Surgical and Experimental Pathology

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# Interesting overlooked findings in melanocytic nevi

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## Abstract

Since histological analysis is the gold standard for melanoma diagnose, to understand possible findings in nevi is the first step to avoid diagnostic errors. The aim of this paper is to describe several histological features that can be found in nevi and may be misunderstood or overlooked. Histological findings were organized into two groups: 1- adaptive findings (neurotization, sebaceous alteration, adipose metaplasia, amyloid deposition and calcifications, pseudovascular lacunae), 2- findings that can occasionally be associated with malignancy (suspicious for angiolymphatic invasion, perineural infiltration, deep mitosis, muscle infiltration). Each finding by itself does not mean that lesion is malignant. We have selected 13 cases of benign intradermal or compound melanocytic nevi excised for aesthetical purposes from our collection to illustrate possible overlooked findings in melanocytic nevi.

**Keywords:** Dermatology, Pathology, Nevus, Histology

## Introduction

Despite melanocytic nevi are very frequent in daily practice, differential diagnose with melanoma can be tough sometimes. In this context, not common features can be challenging for Pathologists that are not used to them (Fernandez-Flores and Cassarino 2016). We might not forget, when a nevus cannot be characterized it might be a melanoma (Massi and LeBoit 2014).

According to the World Health Organization (WHO) book about the classification of skin tumours, the most important differential diagnosis of melanocytic nevi is melanoma. This diagnose is based on clinical, dermatological and histological criteria. On a histological basis the following criteria are analyzed: symmetry, circumscription, ulceration, cellularity, pagetoid scatter, cytological atypia, mitotic activity, failure of cellular maturation, lymphovascular and perineural invasion (Edited by Elder et al. 2018).

The aim of this paper is to illustrate few histological findings that can be found in benign nevi and to provide a brief review.

## Methods

Our illustrative cases were organized into two groups: 1- adaptive findings corresponding to phenotypes such as metaplasia, dystrophic alteration and signs of senescence (neurotization, sebaceous alteration, adipose metaplasia, amyloid deposition and calcifications, pseudovascular lacunae, foreign body reaction). 2- findings occasionally associated with malignancy which by itself do not mean that it is malignant (suspicious for angiolymphatic invasion, nevi cells surrounding the nervi or muscle, deep mitosis) (See Figs. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12).

We have selected 13 cases of benign melanocyte intradermal or compound nevi from our collection which were excised for aesthetical purposes. All lesions were analyzed by two Dermatopathologists, and there were benign.

## Results

Seven patients were female and six patients were male. The mean age was 40 years. Five lesions were

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excised from face, four lesions from limbs and four lesions from trunk; without any favorite location. For description of each case see Table 1.

## Discussion

There are three different morphological spectra of nevi cells. They can be big and epithelioid (type A), small like a lymphocyte (type B) or spindled (type C) (Edited by Elder et al. 2018). Cases with neural metaplasia are rich in type C cells. Most frequently that alteration is found with adipocyte metaplasia . This way, neurotization is considered as the final stage of the developing of intradermal melanocytic nevi. The differential with neurofibromas can be hard and it is only possible when type A or B cells are found in non neurotized areas. We also highlighted melanocytic and neural cells have a common embryological origin from the neuro crest (Fernandez-Flores and Cassarino 2016) and those lesions should be distinguished from melanoma with neural differentiation (Massi and LeBoit 2014).

Pseudovascular lacuna is an alteration characterized as free dilated spaces among melanocytes, also called as Pseudo-Dabska pattern in reference to endovascular papillary angioendothelioma (Fernandez-Flores and Cassarino 2016). The origin of those spaces remains unclear. Most nevi with a pseudovascular lacuna are Unna, Meischer or congenital nevi. That finding is unknown in both Clark and Spitz nevi (Massi and LeBoit 2014).

According to the WHO book congenital nevi may present nevus cells in close proximity or within skin appendages, like a muscle (Edited by Elder et al. 2018). The permeation of a muscle can also be found in malignant lesions as Spitz melanoma (Hashimoto et al. 2012). Those features can be identified in melanocytic acquired nevi, too. It is questionable if those lesions are congenital and they could become visible after the deposit of pigment or they evolve from perineural melanoblasts and colonize the dermis and its adnexa (Massi and LeBoit 2014).

Angioadnexocentric pattern of distribution is also described in the majority of congenital nevi (Fernandez-Flores and Cassarino 2016; Massi and LeBoit 2014). Angiolymphatic invasion is considered most frequently as a sign of malignancy. Nevertheless it can be found in benign lesions. In this context, some capillaries are so superficial which disappear in case of sections for histochemistry or immunohistochemistry stains. In many cases there are not angiolymphatic invasion. In fact, it is only a stromal retraction. There are theories about lymphatic transfer of melanocyte cells to lymph node in order to try to explain the nodal deposits of melanocytic cells (Holt et al. 2004).

Sometimes the findings are not cytological. Architectural pattern is an important part of melanocytic lesions evaluation. Considering angiocentric distribution of nevi cell, at low magnification the lesion could be considered as coat-sleeve-like infiltration of the blood vessels. Nevertheless, when you watch out the lesion you can see some features of melanocytes as nested pattern and pseudo nuclear inclusions confirming an angiocentric nevus (Hashimoto et al. 2012).

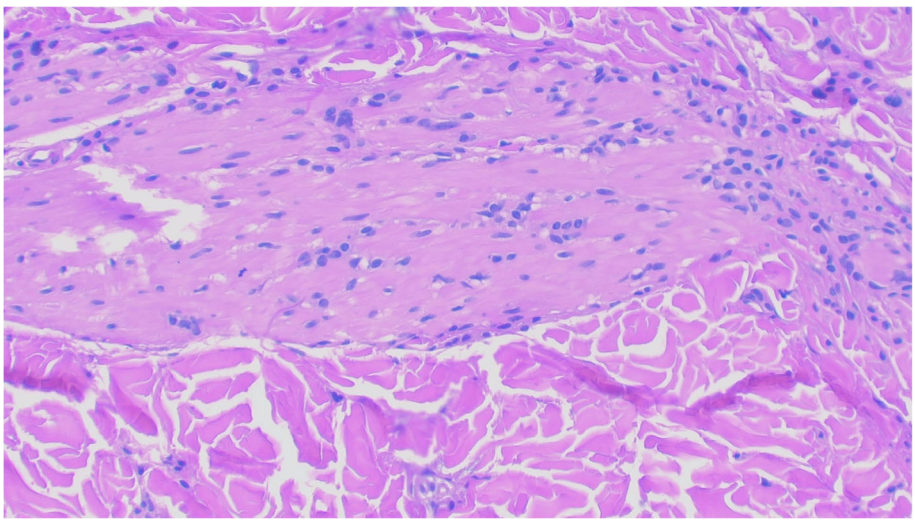

**Fig. 1** Nevi cells surrounding the muscle Hematoxylin and eosin 400X

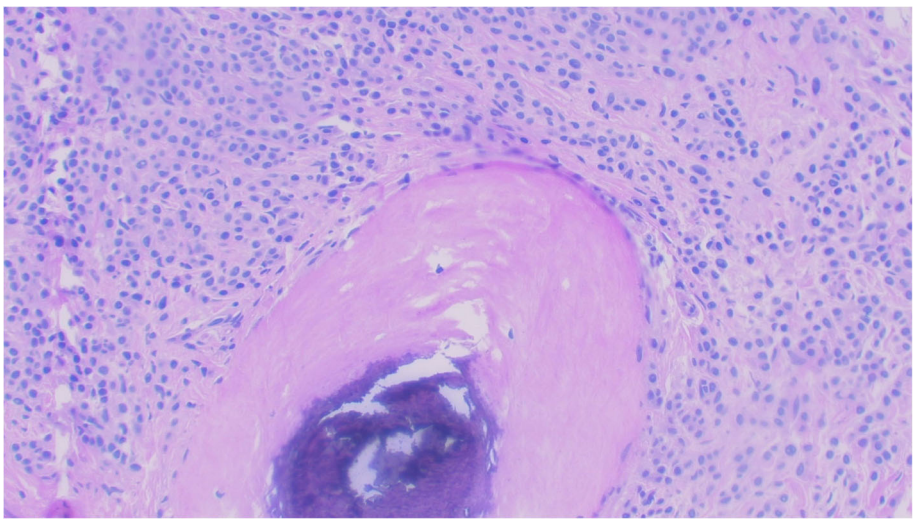

**Fig. 2** Calcification Hematoxylin and eosin 400X

Sebocytes-like melanocytes are described in the spectrum of clear cell changes and it is considered by some authors as part of the spectrum of balloon cell alterations. It is a very common finding with reports around 30% of Unna nevi (Fernandez-Flores and Cassarino 2016).

Mucin deposits can occur in many cutaneous neoplasms. In an important series of melanocytic nevi, mucin alteration was found in 0.55% of the compound melanocytic nevi and 2.75% of the intradermal ones. Three patterns of mucin deposition in melanocytic nevi are described: intercellular formations of fine cords of mucin, formations of various sized myxoid pools in the stroma surrounded by nevus cells or a mixed pattern. The cause of mucin production in melanocytic nevi still remains unclear (Perdiki and Bhawan 2008). Usually the mucin is easily detected in hematoxylin and eosin staining but when it is very focal Alcien blue and colloidal iron can be requested (Massi and LeBoit 2014).

Amyloid deposits associated with melanocytic nevi are quite rare. Usually, eosinophilic deposits are found in papillary dermis above the melanocytic tumor. Two possible explanations are that the deposits are secondary to scratching or they are part of the degeneration process of melanocytic or epithelial cells (Hanami and Yamamoto 2013).

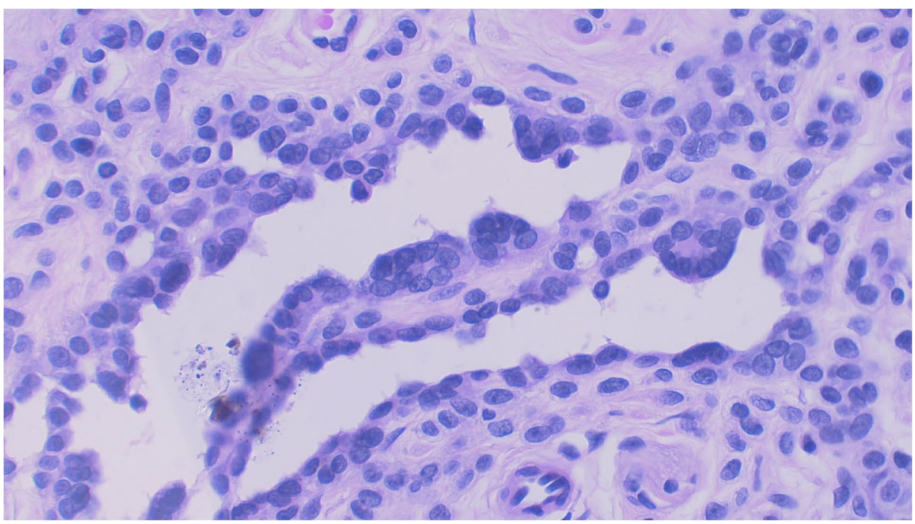

**Fig. 3** Pseudovascular lacunae Hematoxylin and eosin 400X

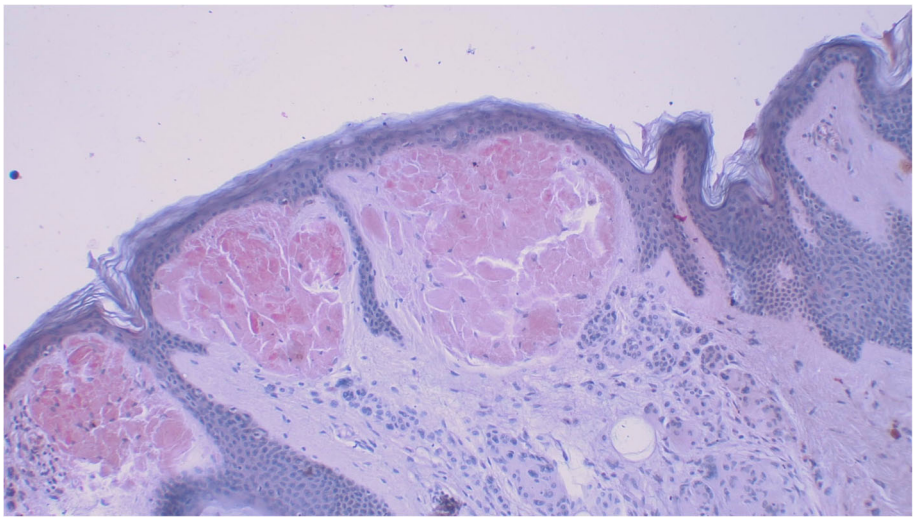

**Fig. 4** Amyloid deposits Congo Red stain 200X

About mitoses, when we are analyzing juvenile pigmented lesion, the pathologist should be careful in order not to overestimate as malignant. Despite the tendency of reduction of frequency of mitoses with the increase of age, about 40% of nevi in young patients had at least one intradermal mitose (Brown and Tallon 2017). Then, for pigmented lesions excised from young patients the mitoses cannot be misunderstood if they are rare and superficial.

Foreign body reaction was described in about 4% of benign nevi. Head and neck are the most common regions of nevi with those alterations. Possible explanation is the previous presence of a vanished epidermal cyst or the strangulation of pilosebaceous unit (Knox et al. 1993). In one of this cases it was also related with calcification.

In conclusion, histological analysis is the gold standard of melanoma diagnose and it is based on criteria which cannot be considered isolated. Nevertheless, clinical and dermatological correlation is recommended. Besides that, alterations as vascular infiltration, perineural invasion, metaplasia, calcification, amyloid or mucin deposits, mitoses, pseudovascular lacuna and foreign body reaction are possible findings in benign melanocytic nevi.

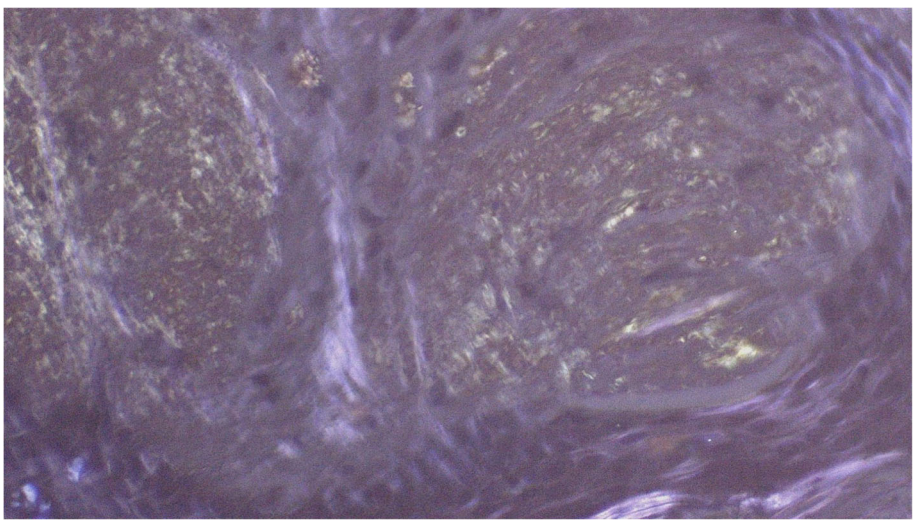

**Fig. 5** Apple-green birefringence of Congo red stained preparations under polarized light 400X

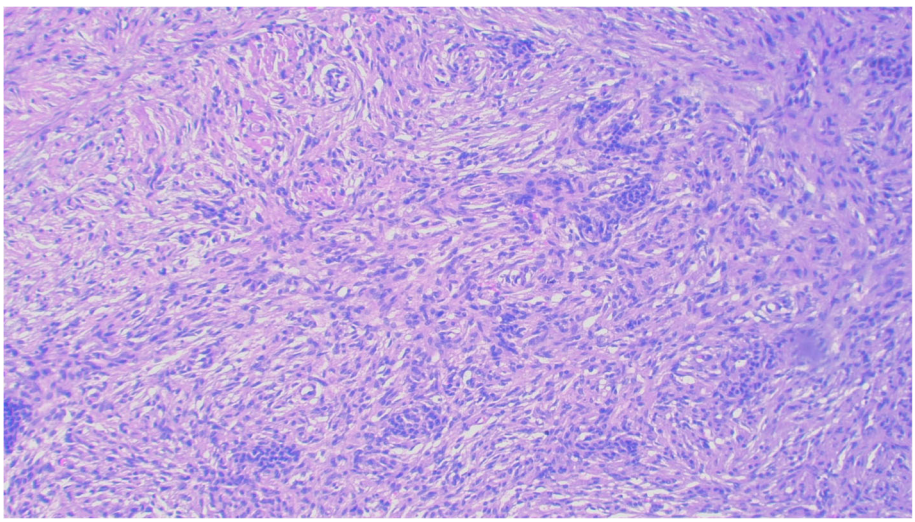

**Fig. 6** Mucin deposits Hematoxylin and eosin 400X

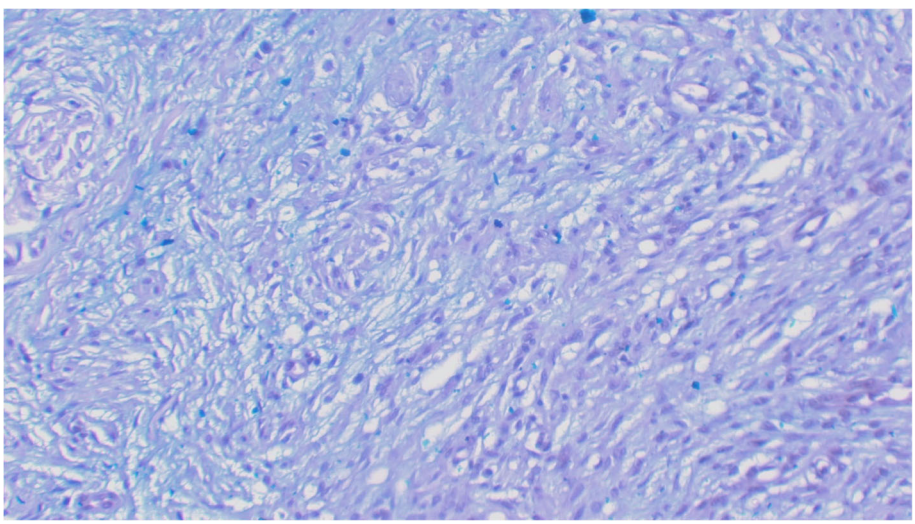

**Fig. 7** Positive Alcien Blue stain 400X

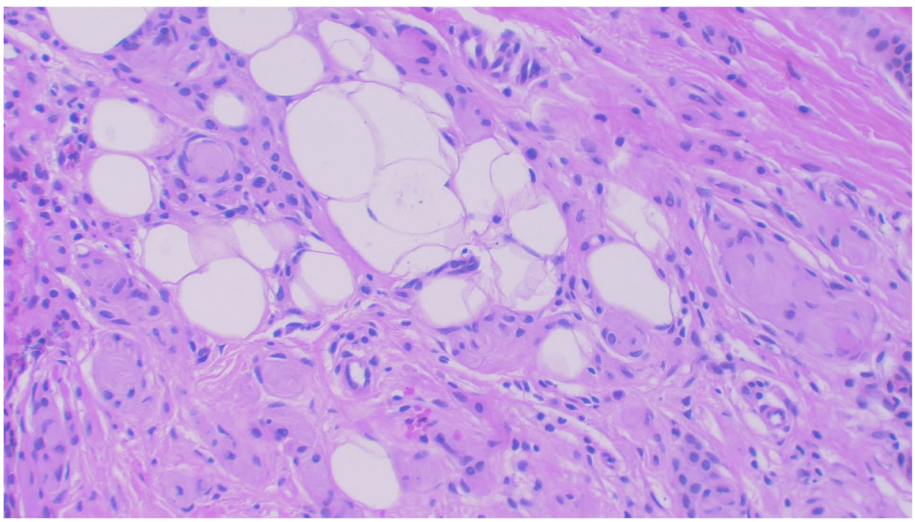

**Fig. 8** Adipocytic and neural metaplasia Hematoxylin and eosin 400X

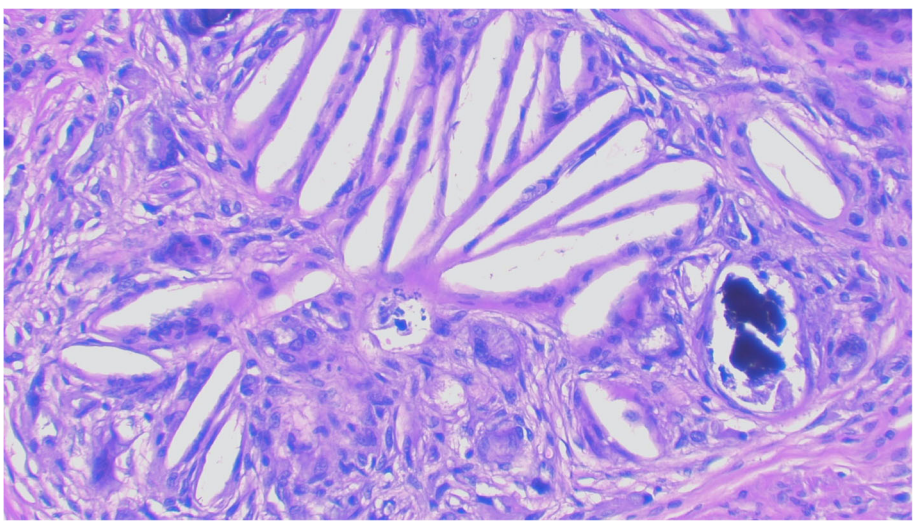

**Fig. 9** Granulomatous foreign body reaction Hematoxylin and eosin 400X

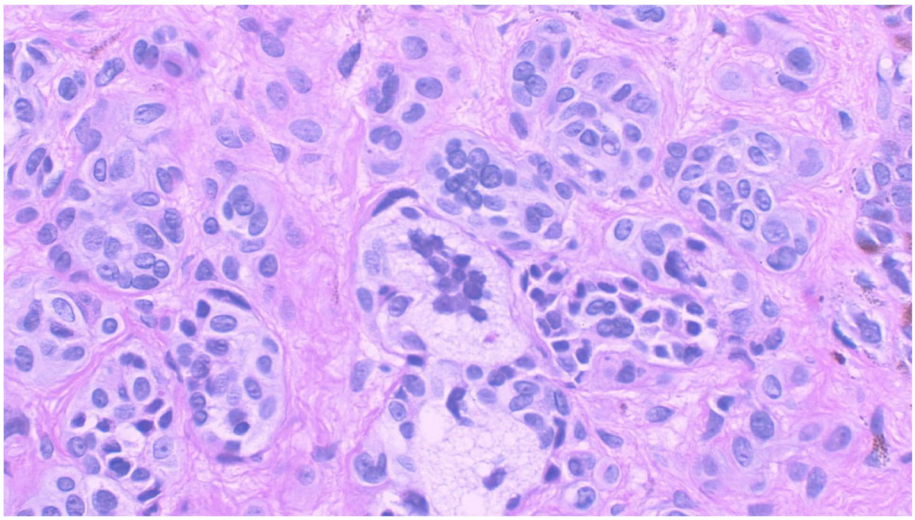

**Fig. 10** Multivacuolated cells (sebocyte-like) Hematoxylin and eosin 400X

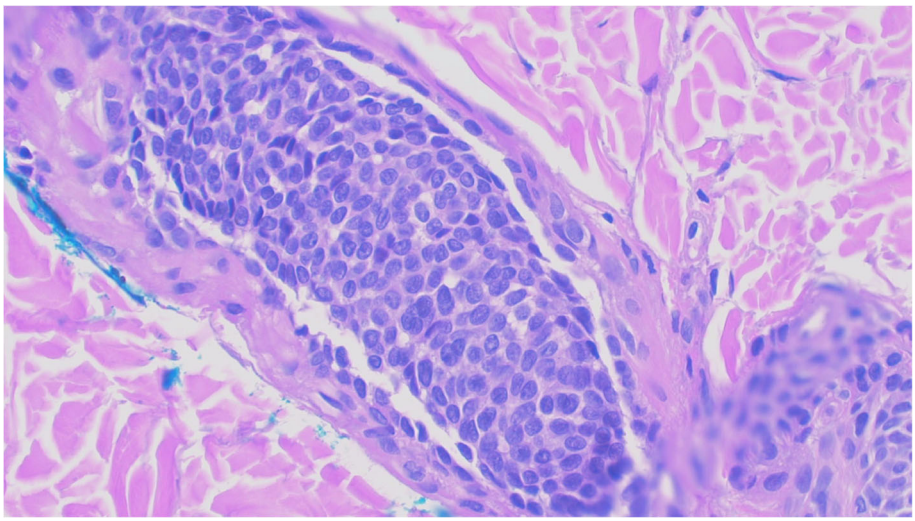

**Fig. 11** Suspicious for vascular invasion Hematoxylin and eosin 400X

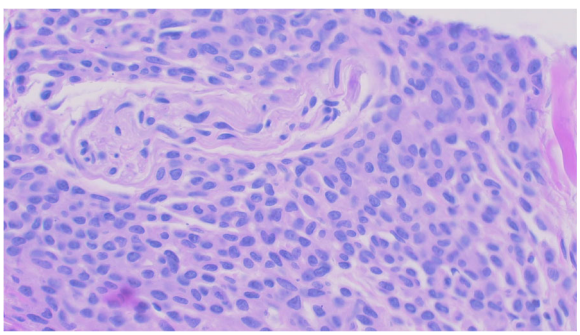

**Fig. 12** Nevi cells surrounding the nerve Hematoxylin and eosin 400X

**Table 1** Cases description

| Case number | Gender | Age (years) | Site | Finding |
|---|---|---|---|---|
| 1 | female | 38 | Scalp | Adipocytic metaplasia and multivacuolated cells (sebocyte-like) |
| 2 | female | 32 | Forearm | Suspicious for vascular invasion |
| 3 | female | 31 | Face | Granulomatous foreign body reaction and calficication |
| 4 | male | 54 | Face | Nevi cells surrounding nerve |
| 5 | male | 41 | Back | Pseudovascular lacunae and nevi cells surrounding nerve |
| 6 | female | 33 | Around the ear | Neural metaplasia |
| 7 | female | 70 | Around the ear | Amyloid deposit |
| 8 | female | 45 | Thigh | Angiocentric pattern |
| 9 | masculino | 13 | Back | Mitose in the bottom |
| 10 | masculino | 31 | Abdomen | Pseudovascular lacunae |
| 11 | female | 46 | Back | Vascular invasion |
| 12 | masculino | 22 | Hand | Nevi cells surrounding nerve |
| 13 | masculino | 60 | Arm | Nevi cells surrounding muscle |

### Abbreviation
WHO: World Health Organization

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None.

### Authors' contributions
JCCXJ Contribution: histological analysis, data collection and article writing. JPOX Contribution: Paper review and critical analysis. DJCJ Contribution: paper review. SCGPD Contribution: histological analysis. NJM Contribution: article writing. All authors read and approved the final manuscript.

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### Consent for publication
Yes

### Competing interests
The authors declare that they have no competing interests.

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