REVIEW

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Skin disorders that mimic melanoma: a review

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ABSTRACT

Malignant melanoma is a skin disorder that originates from the degeneration of melanocyte pigment cells towards malignancy, which is characterized by an increasingly enlarged and irregular and more prominent color change. Many skin disorders have similarities with malignant melanoma, which sometimes makes it difficult for medical personnel to make a diagnosis. Skin conditions that resemble melanoma are categorized into histogenetic lines such as melanocytic (Spitz naevus, Cellular blue naevus, melanocytic naevus with focal atypical epithelioid component/clonal naevus, Deep penetrating naevus), neural (Malignant peripheral nerve sheath tumor, Neurotheceomakell (Sicatrical). When the intraepidermal melanocytic component is subtle or missing, or the tumor displays uncommon histological features, misclassification of melanoma is more likely. The recent implementation of clearer clinical and histopathological criteria with the development of dermoscopy and computer technology has been able to led to the early detection of melanoma, which has contributed to the increased diagnosis of this disease and other skin diseases that may have similarities to melanoma. This review aimed to differentiate melanoma-like skin disorders.

Keywords: Dermoscopy, diagnosis, melanoma, melanoma-like.
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INTRODUCTION

Melanoma is a skin disorder that originates from the degeneration of melanocyte pigment cells towards malignancy, which is characterized by an increasingly enlarged and irregular and more prominent color change.[1] Melanocytes are cells that originate from the neural crest of vertebrates. During the process of embryogenesis, melanocyte precursor cells (melanoblasts) will migrate to the mesenchyme to reach the epidermis and hair follicles. The function of melanocytes is to give different skin colors to each person or race and to synthesize melanin.[2] Many skin disorders have similarities with malignant melanoma, which sometimes makes it difficult for medical personnel to make a diagnosis.[3] These skin disorders include both melanocytic and non-melanocytic tumors. In Indonesia, skin cancer is one of the three most common cancers, with malignant melanoma accounting for 1-2% of all deaths due to cancer.[3] Data from the Dermatology and Venereology Outpatient Unit, Division of Tumors and Skin Surgery at the General Hospital Dr. Soetomo in January — December 2018, showed the incidence of skin cancer as many as 27 (0.88%) cases of skin cancer from a total of 3,368 patients with skin surgery tumors. Misdiagnosis of melanoma (overcalling and undercalling) is common, mainly because melanoma can mimic a variety of other benign and malignant neoplasms.[4] This review aimed to discuss the skin condition that mimics melanoma.

MELANOMA-LIKE SKIN DISORDERS

From the Greek words melas (dark) and oma, the word "melanoma" is formed tumor) It is a malignant tumor that arises from melanocytic cells and therefore can occur anywhere where these cells are found.[5,6] Melanomas can mimic a variety of other benign and malignant conditions, so misdiagnoses of melanoma (overcalling and undercalling) can occur.[3] When the intraepidermal melanocytic component is subtle or missing, or the tumor displays uncommon histological features, misclassification of melanoma is more likely.[4]

Melanoma-like skin disorders are grouped into histogenetic lines such as Melanocytic (Spitz naevus, Cellular blue naevus, Melanocytic naevus with focal atypical epithelioid component/clonal naevus, Deep penetrating naevus), Neural (Malignant peripheral nerve sheath tumor, Neurotheceoma/cellular neurotheceoma), Histiocytic (Juvenile xanthogranuloma, Epithelioid cell histiocytoma, Atypical fibroxanthoma), Epithelial (Spindle squamous cell carcinoma), Mesenchymal (Epithelioid angiosarcoma & Leiomyosarcoma), and Reactive processes (Sicatrical) (**Figure 1**).[7]

Skin conditions that resemble melanomas are classified according to their histogenetic lines, which include melanocytic (Spitz nevus, Cellular blue nevus, melanocytic nevus with focal atypical epithelioid component/clonal nevus, deep penetrating nevus), neural (malignant peripheral nerve sheath tumor, neurotheceoma/cellular neurotheceoma), and histiocytic (Sicatrical).[7]

Spitz nevus is one of the tumors that is often misdiagnosed as melanoma. There have been numerous attempts

to clarify further the histology, immunohistochemical, and molecular criteria that separate these two entities. A Spitz nevus has a symmetrical dome-shaped appearance with varied epidermal acanthosis and hyperkeratosis as its typical histological features. Epithelioid and/or spindled melanocytes make up the lesions (Figure 2).[4,8,9]

Deep penetrating nevus (DPN) often causes diagnostic confusion with melanoma. DPN has a dome-shaped lesion and is most common in the second and third decades of life in both men and women. The DPN on histologic appears to be well demarcated and shows a wedge-shaped configuration with the broad aspect of the lesion aimed at the upper epidermis, and the dermal component shows vertically oriented and highly pigmented melanocytic nests (Figure 3).[7]

It was once thought that cellular blue nevus was a type of melanoma. The blue nevus is a variation of this disease, which is now understood to emerge when the skin does not fully acquire melanocytes during its embryonic migration from the neural crest. It appears hourglass-shaped or like a dumbbell under histologic magnification, with a lobular pattern, subcutaneous involvement, and a rounded margin push (Figure 4). The common blue naevus frequently exhibits the zonal configuration, which is characterized by highly pigmented dendritic or spindled melanocytes arranged in sclerotic stroma on the superficial and periphery aspects of the lesion and ovoid, fusiform, or spindled melanocytes restricted to the center area (Figure 5).[10,11]

Dermoscopy features of melanocytic lesions, such as black-brown spots or lumps, blue or white veil-like structures, and non-abortizing Ossels, can be seen in pigmented basal cell carcinoma (BCC). The only way to accurately identify BCC and choose the best course of treatment is through a biopsy. It has been demonstrated that punch and shave biopsies are similarly accurate.[11] At least one of the following positive characteristics, such as leaf-like or structureless patches on the lesion's periphery, numerous blue-gray globules, enormous blue-gray ovoid nests, focal ulceration, and spoke wheel areas, separates basal cell carcinoma from melanoma.[12]

Nodular hidradenoma is a rare, benign, adnexal neoplasm ascribed to apocrine origin, characterized by a well-defined but not encapsulated tumor consisting of a lobulated mass of cystic cells mainly located in the upper or middle dermis but occasionally extending into the subcutaneous tissue.

Figure 1. Overview of 5 different morphological clusters of melanoma identified by Clark Level grouping.[7]

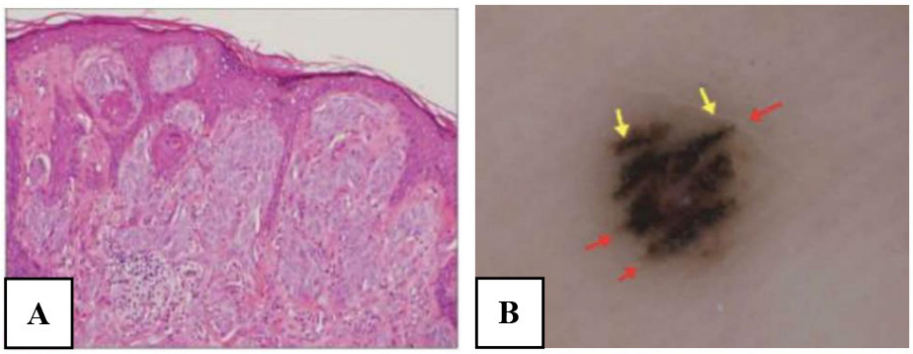

Figure 2. Histology of Spitz Nevus. The image shows the dominant melanocytes at the dermal-epidermal junction, the artifactual cleft surrounding the nest and maturity to depth (Hamatoxylin & eosin, × 100) (**A**).[9] Dermoscopy examination showing parallel groove pattern (yellow arrow) with peripheral projection (red arrow) (DL3, Contact polarized mode without fluid interface x 10) (**B**).[9]

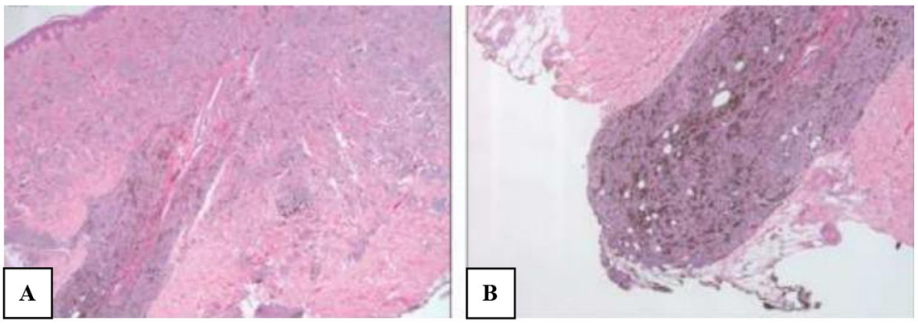

Figure 3. DPN photomicrograph. A nevus located in the skin penetrates around the hair follicle without damaging it (**A**). Distinctive deep penetration with the appearance of pushing borders (Hematoxylin & eosin, × 40) (**B**).[4]

Various cell types are seen in nodular hydradenoma in varying proportions and combinations, including primarily eosinophilic polyhedral cells, squamous cells, and oxyphilic or transitional mucous membranes. Tract-like structures are present in most tumors and generally contain cystic cavities of varying size.[13]

Seborrheic keratosis (SK) is a common epidermal tumor in middle-aged and elderly individuals. Although it is a benign tumor, there is some morphological overlap with other malignant skin lesions.[14] Seborrheic keratosis also displays a granular pattern similar to the peppery appearance found in melanoma.[16] SK dermoscopically mimics melanoma and basal cell carcinoma by the presence of a globular-like structure. The structural findings on dermoscopy of SK can include abnormalities such as multiple milia-like cysts, pseudofollicular (comedo-like) openings, hyperkeratosisifissure (sulci and gyri).[15]

Solar lentigines are age spots, which can be light brown to black pigmented lesions of varying size (several mm to several cm that usually develop on chronically sun-exposed skin. The histopathology of solar lentigo revealed club-shaped rete ridges with elongated shapes, many melanocytes, and increased melanin production without cellular atypia.[16] Solar lentigo is caused by mild localized basal melanocyte proliferation brought on by prolonged ultraviolet exposure, which is followed by an increased in melanization.[17]

Vascular lesions need dermoscopy to increase the clinical evaluation of pigmented skin lesions' diagnostic accuracy, and are also very helpful in making the diagnosis. In vascular lesions, red, blue, or red lacunae and bluish red or blackish red in homogeneous areas are the most frequent dermoscopic findings. In the meantime, the "rainbow pattern" polarized dermoscopic findings in seborrheic keratosis will arise.[12]

The benign fibrohistiocytic mesenchymal growth known as dermatofibroma, also referred to as fibrohistiocytoma, commonly develops on the skin. Clinically, dermatofibromas include "dimple marks" and lateral skin depressions. The distinction between dermatofibromas and other skin tumors, with the exception of melanoma, is crucial. These traits include peripheral pigment networks, center white scar-like patches, various vascular structures, white networks, and the absence of melanocytic features. A core white patch and peripheral pigment tissue were the most typical dermatoscopic patterns in the study group.[15]

One of the most prevalent cutaneous vascular proliferations, cherry angioma (also known as cherry hemangioma, senile angioma, or Campbell de Morgan spot), most frequently affects the chest and arms but is highly uncommon to occur on the face, palms and soles, hands, or feet. This disease typically presents as a round to oval, bright, red, dome-shaped papule and pinpoint macules.[18]

Tattoo pigment on lymph nodes frequently presents as a skin condition resembling melanoma. For the treatment of cutaneous melanoma, sentinel lymph node biopsy (SLNB) with lymphoscintigraphic mapping is presently used extensively. One of the most reliable indicators of the prognosis and cure rate for patients with primary melanoma is the condition of the regional lymph nodes. When compared to regional lymph node dissection, SLNB is a minimally

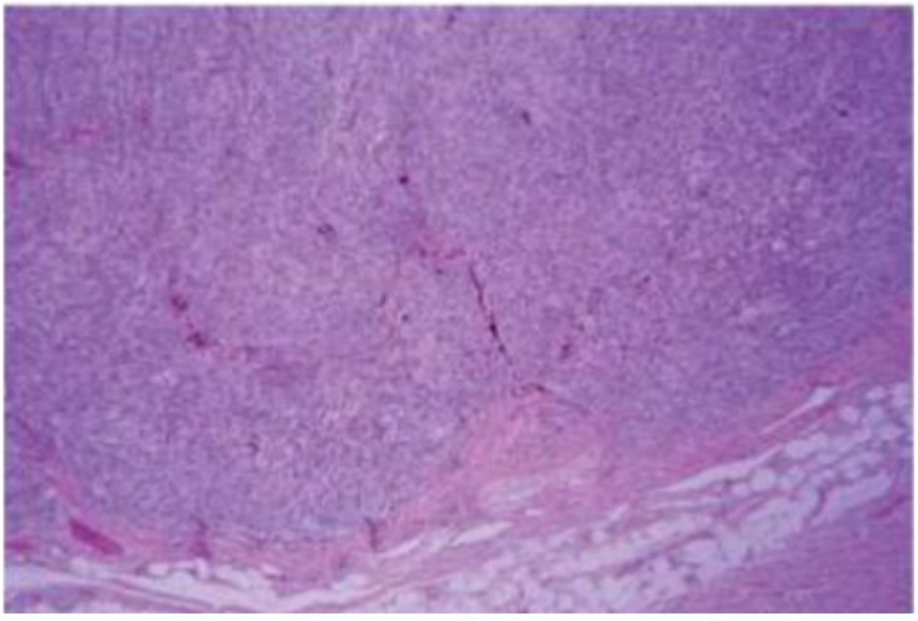

Figure 4. Cellular blue naevus. The archetype of subcutaneous involvement is shown by pushing a fine margin (Hematoxylin & Eosin, 40x).[4]

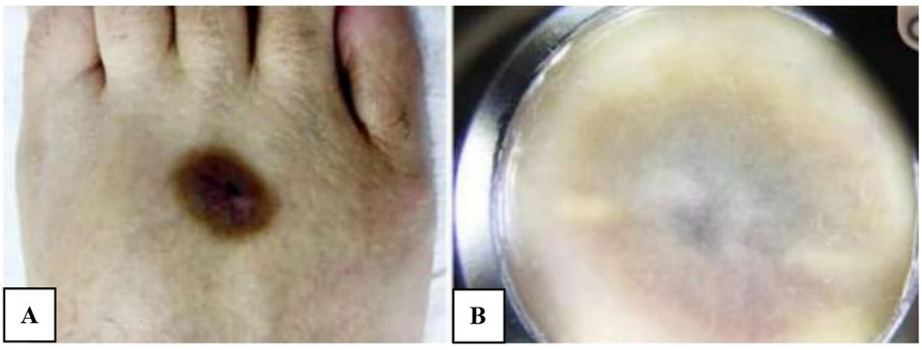

Figure 5. Brownish macula with a bluish center on the dorsum of the right leg (**A**). Dermoscopy shows steel-blue pigmentation in one area and purple in the other with hypopigmented areas (**B**).[11]

invasive operation. In situations with histopathologically positive lymph nodes, complete dissection of local lymph nodes is advised. The tattoo pigment in malignant melanoma patients with nearby tattoos looks clinically like metastases.[19]

CONCLUSION

The recent implementation of clearer clinical and histopathological criteria with the development of dermoscopy and computer technology has been able to led to the early detection of melanoma, which has contributed to the increased diagnosis of this disease and other skin diseases that may have similarities to melanoma. Dermoscopy is a straightforward, affordable, and non-invasive method that raises the diagnostic reliability of other skin conditions that could be related to melanoma. Misdiagnosis of melanoma (overcalling and undercalling) can occur mainly because melanoma can mimic a variety of other benign and malignant neoplasms. Additional examinations, such as biopsy and histopathology, are also needed for further diagnosis and management. In intradermal melanocytic tumors that are not visible, such as Spitz nevus, deep penetrating naevus, and cellular blue nevus, the histology results even have similarities with the histological structure of melanoma.

CONFLICT OF INTEREST

The authors declare that they have no potential conflict of interest.

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AUTHORS CONTRIBUTIONS

All authors contributed to the literature review, manuscript preparation, and publication.

GENERATIVE ARTIFICIAL INTELLIGENCE (AI) DISCLOSURE

There is no involvement of AI in this literature review.

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