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Case Report

Nevus Blue as a Sporadic Finding in a Patient with a Blue Toe?

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Abstract

BACKGROUND: Blue nevus is an interesting finding, which aetiology and risk of locoregional and distant metastasis have not yet been fully clarified. It may be inherited or acquired, with sporadic cases usually presented as solitary lesions. It is often localised in the area of the head and less often on the arms, legs or trunk. Blue nevi are formations with relatively low but still possible potential for switching to melanoma.

CASE REPORT: The patient we described was hospitalised for pronounced cyanosis of the small toe of the right foot, accompanied by painful symptoms at rest and pain symptoms for a few weeks. Using inpatient paraclinical and instrumental tests, the patient was diagnosed with cholesterol microembolism. During the dermatological examination, blue nevus on the contralaterally localised limb was also diagnosed as a sporadic finding. According to the patient's medical history, the finding had existed for many years, but in the last few months, the patient has observed growth and progression in the peripheral zone of the nevus without any additional clinical symptoms.

CONCLUSION: Due to the risk of progression to melanoma, the lesion was removed by radical excision, and the defect was closed by tissue advancement flap.

Introduction

Blue nevi are melanocytic tumours of dermal origin. Their prognosis is usually very good, and in most cases, they remain completely benign, asymptomatic and unchanged throughout life [1]. But there is a spectrum of "blue" lesions ranging from common benign to lesions of unknown potential as heavily pigmented epithelioid melanocytomas to aggressive malignant tumours such as the so-called "blue nevus associated melanoma" [1] [2] [3] [4]. According to blue nevi need a thorough histological work-up not to overlook a malignant transformation, in particular in adult patients where blue nevi are less common than in adolescents. Therefore, the dilemma often arises whether surgical removal of the nevus should be a priority.

Case report

A 49-years-old man is presented in good general status. He was a smoker for 20 years (10-15 cigarettes per day). There is no evidence of family history, concomitant diseases or medication. The patient was first hospitalised at the clinic for a blue formation on the small toe of the right foot that had occurred approximately two weeks before.

During the dermatological examination, we made two independent findings: 1) cyanosis on the small toe of the right foot (Fig. 1a, and 2) nevus with blue colour on the left leg above the ankle (Fig. 1b, 1c). The patient complained of pain at palpation of the cyanosis toe, foot pain at rest and improvement of the status of the movement.

The inpatient instrumental and paraclinical examinations showed no significant abnormalities: a panoramic image of teeth – 17, 23, 27, 32 roots with granuloma; PSA (< 4.0) – negative; CEA (< 5.0) – negative; Protein C (109.7%) – normal; Protein S (119.3%) – normal; antithrombin III – normal; Factor V Leiden – normal; anti-phospholipid antibodies – 1.3 U/ml (< 10); anti-cardiolipin antibodies – 1.4 U/ml (< 10); anti beta2-glycoprotein antibodies – 3.3 U/ml (< 10); ANA-1: 100 (boundary titre), anti-streptolysine titre – normal; INR – 1.04.

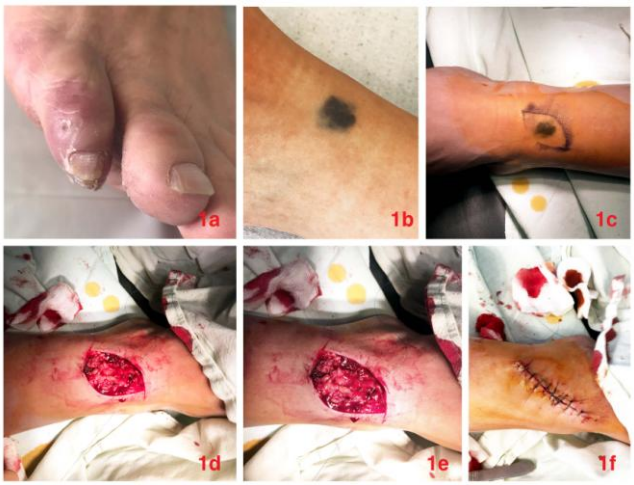

Figure 1: 1a) Cyanotic toe; 1b) Blue nevus localized on the left lower leg, above the ankle; 1c) Outlining the resection boundaries; 1d, 1e) Elliptical excision of the blue nevus with boundaries of surgical security 0.5 cm; 1f) Closure of the surgical defect by means of stretch plastic surgery

The Doppler echography of the lower limb vascular system followed by consultation with a vascular surgeon showed no evidence of thrombosis or thrombophlebitis. Surface and deep venous system – without evidence of reflux; preserved pulsations at the levels of the foot and digital arteries of both limbs. Echocardiography showed evidence of dilated and hypertrophied right ventricle. The blue toe was found to be most likely due to cholesterol microembolism.

For microembolism, a therapy with low molecular weight heparin – Nadroparin calcium 0.4 x 1/d subcutaneously for 7 days and topical Heparoid ungentum for 7 days was introduced. After a consultation with a vascular surgeon, outpatient therapy with Cilostazol 100 mg x 2/d for 1 month and Clopidogrel 75 mg x 1/d for 1 month was assigned.

Due to the patient's current history of the observed growth of a blue formation and the likelihood of malignant transformation to melanoma, radical removal was performed under local anaesthesia. Elliptical excision with a 0.5 cm surgical field security was used (Fig. 1d, 1e), followed by gradual closure of the defect by tissue advancement flap (Fig. 1f). The histological examination confirmed the diagnosis of cellular blue nevus with free resection margins.

Discussion

Blue nevus is a flat or slightly raised macula, papule or plaque with grey-blue to bluish-black colour [2]. It is believed that blue nevi are a collection of pigment-producing melanocytes in the dermis [1] [2]. They may be congenital or acquired [3]. They are usually presented as single lesions and are found in the area of the head, neck, and sacral region, the back of the upper and lower limbs [1]. In dermoscopy with polarised light popular exophytic lesions present with a homogenous blue-greyish globular pattern, and striking colour changes resembling the colours of a rainbow. Such a pattern is usually seen in vascular lesions only. In flat lesions, the dermoscopic pattern may resemble seborrheic keratosis. Dermoscopy alone is not a substitute for histopathology.

Although in most cases blue nevi are considered benign, there are occasions when they are likely to progress to melanomas [3] [4] [5]. Determination of the risk of occurrence of a possible melanoma based on a blue nevus, as well as which of the occurred or congenital blue nevi will have an aggressive course, may be a significant challenge for the clinician [3] [4]. In these cases, identification of certain genetic changes would help to individualise and refine their prognosis [4].

Benign and malignant lesions are characterised by genetic peculiarities. Benign blue nevi harbour mutations of the G-protein-coupled receptor subunits *GNAQ* and *GNA11*. Also, the *c-kit* (CD117) gene may be used, which is strongly positive in immunohistochemical staining for benign cellular blue nevi, in contrast to the invasive melanomas, in which this gene has a lower intensity of staining [1].

Several histological types of blue nevi are known: simple blue nevus, cellular blue nevus, atypical cellular blue nevus, combined blue nevus, blue nevus-like melanoma, and malignant blue nevus – with the worst prognosis [3] [4] [5].

The frequency of malignant transformation of blue nevi is between 5.2 and 6.3% [6]. No consensus has yet been reached on the histological features indicating malignancy in blue nevi, and this poses significant diagnostic difficulties in attempting to distinguish between benign and malignant blue nevus [7]. The presence of irregular edges with satellites (satellitosis) is considered a strong precondition for malignancy [5]. Other signs considered to be indicative of possible malignant transformation are infiltration boundaries, common mitoses, nuclear pleomorphism, hyperchromasia [7]. According to many authors, the most important histopathological sign distinguishing benign and malignant blue nevi is the widespread necrosis [7].

Malignant blue nevi are "aggressive neoplasias" that most commonly metastasises in the regional lymph nodes [3] [6] [9]. Migration or infiltration

of nevus cells to distant lymph nodes is also possible [8]. Interestingly, it is possible to have infiltration of the lymph nodes by single cells also in the event of a benign type of cellular blue nevus without any histological evidence of malignancy [1] [6] [10]. Literature data are of interest, in which axillary lymph node biopsy (performed to suspicion of breast cancer metastasis) indicates the presence of a combined blue nevus adjacent to benign non-pigmented nevus cells (within the same lymph node). This speaks in favour of the fact that blue nevus may occur as a primary finding in the lymph nodes without a skin manifestation or primary skin manifestation [11].

Virtually, the cases of enlarged lymph nodes within the congenital or acquired cellular blue nevus camouflage the clinical picture and may be misinterpreted as melanoma metastases [12].

Atypical cellular blue nevus is presented with median histology between the “malignant blue nevus” and melanoma [3]. This type of blue nevus is associated with the highest risk of proliferation to malignant melanoma and metastasis in the lymph nodes [3] [13]. There are in fact cases of “metastatic malignant melanoma”, which are often the result of incorrect diagnosis or interpretation of the available histopathological evidence indicative of a “malignant blue nevus” [13].

As on many other topics in the field of medicine, there are many questions here as well [14]. On the one hand, the underestimated blue nevi may become melanomas with metastasis in the lymph nodes, and on the other, the lymph nodes that are not always enlarged, in combination with blue nevus show progression to malignant melanoma [11] [13] [16]. According to studies evaluating the 5-years survival in cases of lymph nodes involvement from benign nevus cells, it does not differ from that in patients lacking lymph nodes involvement [17]. Currently, the recommended approach in case of lymph nodes involvement is the removal of the primary skin lesion and lymph nodes biopsy, followed by histological and immunohistochemical analysis to consider further actions [17].

Several years after lymph nodes dissection has seemed to be mandatory for the detection of a malignant blue nevus with lymph nodes metastases [18]. Complete lymph node dissection is seen today more critical especially in patients with low-risk sentinel lymph node tumour load since the prognosis is not improved by this way [19] [20].

A case of a patient with a blue nevus leading to the development of orbital-palpebral and intracranial melanoma has also been described [21].

Any case of increasing and extending blue nevus boundaries is a major indication of their surgical removal [7] [11]. The excision should be through a technique leading to complete elimination of the lesion and should ensure compliance with the boundaries of surgical security [22]. This is easily and quickly accomplished by radical excision and closing the defect using a tissue advancement flap [20]. Each patient with a resected blue nevus requires a histological examination of the lesion removed and long-term monitoring of the operative zone and the locoregional lymph nodes [6] [11] [14].

In conclusion, despite the “predominantly” benign course of the blue nevi, some of them are related to a risk of switching to malignant melanoma. This makes the early surgical removal a priority approach. The aesthetically and therapeutically acceptable surgical decision for blue nevi is the radical excision, followed by closure of the occurred skin defect using stretch plastic surgery.

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