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Case Report

The diagnostic challenge of amelanotic melanoma – case reports and short review of the literature

[1]Loredana Ungureanu, [1]Rodica Cosgarea, [2]Liliana Rogojan, [1]Simona C. Șenilă
[1] Department of Dermatology, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [2] Department of Histopathology, Cluj-Napoca Emergency County Hospital, Romania.

Abstract. Amelanotic melanoma is a type of cutaneous melanoma characterised by the absence of pigment. The clinical diagnosis of amelanotic melanoma represents a challenge for the practitioner because it can mimic benign or malignant skin tumours and even inflammatory skin disorders. Although the dermoscopic criteria for amelanotic melanoma are not so well established, dermoscopy proves to be a useful tool for the diagnosis. We present two cases that illustrate the challenge in the diagnosis of amelanotic melanoma.

Key Words: amelanotic melanoma, dermoscopy.

Corresponding Authors: L. Ungureanu, e-mail: danaszent@yahoo.com

Introduction

Cutaneous melanoma represents a very aggressive type of cancer that has one of the fastest growing incidences worldwide, with over 150000 new cases estimated in developing countries in 2010 (Jemal et al 2011). Although it represents only 10% of the total cutaneous malignant tumours, melanoma is responsible for over 90% of the deaths caused by these tumours (Jemal et al 2011). Amelanotic melanoma (AM) accounts for 2-8% of all melanomas (Jaimes et al 2012) and represent an atypical form of presentation that may not be easily recognized as malignant melanoma (McClain et al 2012). Studies show that survival after diagnosis of amelanotic melanoma is poorer than after pigmented melanoma, probably because the diagnosis is difficult and is made in more advanced stage (Thomas et al 2014). Clinically, the term of AM reffers to any melanoma lacking pigment, however there are also melanomas that produce low-levels of melanin (hypomelanotic melanoma - HM) and may appear to have no pigment (Jaimes et al 2012). Because of their lack of pigment, such lesions may be misdiagnosed as other benign or malignant skin tumors or even as inflamatory disorders, and the treatment can be delayed until advanced stages when the lesion becames nodular, vascular or ulcerated (Bono et al 2001). Dermatoscopy is an in vivo, non-invasive technique that allows a 10x magnification of the skin which enables the clinician to analyse the morphological structures within pigmented lesions that are not visible with the naked eye, structures with a well-defined histological correspondent. Various studies have demonstrated the improved capacity of dermatoscopy in differentiating benign lesions from malignant ones, bringing a valuable contribution to the early diagnosis of melanoma (Kittler 2008; Argenziano et al 2012; Argenziano et al 1997). Although dermoscopic evaluation has been shown to improve the accuracy of pigmented melanoma diagnosis compared with naked eye examination, less literature is found regarding melanomas lacking significant pigment. Still, dermoscopic evaluation has been shown to be superior to naked eye examination for the diagnosis of amelanotic or hypomelanotic melanoma (Pizzichetta et al 2004; de Giorgi et al 2006)

We report two unusual presentations of amelanotic melanoma resembling squamous cell carcinoma and basal cell carcinoma, two types of malignant skin tumours with completely different prognosis from AM. Both patients signed an informed consent for their data and pictures to be used for scientific purposes.

Case 1

A 75-year-old Caucasian women presented with a relatively rapidly growing solitary lesion on the right cheek. The lesion was first noted by the patient two years before the presentation as a red, slowly enlarging plaque. The lesion was diagnosed by the general practitioner as a dermatitis and treated with corticosteroids for three weeks. One year after these treatment and four month prior to the presentation, the lesion started to grow rapidly. On physical examination, there was a firm, dome-shaped, pink, 1.5 cm nodule, with a central ulceration covered by a yellow fine crust and fine scales (Fig. 1a). The clinical examination of the lymph nodes revealed firm, painless submandibular and laterocervical lymphadenopathy. Dermoscopic examination revealed white-yellow circles, white-yellow structureless areas, milky red areas, reticular white lines and a polymorphous vascular pattern (Fig. 1b). The clinical picture supported the diagnosis

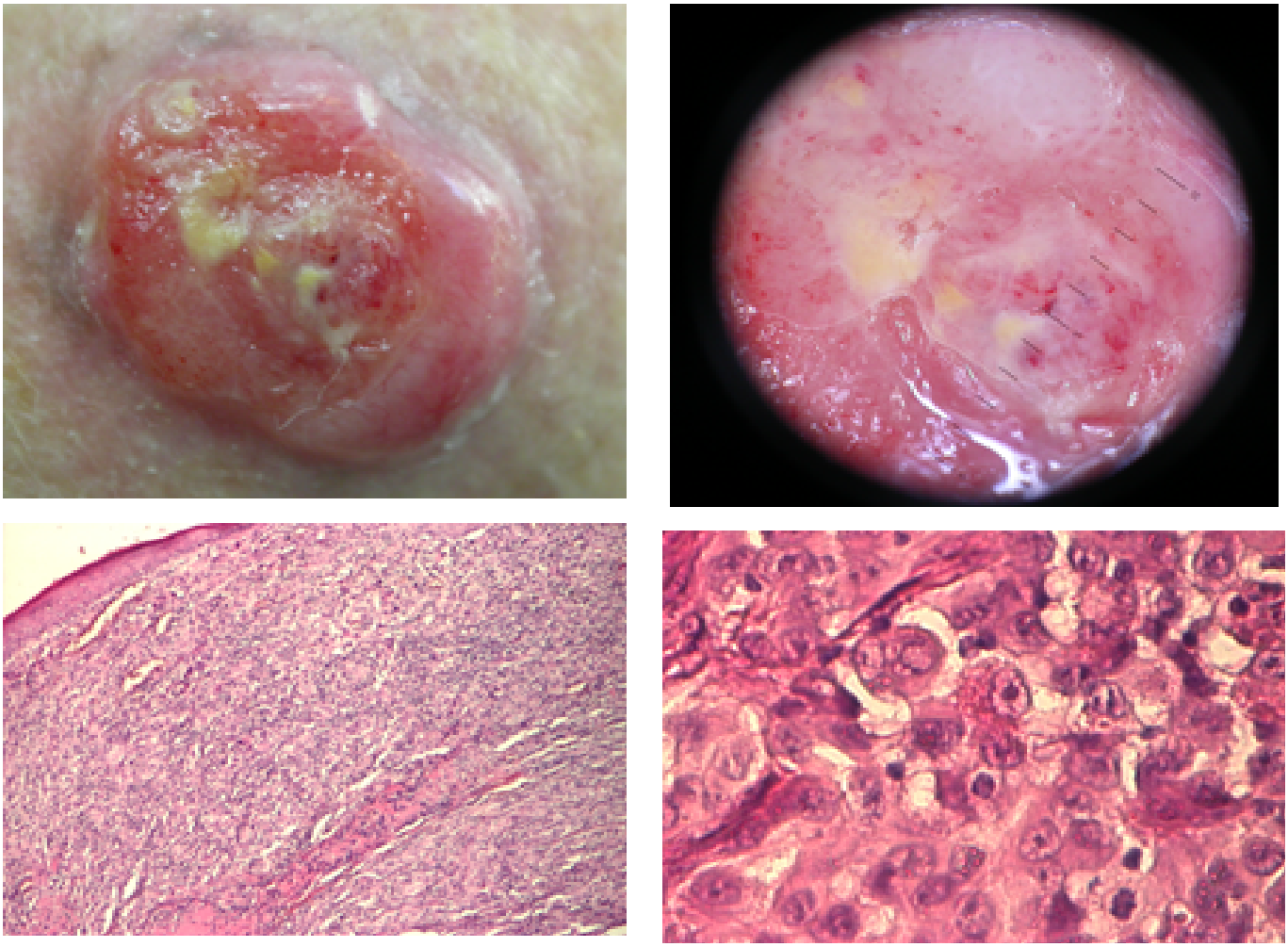

Figure 1. Amelanotic melanoma a. Clinical picture - firm, dome-shaped, pink, 1.5 cm nodule, with a central ulceration covered by a yellow fine crust and fine; b. Dermoscopy - white-yellow circles, white-yellow structureless areas, milky red areas, reticular white lines and a polymorphous vascular pattern; c,d. Histopathological picture (H-E stain 4X, 10X) - 5.8-mm thick (according to Breslow), Clark level IV, ulcerated non-pigmented melanoma without regression structures, with a high mitotic rate of 22 mitosis/mm^2.

of squamos cell carcinoma but the presence of milky red areas, reticular white lines and polymorphous vascular pattern on dermoscopy raised the suspicion of amelanotic melanoma. The lesion was excised and the histopathological evaluation revealed a 5.8-mm thick (according to Breslow), Clark level IV, ulcerated non-pigmented melanoma without regression structures, with a high mitotic rate of 22 mitosis/mm^2 (Fig. 1c).

Case 2

A 60-year-old Caucasian men presented with a slowly growing solitary lesion on the posterior thoracic region. The lesion was first noted by the patient one year before the presentation and it grew slowly during the mentioned period of time. On physical examination, there was a flat, pink, 1.5/2 cm plaque with slightly raised borders, with a 1/1cm dome-shaped, pearly, pink, multilobular nodule on the surface; small brown-blue areas and large, irregular telangiectatic vessels were visible on the surface (Fig. 2a). Dermoscopic examination revealed large blue-grey ovoid nests, multiple brown and blue-grey globules and linear telangiectatic vessels corresponding to the nodular area, while on the flat part of the lesion it showed milky red areas and a polymorphous vascular pattern (Fig 2b). The clinical picture supported the diagnosis of pigmented basal cell carcinoma, the only clues for an amelanotic melanoma being the presence of milky red areas, brown globules and polymorphous vascular pattern on dermoscopy. The lesion was excised and the histopathologic evaluation revealed a 2.5-mm thick (according to Breslow), Clark level III, non-ulcerated, slightly pigmented melanoma, without regression structures, with a low mitotic rate of 2 mitosis/mm^2 (Fig. 2c). The lesion was re-excised according to the guidelines and a subsequent sentinel lymph node biopsy was negative for regional nodal metastases.

Discussions

Amelanotic / hypomelanotic melanoma (AHM) is a subtype of cutaneous melanoma characterised by little or no pigment on clinical examination (Pizzichetta et al 2004). Hypomelanotic melanomas are more frequent than completely amelanotic forms, the last being very rare (Pizzichetta et al 2004; Moloney et al 2011). Although the incidence of AHM is appreciated to be 2-8% of all melanomas, the real incidence is difficult to estimate due to misdiagnosis (Stojkovic-Filipovic et al 2014). The

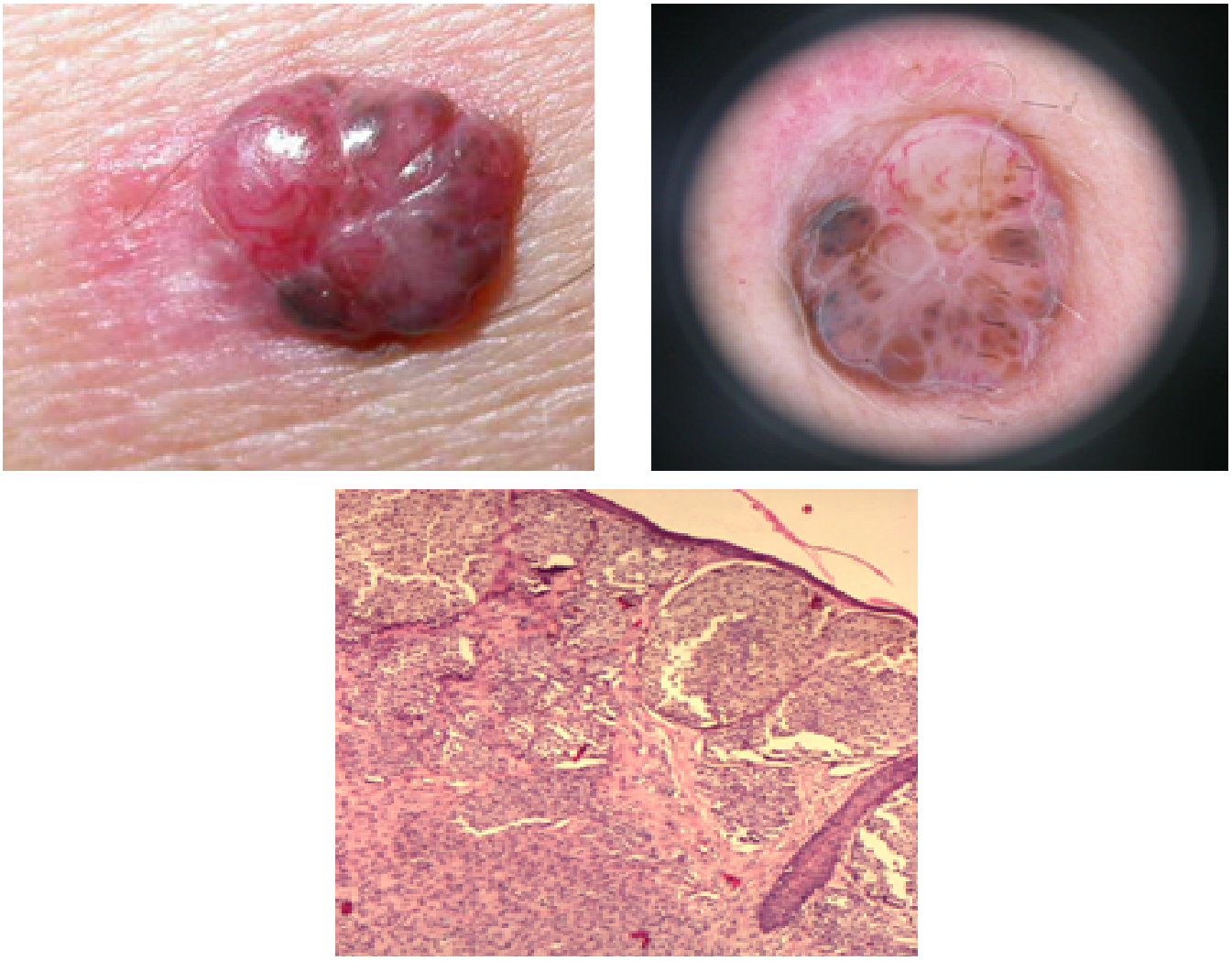

Figure 2. Hypomelanotic melanoma a. Clinical picture - flat, pink, 1.5/2 cm plaque with slightly raised borders, with a 1/1cm dome-shaped, pearly, pink, multilobular nodule on the surface; small brown-blue areas and large, irregular telangiectatic vessels on the nodule; b. Dermoscopy - large blue-grey ovoid nests, multiple brown and blue-grey globules and linear telangiectatic vessels corresponding to the nodular area; milky red areas and a polymorphous vascular pattern on the flat area; c. Histopathological picture (H-E stain 4X) - 2.5-mm thick (according to Breslow), Clark level III, non-ulcerated, slightly pigmented melanoma, without regression structures, with a low mitotic rate of 2 mitosis/mm.

explanation for the lack of pigment it is thought to be the poor differentiation of melanoma cells (Cheung et al 2012).

AHM appears usually in older individuals, on the trunk in men and on the limbs in women and can appear as nodular or superficial spreading melanoma (Cheung et al 2012). From a clinical point of view, AHM can appear in different forms, simulating other benign or malignant skin tumours or even inflammatory disorders like eczema or contact dermatitis (Pizzichetta et al 2004). Studies show that prognosis in amelanotic melanoma is poorer than in pigmented melanoma, probably because the diagnosis is difficult and is made in more advanced stage (Thomas et al 2014). Moreover, the prognosis of metastatic amelanotic melanoma is poorer than for metastatic pigmented melanoma (Koch et al 2000).

Dermoscopy, a non-invasive diagnostic method, improves the diagnostic accuracy of AHM (Pizzichetta et al 2004; de Giorgi et al 2006; Stojkovic-Filipovic et al 2014). Due to the lack of pigment, the dermoscopic criteria for AHM rely mainly on the vascular pattern analysis. It has been shown that vessel morphology differs in flat and raised AHM (Stojkovic-Filipovic et al 2014). While flat lesions are characterised mainly by dotted vessels, in raised lesions linear vessels become more prominent (Stojkovic-Filipovic et al 2014). Dotted vessels, presenting as red dots, are specific for flat lesions, but can be found in raised lesions too, especially in combination with other type of vessels resulting in the so called polymorphous vascular pattern (Jaimes et al 2012). Linear vessels can present in different forms: irregular linear vessels, serpentine vessels, glomerular vessels, looped vessels (Stojkovic-Filipovic et al 2014). Rosendahl et al (2014) suggested that flat AHM are characterized by a polymorphous pattern of vessels that include dotted vessels, while nodular AHM should be suspected when a non-pigmented nodule lacks a specific distribution of vascular structures and a specific benign diagnosis cannot be made with confidence. Milky red areas and milky red globules are another vascular dermoscopic structure present in AHM and is considered one of the most important feature for the diagnosis of truly amelanotic melanoma (Cavicchini et al 2007). Other dermatoscopic clues are scar-like depigmentation mainly in regressed melanomas, ulceration in thick melanomas, white lines and the presence of melanocytic structures (Stojkovic-Filipovic et al 2014).

Our cases illustrate the challenge in the diagnosis of AHM and the usually advanced stage in the moment of diagnosis. Both patients were misdiagnosed as having other skin tumours based on the clinical aspect, although dermoscopy offered clues for the correct diagnosis. Consequently, dermoscopy proves to be a useful tool to improve AHM detection and should be routinely used in the evaluation of non-pigmented skin tumours.

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Authors

•Loredana Ungureanu, Department of Dermatology "Iuliu Haţieganu" University of Medicine and Pharmacy, 3-6 Clinicilor Street, 400006, Cluj-Napoca, Cluj, Romania, EU, email: danaszent@yahoo.com

•Rodica Cosgarea, Department of Dermatology "Iuliu Haţieganu" University of Medicine and Pharmacy, 3-6 Clinicilor Street, 400006, Cluj-Napoca, Cluj, Romania, EU, email: cosgarear@yahoo.com

• Liliana Rogojan, Department of Histopathology "Iuliu Haţieganu" University of Medicine and Pharmacy, 3-6 Clinicilor Street, 400006, Cluj-Napoca, Cluj, Romania, EU, email: lilianarogojan@yahoo.com

•Simona C. Şenilă, Department of Dermatology "Iuliu Haţieganu" University of Medicine and Pharmacy, 3-6 Clinicilor Street, 400006, Cluj-Napoca, Cluj, Romania, EU, email: simonasenila@yahoo.com

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