Diffuse cutaneous melanosis: rare complication of metastatic melanoma*

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Abstract: Diffuse cutaneous melanosis is a rare complication of metastatic melanoma related to a worse prognosis. There are few cases reported in the literature. Its pathogenesis has not been completely elucidated, although studies have suggested certain mechanisms for its occurrence. It is clinically manifested as a blue-gray discoloration of the skin and mucous membranes in a cephalo caudal progression and usually associated with melanuria. Skin and mucosa histopathology reveals only the presence of melanophages in the dermis, mainly perivascular, and free interstitial melanin. We report the case of a 68-year-old male with metastatic melanoma, diffuse hyperpigmentation of the skin and melanuria.
Keywords: Melanosis; Melanoma; Paraneoplastic syndromes

INTRODUCTION

Diffuse cutaneous melanosis (DCM) is a rare complication of advanced metastatic melanoma, with few reported cases in the medical literature since it was first described by Wagner in 1864.[1–6]

It is characterized by progressive and diffuse blue-gray hyperpigmentation of the skin and mucous membranes, secondary to the abnormal deposit of melanin in the dermis.[1–5] Histopathology findings consist in the deposition of perivascular histiocytes filled with melanin and free pigment in the dermal connective tissue.[1–3,6] The gray color of the skin is due to the depth where the melanin is found. Rarely, melanoma cells are seen in the skin and there are few reports of increased melanin and melanocytes in the skin.[1–3] The dark urine color — melanuria — is a frequently associated finding with this condition.[1,2,4] Other manifestations besides cutaneous, mucosal and urine pigmentation, such as darkening of hair, of the peritoneal fluid, sputum and internal organs can also be found.[1,2]

We report the case of a patient with diffuse melanoderma and history of an advanced melanoma removed six years prior, with no previous diagnosis.

CASE REPORT

A 64-year-old man, farmer, Fitzpatrick phototype I, presented with diffuse gray-blue coloration of the skin, with a cephalocaudal progression over the past three months (Figure 1). There was also history of weight loss (7Kg) in seven months, dyspnea, cough and dark urine (Figure 2). On physical examination, the abdomen was enlarged and there was hepatomegaly. He had no comorbidities. As past history, a pigmented skin lesion had been excised from the left lumbar region six years prior, in another hospital, but he had no knowledge of the histopathology.

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The patient was admitted to the gastroenterology ward at the university hospital for investigations. Chest radiography and chest and abdomen computed tomography were performed, that showed multiple nodular images in the lungs and liver (Figure 3). Laboratory tests detected abnormalities in the liver enzymes (AST = 98 U/L, ALT = 196 U/L, AF = 1724 U/L, GGT = 462 U/L) and raised LDH (817 U/L). Colonoscopy demonstrated melanosis colis, with no other abnormalities. A skin biopsy was performed in the area of hyperpigmentation on the face, and histopathology showed perivascular melanocytes in the superficial and deep dermis, and liver biopsy showed melanoma metastases (Figures 4 and 5).

The patient was discharged and referred to an outpatient clinic of Oncology at a tertiary hospital, but died in less than 1 month.

DISCUSSION

DCM is a rare condition associated to metastatic melanoma. According to a systematic world literature review, 70 cases of this condition were published.[1] Data from the systematic review show that men are more commonly affected than women, with 60% of cases.[1] Most patients were Caucasian (95%) and mean age at diagnosis was of 50 years and 4 months.[1] The back was the most commonly affected site for the primary melanoma (50%), and the association with melanuria was described in 77% of cases.[1] Two reports described melanuria in about 15% of cases.[2,4]

The case reported has epidemiological (white male) and clinical (site of the primary lesion, predilection of the melanosis for photo-exposed, melanuria and survival) features similar to those found in all publications.

The physiopathogenesis of DCM has not been completely stablished.[1,2,4,6,7] The most accepted theory is that metastatic mela-

Figure 1: Diffuse gray-blue color of the skin, predominantly on photo-exposed areas

Figure 2: Melanuria

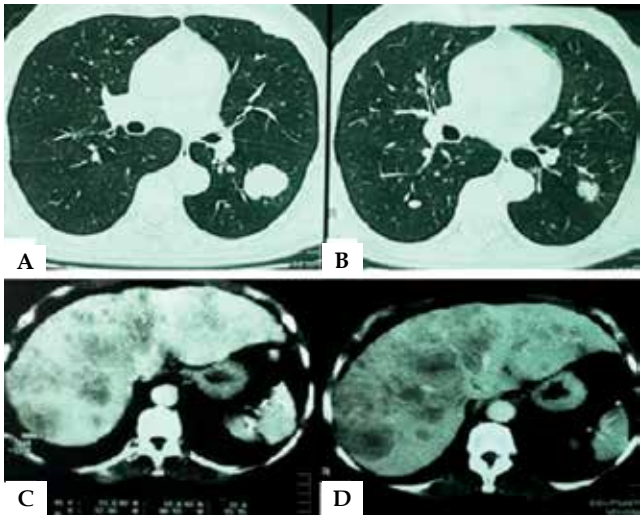

Figure 3: Chest and abdomen computed tomography. **A and B:** Multiple nodules in the lungs and a mass in the left inferior lobe. **C and D:** Multiple nodules in the liver

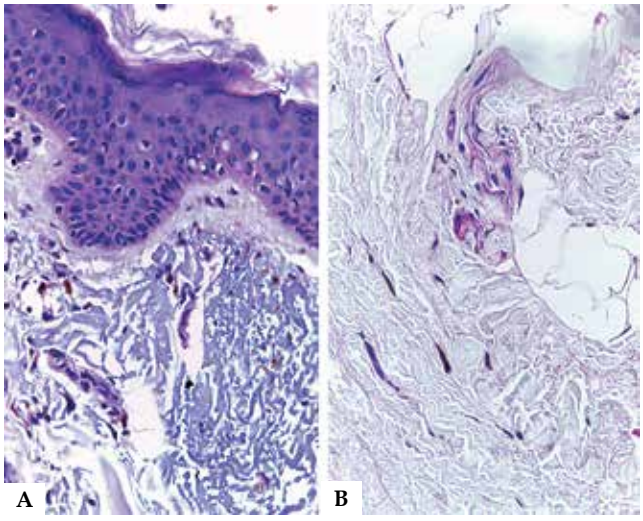

Figure 4: Skin histopathology. **A:** Perivascular and interstitial melanocytes in the dermis (Hematoxylin & eosin, X40). **B:** Interstitial melanophages in the deep dermis, adjacent to subcutaneous tissue (Hematoxylin & eosin, X40)

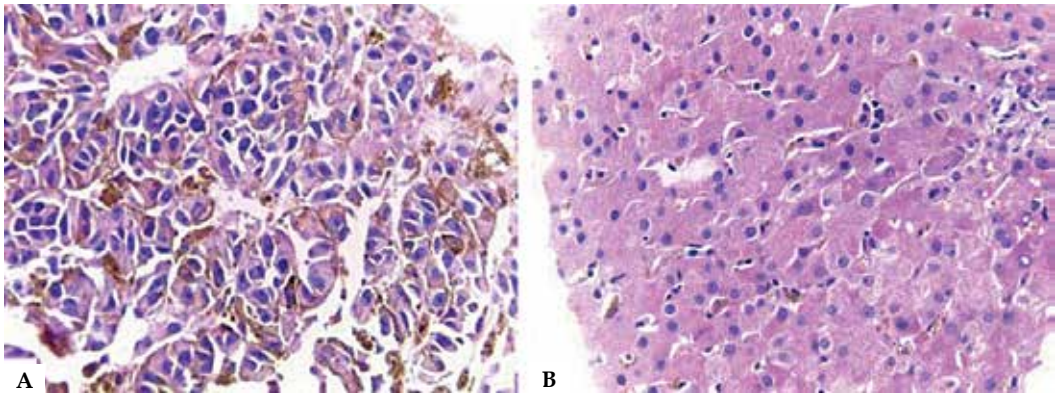

Figure 5: Liver histopathology. **A and B:** Cells of metastatic melanoma among hepatocytes and melanin in the liver sinusoids (Hematoxylin & eosin, X40)

noma undergoes cytolysis by central ischemia, immunological responses or oncologic treatments, releasing great amounts of melanin precursors, free melanin and melanosomes.[1,3] Melanin precursors are released into the blood stream, where they can be converted into melanin by serum oxidants or phagocytosed and processed by macrophages/histiocytes, and converted into melanin by the action of lysosomes.[1,3,4] When lodged in the dermis, the consequence is melanosis. Melanophages are eventually degraded on the site, forming residues of melanosomes and melanin that also contribute to melanosis.[1,3] Circulating melanin precursors are capable of invading the glomeruli and be excreted in urine, explaining melanuria, which becomes more marked after exposure to oxygen in the environment, due to the oxidation of melanin.[1,2] The melanin buildup in the renal tubules and glomeruli endothelial cells can lead to renal dysfunction and increase in the nitrogenous compounds.[2]

The perivascular distribution of histiocytes containing pigment in their interior supports the theory that these melanophages come from the circulation instead of originating locally.[1] The progressive and diffuse nature of DCM suggests a continuous influx of pigment in the blood stream. Its cephalocaudal progression and predilection for phot-exposed areas are well described in the literature.[1]

Patients with DCM have a poor prognosis, with an average survival of four to six months after the onset of pigmentation.[1,2,4]

This case report is justified by the rarity of this kind of clinical presentation of the melanoma and for the fact that the authors found only one case in the literature reported by Brazilians.[8] ❑

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