ID Design Press, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2018 Jan 25; 6(1):143-145.
Special Issue: Global Dermatology-2
https://doi.org/10.3889/oamjms.2018.016
eISSN: 1857-9655
Case Report

Medium Sized Congenital Melanocytic Nevus with Suspected Progression to Melanoma during Pregnancy: What's the Best for the Patient?

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Citation: Tchernev G, Dzhelyatova GA, Wollina U, LozevI, Lotti T.. Medium Sized Congenital Melanocytic Nevus with Suspected Progression to Melanoma during Pregnancy: What's the Best for the Patient? Open Access Maced J Med Sci. 2018 Jan 25; 6(1):143-145. https://doi.org/10.3889/oamjms.2018.016

Keywords: Congenital melanocytic nevus (CMN); Pregnancy; Melanoma; Malignant transformation

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Received: 20-Aug-2017; **Revised:** 17-Sep-2017; **Accepted:** 24-Sep-2017; **Online first:** 13-Jan-2018

Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Congenital melanocytic nevi (CMN) are pigmented skin lesions usually present at birth. Rare varieties can develop and become clinically very large. Although they are benign nevomelanocytic neoplasms, all CMN may be precursors of the melanoma, regardless of their size. Individual risk of malignant transformation of melanocyte is determined by simultaneous action of exogenous and endogenous factors. The major exogenous risk factor is ultraviolet radiation. Leading roles among the endogenous factors are attributed to skin phenotype, gene mutation, sex hormones and their significance.

CASE REPORT: We present a case of a 27 – year - old pregnant female patient with a congenital melanocytic nevus, which increased significantly in size, during her pregnancy. Estrogen levels increase during pregnancy and clinical evidence has suggested that melanocytes are estrogen - responsive. Nevi in a pregnant patient would exhibit increased expression of estrogen receptor β (ERβ) and thus enhanced the potential to respond to altered estrogen levels.

CONCLUSION: All pigmented skin lesions should be carefully observed during pregnancy by a dermatologist due to the increased risk of malignant transformation, associated with the endocrine dependence. All lesions with visible changes should be removed surgically with appropriative anaesthesia.

Introduction

Despite aesthetic, congenital melanocytic nevi can cause health problems. Usually they are classified by size: small (< 1.5 cm in diameter), medium (1.5 – 19.9 cm) and large or giant (≥ 20) [1]. Independently of their size, all congenital melanocytic nevi are associated with increased risk of development of melanoma [1]. The risk of malignant transformation is higher in giant congenital nevi, and they should be carefully monitored biopsied if indicated [2].

The most prominent and predictable progression could be seen in the middle sized melanocytic nevi by dermoscopic and clinical evaluation, because:

1. The giant congenital melanocytic nevi often show areas which are clinically and dermoscopically difficult to differentiate from melanoma [3]. In these cases (patients with giant congenital melanocytic nevi) surgical excision is rarely due to the enlarged size of the lesions [4][5]. Confocal laser dermoscopy and PET CT can be useful to diagnose melanoma [6].

2. Small congenital melanocytic nevi or so-

called congenital pseudomelanomas are often clinically and dermoscopically indistinguishable from real melanomas. Histopathological verification of the above-mentioned lesions are also subjected to lively discussions; therefore differentiation of melanoma is extremely difficult.

These two facts are giving a new perspective on diagnosis and choosing of the most appropriate treatment option for the medium-sized melanocytic nevi, namely by surgery [3][4][5]. Progression of normal and dysplastic nevi to melanoma during pregnancy is an interesting topic which at the moment does not find a definitive solution [7].

Case report

We present a case of a 27 – year - old female patient, with a pigmented lesion measuring 3 x 5 cm, located above the right gluteal area since early childhood. The lesion was asymptomatic and had not shown any changes in size or colour for the last 20 years. There was no evidence of significant comorbidities or medical treatment. During pregnancy, the patient noticed peripheral enlargement of the lesion as well as the intensification of the dark hue. The latest changes prompted the patient to seek medical consultation at the dermatological clinic. A large melanocytic nevus was established within the clinical examination, located above the right gluteal area with asymmetric shape, uneven boundaries at the periphery, no uniform colour in the different areas of the lesion as well as the difference in diameter – east, west, north, south, but no elevation of the lesion.

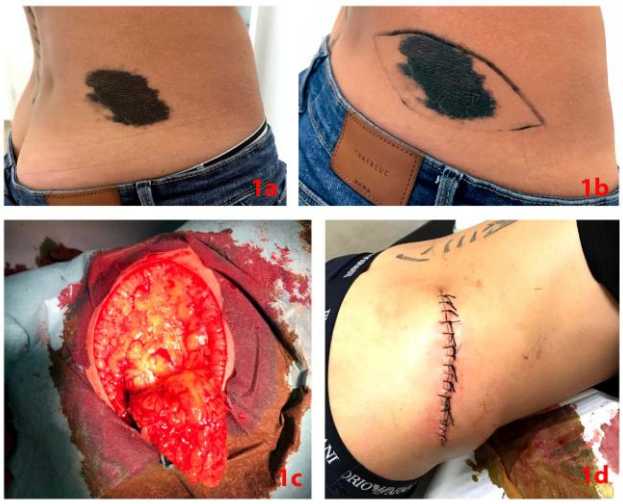

Figure 1: a, b) Clinical view of the lesion located above the right gluteal area; c, d) Consecutive stages within the excision of the lesion

The diagnosis of medium-sized congenital melanocytic nevus was confirmed by the medical history, dermoscopic and clinical signs of dysplasia and progression during pregnancy. The lesion was surgically removed under local anaesthesia (Fig.1 a, b, c, d). The histopathological evaluation concluded the diagnosis of medium-sized congenital pigmented congenital melanocytic nevus with minimal cytological atypia and clear surgical margins.

Since pregnancy is a sure risk factor for the progression of normal nevi to dysplastic or dysplastic nevi to melanoma, we recommend surgical treatment as a preferable option.

Discussion

It is well known that the frequency and prognosis of melanoma in women are influenced by hormonal and reproductive factors [7]. It is also well established that the prognosis and survival rate in premenopausal women is better than postmenopausal [8]. In the last years there has been increased interested and discussion about the impact of pregnancy on nevi and their malignant transformation [7][9][10]. New theories and approaches have been advanced to explain the interplay between hormones and pathological changes in nevi [11]. One of the hypotheses is the influence of estrogen expression. Beneficial and protective effects on the skin have estrogen receptors: estrogen – receptor α (ERα) and estrogen - receptor β (ERβ) [12]. Significant differences in the concentrations of these receptors have been established in sections of melanocytic lesions and those with healthy skin as well as in pregnant and non- pregnant women's skin [13]. Subtype β is a predominant receptor in melanocytes and its protective function is well known [12]. ERβ is antagonist against uncontrolled cell- proliferation and tumor growth [12][14]. An increased in the immunoreactivity for ERβ was observed in normal nevi during pregnancy [15]. The immunoreactivity for ERβ was found to decreases with such deeply extending cells [16][17]. Loss of ERβ expression and its presumed inhibitory effects may promote transformation into melanoma, which is a key event in neoplastic progression [18]. Several studies show reduced expression of ERβ in metastatic stages of malignant melanoma [19], in the presence of a greater thickness of the dysplastic nevi [20]. The clinical implications of such altered ERβ expressions remains underestimated. Different hypothesis explains the higher risk of malignancy during pregnancy with the increased levels of male sex hormones- androgens [21]. There is a theory that endocrine effect reduces after first pregnancy. During second and third pregnancy the risk of development of malignant melanoma (MM) is lower due to the presence of antibodies against tumor-associated fetal antigens. Thus, during first pregnancy the risk of malignant transformation is increased, while every subsequent

pregnancy has a protective effect [22]. Recently, mutations in two tumor suppressive gens - BAP1 (BRCA - associated protein 1) and BRAF (V - raf murine sarcoma virus oncogene homolog B1) have been associated with increased susceptibility for development of MM and other atypical epithelial lesions [23][24]. Screening for mutation/loss/ inactivation of BAP1 and BRAFV600E can be performed by immunohistochemistry. Most melanocytic lesions show positive BAP1 nuclear staining. BRAFV600E is positive in 5% of congenital melanocytic nevus [23][25]

The potential relationship between dysplastic nevi and malignant transformation during pregnancy is underestimated [26][27]. However, all pigment skin lesions should be carefully observed during this period [26][27]. In our case of a 27 – years - old pregnant woman, with CMN, which significantly increased its size and changed its colour and therefore, we decide to remove the lesions surgically, because of the increased risk of malignant transformation.

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