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NEVOID MELAMOMA - THE UNIQUE HISTOLOGICAL AND IMMUNOHISTOCHEMICAL APPEAREANCE

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Abstract: *Nevoid melanoma is a rare tumor with the origin in the melanin producing cells called melanocytes. The main particularity of this tumor is the resemblance with a benign tumor, a compound of intradermal nevi, despite the malignant behaviour and aggresivity. On the usual stain, we generally observe a tumoral proliferation with a solid architecture, with cells organized in nests. The cytological atypia is observed with high power fields; pagetoid migration is common. The cases described so far in the literature are limited and the incidence has not been established due to the variety of diagnostic the definitions for this particular tumor.*

Key words: *nevoid melanoma, histology, immunohistochemistry.*

1. Introduction

Melanoma is a malignant tumor derived from the cells that are producing melanin, called melanocytes. These cells, due to a series of factors with various origins, can become malignant and lead to melanoma. The tumor is considered to be one of the most aggressive neoplasms known until present days and the excision in an early stage is vital for patients. Looking further into the prognosis, it is known that patients with melanoma in situ have a survival rate of almost 97% at five years, while for patients in stage IV, this percentage goes below 10% [1].

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Over years, melanoma has become a challenge for clinicians and pathologysts. The need for a fast, clear diagnosis and a proper treatment are the ultimate goals when encountering this tumor. Therefore, all the lesions that clinically present atypia are being surgically removed and sent for analysis. The etiology of melanoma is related to the exposure to UV (A and B), genetic patterns (people with relatives who presented with melanoma have a higher risk), multiple atypical nevi, personal features of an individual (for example light skin, sensitive skin that presents reactions after sunlight exposure, immunosuppression) or a poor socio-economical status, which is leading to a late diagnosis [2].

Cutaneous melanoma can appear de novo (on a healthy skin) or can develop on another lesion (such as displastic nevi, cellular blue nevus, congenital nevus, common acquired nevus), usually on areas exposed to the sun. Melanoma can also develop on the mucosa, and this type of tumors are also not associateds with UV exposure [2, 3].

Clinically, the suspicion of melanoma can arise when we encounter the following changes in a melanocytic lesion: asymetry, irregular borders, color variations, diameter larger than 6 mm and elevated surface.

Histologically, the most comon type of melanoma is superficial spreading melanoma. This type of tumor is followed in incidence by nodular melanoma, lentigo maligna melanoma and acral melanoma [4]. Nevoid melanoma is a rare type of melanoma which has particular histological features that resemble nevi. Despite its name, it is important to remember that the “nevoid” term is not implying a better outcome, because this tumor has the same prognosis as the other types of melanoma, in particular nodular melanoma [5].

2. Materials and Methods

We describe the case of a 45 year old patient who presented to the Surgery Department with a cutaneous tumor located on the left side of his face. Surgical excision was performed and the sample was sent for analysis to the Pathology Department of Mureș Clinical County Hospital for analysis. Tissue samples from the specimen were collected and processed by routine techniques: samples were fixed in 10% buffered formalin, paraffin embedding and staining with Hematoxylin–Eosin (HE). An immunohisto-chemical analysis was performed on 4 µm-thick sections prepared from formalin-fixed paraffin- embedded tissue by using an automated immunostainer.

3. Results

The clinical appeareance showed a well defined papilomatous lesion, highly pigmented, without any other particularities. On the gross examination, the cutaneous specimen presented an ellipsoid shape along with a round, black nodule of 8 mm diameter. On the microscopy, we observed a tumoral proliferation that extended from underneath the epidermis towards the reticular dermis (figure 1). The tumor presented a solid architecture and the cells were organized in nests. Towards the depth of the lesion, the cells became smaller and the nests were less visible (Figure 2). With the high power field,

cellular details appeared more proeminent. The tumoral cells presented an ovoidal or polygonal shape, with a pale eosinophilic cytoplasm. The nuclei were enlarged, pleomorfphic, with hyperchromasia, showing proeminent, eosinophilic nucleoli (Figure 3). In the epidermis, malignant melanocytic cells were observed extending to the corneus layer. Mitoses were also noticed (2-3 mitoses/ 10 HPF) and maturation elements were present in the peripheral area of the tumor (nevus component).

The particularities of the tumor included the following: for the malignant component, Breslow index of 0,9 mm and Clark invasion III, no ulceration, TIL brisk, radial growth phase, pagetoid migration. The benign component presented a depth of 1 mm (1,9/total), Clark invasion IV.

Immunohistochemestry staining showed positivity for the following markers: S100 (nuclear marker, figure 4), SOX10 (nuclear marker, figure 5), MelanA (cytoplasmatic marker, showing intense staining in the malignant component, figure 6) and ki67 (proliferation index with expression between 40% in the malignant component and 2% in the deep side of the lesion corresponding to the nevus).

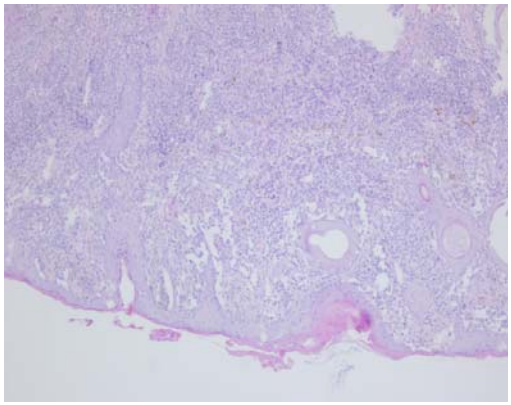

Fig. 1. *Nevoid melanoma, low magnification, Hematoxilin-Eosin stain, 5x*.

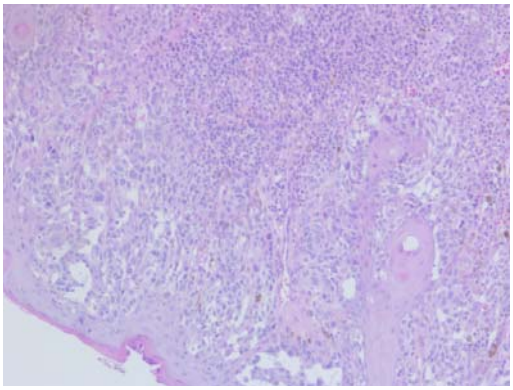

Fig. 2. *Nevoid melanoma, low magnification, Hematoxilin-Eosin stain, 5x.*

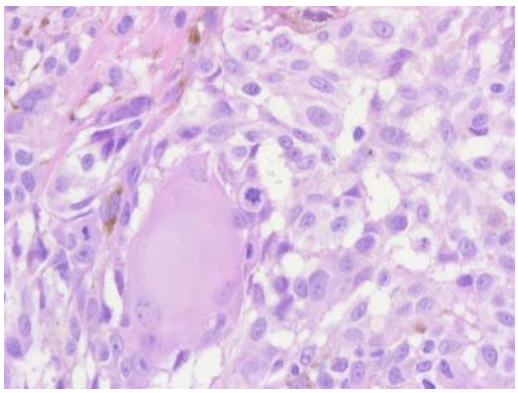

Fig. 3. *Nevoid melanoma, high magnification, Hematoxilin-Eosin stain, 40x.*

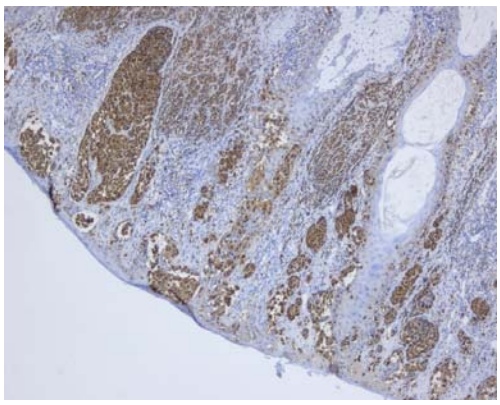

Fig. 4. *Nevoid melanoma, Immunohistochemistry stain-S100, 5x.*

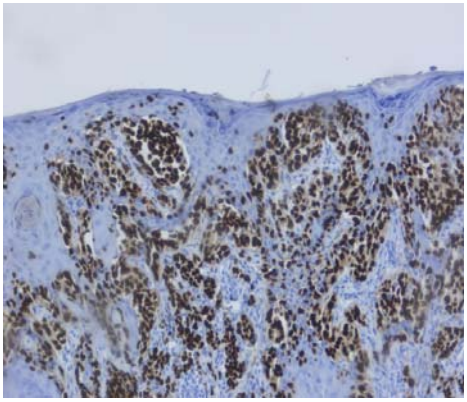

Fig. 5. *Nevoid melanoma, Immunohistochemistry stain- SOX10, 5x. Pagetoid migration is observed in the epithelium*

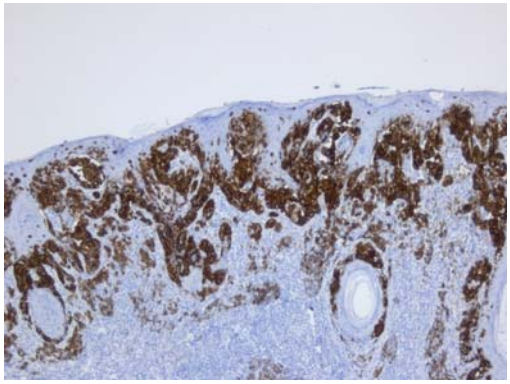

Fig. 6. *Nevoid melanoma, Immunohistochemistry stain-Melan A, 5x.*

4. Discussion

On the gross examination, according to Lazar et all, nevoid melanoma can appear as a papulae or a verrucous lesion, with smooth borders. On the cut surface, the lesion can be pigmented or can present with an amelanotic appeareance and a pink coloration. In our case, the tumor showed dark coloration and presented as a round, well defined nodule [6].

The histological examination showed a large variation in the appeareance of the epidermis. Some cases are described as "normal", others show acanthotic epithelium, a verrucous appeareance or even atrophia. In the case of our patient, the epidermis showed the presence of malignant melanocytes that extended in the entire depth of the epithelium. Many of the cases do not present an intraepidermal component associated (for example melanoma in situ or pagetoid migration). Some authors consider nevoid melanoma as a subtype of nodular melanoma as well. Others will describe an extension of e melanoma in situ in the intradermal component of the nevi. The major challenge in this particular case is identifying the border of the malignant component and assess the Breslow index. Ulceration can be present and when it is seen, it's a sign of poor prognosis. It is important to remember that nevi do not present this feature. In our case, ulceration was absent [7-10].

The component located in the dermis is, like the name suggests, nevoid, and maturation can be observed at low power. The cells are distributed in nests and they decrease in size towards the reticular dermis. The same appeareance was highlighted in our case. On the superficial part of the proliferation, corresponding to the papilar dermis, the tumoral cells showed nesting and were round, ovoidal, polygonal, similar to an intradermal nevus [11-13].

At the base of the lesions, the cells have a bland appeareance and become smaller. In our case, maturation was observed as well. Towards the depth of the lesion, the tumoral cells lost the nesting phenomenon and were distributed diffusely, surrounding the sebaceous glands present at that level, with minimal to no atypia [13-15].

Using the high power field, atypia is usually observed. In the superficial side of the tumor, the cells are enlarged and present nuclear atypia with pleomorphism, irregular contur, hyperchromasia and-characteristic for melanoma-eosinophilic nucleoli. The high-power examination was the most important part of our analysis on the Hematoxilin-Eosin stain. Looking closely at the tumoral cells, we observed enlarged nuclei with irregular contur and proeminent nucleoli. Therefore, the suspicion of melanoma arrised [16-18].

The immunohistochemical appeareance, according to WHO, describes a variability of HMB45. When this marker is positive, aberrant patterns are common. For MelanA staining, all the melanocytic cells present should be marked. In our case, MelanA showed intense positivity for the malignant component of the tumor, while the intensity of the stain progressively decreased towards the depth of the lesion, in the nevus component. SOX10 is a highly specific marker for melanoma and it shows intense nuclear staining in the tumor. In our case, the marker was positive as well. S100 is a widely used marker for melanocytic lesions and it shows positivity in both nevi and melanomas. In our case, the marker was positive as well. The proliferation index revealed by staining with ki67 is used in order to determine the activity of the tumoral cells. In our case, the expression was intense in the malignant component, to a maximum of 40%. In the nevi component, the expression reached 2% [19-22].

Clinically, it is important to differentiate the lesion from other type of skin tumors. For example, some of the entities that we need to consider are pigmented papilomatous lesions (other than melanocytic lesions) such as basal cell carcinoma or pigmented seborrhoeic keratosis.

The main differential histological diagnoses for this tumor are exophitic intradermal nevi, Spitz nevi and deep penetrating nevi. The most important key in the diagnostic for nevoid melanoma, which differentiate it from benign intradermal nevi, is the presence of atypical pleomorphic cells and mitoses. When taking into consideration penetrating deep nevi, one of the most important criteria for diagnosis is the absence or rare mitoses (one or two), the depth of the lesion, absence of pagetoid migration and the presence of spindle cells [23]. Spitz nevi are usually symmetrical and well circumscribed. The most important elements for the differential diagnosis in these cases are represented by the presence of Kamino bodies (eosinophilic hyaline globules), well demarcation from the epidermis with “raining down” appeareance. Focal

pagetoid migration can be observed in Spitz nevi, but it is located in the center of the lesion and it is minimal [24].

5. Conclusion

Nevoid melanoma is a rare melanocytic tumor which represents a diagnostic challenge due to the resemblance with benign melanocytic tumors. The lesion should be carefully analysed and the characteristic immunohistochemical markers for melanoma should be used in order to obtain a proper diagnosis.

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