggregation of oval/spindle melanocytes with pale cytoplasm into discrete expansile nodules features a "cellular" blue nevus.[2] The cell components of blue nevus consist of arrested embryonal melanocytes migrating from the neural crest into the epidermis during embryonic development.[3] Immunohistochemically, they usually express melanoma-associated antigen HMB45, together with S100 protein and Melan A/Mart-1. These cells are the sole or the main components of several other melanocytic lesions named "dermal dendritic melanocytic proliferations".[3] Three categories of dermal dendritic melanocytic proliferations have been identified in the classical dermatopathology literature: (a) hamartomatous dermal melanocytoses (Mongolian spot, nevus of Ota, and is nevus of Ito); (b) classic and cellular blue nevus; and (c) malignant blue nevus.[3]

In recent years, a number of additional histopathological variants of blue nevi have been described,[3] such as common and cellular, sclerotic and mucinous, sclerotic and hypo-amelanotic (G. Ferrara *et al*. submitted). Within the benign lesions of the blue nevus family we can also include "atypical" variants.[3,4] These are defined as blue nevi, most often of the cellular type, in which histopathology shows one or several atypical features, including mitoses (not atypical and up to 3–4/ mm^2), ulceration, large size/deep extension, nuclear pleomorphism and

focal necrosis. This concept has been criticized in the name of a "dual" (benign vs. malignant) concept of nosology.[5] Indeed, if defined according to strict morphological criteria, atypical blue nevi have a completely benign biological behavior.[5]

Finally, some dermal dendritic melanocytic proliferations are overtly malignant,[2] but the term "malignant" or "metastasizing" blue nevus is an oxymoron and should be therefore avoided. Melanoma can seldom arise in the context of a cellular blue nevus. Preliminary molecular data suggest that it has a different pathway to tumorogenesis than that of conventional melanoma.[6]

Common or classic blue nevus is a small (gray-blue or blue-black macule, papule, or plaque usually located on the head, neck, perisacral region, or distal extremities.[7] Exceptional extracutaneous locations have also been described.[8,9] It is almost invariably acquired during the second decade of life; most patients belong to phototypes III–IV.[2] The cellular variant is a much larger blue-black nodular lesion whose typical location is the gluteal region.[2,6] The scalp and the extremities are less commonly affected. Unusual clinical features of blue nevi include congenital, familial, eruptive, plaque-like, targetoid, and linear forms.[8,10,11] The term "agminated blue nevus" has been used for multiple blue nevi sometimes arising within a Mongolian spot.[2,11] Most lesions belonging to the blue nevus family show demographic and clinical features which are similar to those of common and cellular blue nevi. In particular, "hypochromic" variants of blue nevi do not seem to be "ancient" blue nevi because of the young age of most of the patients (G. Ferrara *et al*. submitted). Remarkably, these variants of blue nevus are rarely recognized as such on clinical grounds. In fact, the paucity of melanin often imparts a grayish or even a grayish-brown color.[3] Epithelioid blue nevus also resembles blue nevus from a clinical point of view, but is histopathologically distinctive.[8] The majority of epithelioid blue nevi are detected as multiple elements associated with other cutaneous lesions (lentigines and myxoid neurofibromas) in the clinical context of a Carney (myxoma) syndrome.[12] This is an autosomal-dominant disorder typified by the triad: cutaneous lesions; cardiac myxomas; and hormonal hyperfunction (adrenal hyperplasia, pituitary adenomas, testicular tumors). These alterations are summarized into the acronyms LAMB (Lentigines, Atrial myxomas, Mucocutaneous myxomas, Blue nevi) and NAME (Nevi, Atrial myxomas, Myxoid neurofibromas, Ephelides).[13]

The dermoscopic features of common blue nevi are considered to be peculiar enough as to help their clinical recognition.[14] In fact, they are described as showing a homogeneous pattern with a characteristic steel-blue pigmentation – either in a diffuse "structureless" or, less commonly, in a "dotted-globular" pattern.[14] When pressing with the lens plate, a skin folding above the peripheral area of the lesion often appears as a circular whitish line. Both arborizing vessels and peripheral streak-like extensions are sometimes discernible as typically out-of-focus structures. Indeed, the "blue nevus family" is composed by lesions which are not always "blue" on dermoscopy. Large, often ovoid areas of discoloration due to loss of melanin and/or to stromal response are definitional for "white" blue nevi. These lesions represented 46.8% of all excised blue nevi in a recent series (G. Ferrara *et al*. submitted). Much less commonly, a black lamella – namely, a homogeneous, black, disc-like area which can

be removed by tape stripping – covers most of the surface of blue nevi, thus featuring "black" blue nevi (G. Ferrara *et al*. submitted). Finally, a minority of these nevi are either tan ("brown" blue nevi) or variegated ("polychromous" blue nevi) in their dermoscopic color. Interestingly, deep penetrating nevus, an unusual melanocytic neoplasm belonging to the blue nevus family, has been recently described as a polychromous lesion which can undergo rapid dermoscopic changes (G. Ferrara *et al*. submitted).

The clinical recognition of a blue nevus is commonly not problematic. A dermoscopic diagnosis of nodular pigmented basal cell carcinoma can be sometimes evoked because of the presence of arborizing vessels. In blue nevus, however, these vessels are typically out of focus. Some adnexal neoplasms (e.g., trichoblastoma, pigmented intradermal poroma) are characterized by a diffuse bluish pigmentation. As a rule, patients report the onset of these lesions as more recent than that expected for a blue nevus. Apocrine hydrocystoma is an adnexal lesion which is typically located in the periocular area. Its consistency is floating or elastic; not uncommonly, patients report its sudden onset. "Hypochromic" variants of blue nevi can be clinically hard to differentiate from dermal nevi or dermatofibromas.[5] Dermoscopy can help their recognition by showing foci of steel-blue pigmentation which could not be discerned by the naked eye.[5] Pigmented Spitz/Reed nevus must be differentiated from deep penetrating nevus clinically[15] and from common blue nevus dermoscopically.[14] However, when present, peripheral extensions of blue nevus are different from true radial streaks/pseudopods of pigmented Spitz/Reed nevus because they are typically grayish-blue in color and out of focus. The most important differential diagnosis must be made between blue nevus and melanoma. Dermoscopy can aid the recognition of nodular melanoma by showing subtle differentiating features (vascular pattern, remnants of pigment network, blue-whitish veil).[8] Exceptional cases of metastatic melanoma can strictly mimic the clinical and dermoscopic features of blue nevus. Anamnestic data are relevant, but not always clear-cut. A peripheral halo of erythema in metastatic melanoma is quite characteristic but inconstant.[14] In these cases, the "golden rule" is to not schedule any follow-up for a nodular lesion and to excise it. The histopathological pattern of common blue nevus is defined as dendritic–sclerotic.[16] This is typified by the presence of elongated, finely branched, heavily pigmented dendritic melanocytes interspersed with some melanophages among thickened bundles of collagen in the mid and the upper dermis. A thick grenz zone usually separates the lesion from the unaffected epidermis. Not uncommonly, some areas of otherwise typical blue nevi are composed of oval, often plump, melanocytes almost devoid of any pigment. When the pigment loss is sizable, but involves less than 95% of the lesion, the term "hypomelanotic" blue nevus seems to be appropriate (G. Ferrara *et al*. submitted). Cases in which pigment loss involves at least 95% of the lesion can be labeled as "amelanotic".[17] A minority of blue nevi show a marked degree of fibrosis (sclerosing blue nevi; G. Ferrara *et al*. submitted) and/or myxoid changes of the.[3,18] It has been noticed that transition types between hypoamelanotic and sclerosing blue nevi also exist, these lesions can therefore be grouped together into "hypochromic" blue nevi. On dermoscopy

most "hypochromic" lesions appear as "white" blue nevi (G. Ferrara *et al*. submitted). In rare instances, blue nevus is located superficially and some dendritic melanocytes are arranged in single units within the epidermis. These cases have been labeled as "compound blue nevi"[16] or "blue nevi, superficial type, with prominent intraepidermal dendritic melanocytes" [or, simply, "Kamino nevi".[6] On dermoscopy, these lesions often appear as "black" blue nevi.[4] A nevus of another kind is occasionally associated with a blue nevus: such a lesion is termed "combined blue nevus".[14,16] Some authors[6] have noticed that combined blue nevi are often "brown" blue nevi on dermoscopy. The histological pattern of "cellular" blue nevus is defined as spindle/fascicular.[16] It is composed by dendritic melanocytes together with islands of epithelioid and plump spindle cells with abundant pale cytoplasm and usually little pigment. Melanophages are found between the cellular islands. The tumor often bulges into the subcutaneous fat as a nodular downgrowth with a typical clapper-like silhouette.[2,3,9] Stromal desmoplasia and balloon-cell changes are rare occurrences.[2] A peculiar lesion which is placed somewhat in between combined cellular blue and Spitz (Blitz) nevus[19] and epithelioid blue nevus[10] is deep penetrating nevus.[14] It is a dermal V-shaped lesion that bulges into the subcutis. Typically dendritic and spindle melanocytes are its main components, with some interspersed epithelioid (spitzoid) cells whose morphological hallmark is a finely vacuolated (sebocyte-like) cytoplasm. The dermoscopic appearance of this lesion is often "polychromous" (G. Ferrara *et al*. submitted).

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