Journal of Oncological Science 2 (2016) 71–72

Contents lists available at ScienceDirect

Journal of Oncological Science

journal homepage: https://www.elsevier.com/locate/jons

A metastatic malign melanoma case with diffuse cutaneous melanosis

Zeynep Oruç*, Muhammet Ali Kaplan, Halis Yerlikaya, Zuhat Urakçı, Mehmet Küçüköner, Abdurrahman Işıkdoğan

Dicle University, Faculty of Medicine, Department of Medical Oncology, Diyarbakır, Turkey

ARTICLE INFO

Article history:
Received 1 April 2016
Accepted 8 August 2016
Available online 7 October 2016

Keywords:
Diffuse cutaneous melanosis
Malignant melanoma
Paraneoplastic syndromes

ABSTRACT

Diffuse Cutaneous Melanosis is a rare clinical condition characterized by rapidly acquired skin pigmentation that can occur in the course of advanced metastatic melanoma. A 59 year old patient with malign melanoma who developed diffuse cutaneous melanosis in the course of the disease is presented. He had multiple hepatic metastasis, lung metastasis, and multiple bone metastases. After the initiation of chemotherapy, he developed progressively darkening of the entire skin, darkened urine. Four months after the onset of melanosis, the patient died. The prognosis are poor in patients with diffuse cutaneous melanosis associated with malign melanoma.

1. Introduction

Diffuse Cutaneous Melanosis (DCM) is a rare clinical condition characterized by rapidly acquired brown gray skin pigmentation that occurs in the course of advanced metastatic melanoma. The sclera and hair may be affected. Dark urine associated with melanüri, darkening of the serum and peritoneal fluid can be also seen.[1,2] The discoloration of DMC has been reported to have a cephalo-caudal progression and to be most pronounced in sun exposed areas.[3] DCM is often associated with liver metastases.[4] But the pathogenesis is currently controversial. The differential diagnosis of diffuse cutaneous melanosis includes addison disease, porphyria cutanea tarda and hemochromatosis.[5]

We present a patient who developed diffüse cutaneous melanosis due to metastatic malignant melanoma.

2. Case presentation

A 59 year old patient presented with a dark pigmented lesion on the sole of the right foot. At the time of the first diagnosis, there were no clinical/radiological signs of metastatic disease. Primer lesion excision and right inguinal sentinel nodes was performed. After the positive sentinel lymph node biopsy, he underwent complete inguinal lymph node dissection postoperative pathology examination was reported as malignant melanoma, with Clark level III, tumor thickness 5 mm according to Breslow, positive lymph nodes (2/6). The tissue showed the presence of wild type BRAF. The patient rejected adjuvant treatment.

Nine months later, the patient was admitted with abdominal bloating, black skin nodules, back pain and weight loss. General exam revealed hepatomegaly, inguinal lymphadenopathy and cutaneous metastasis. In laboratory studies, LDH: 3800 (125–243), ALT; 60 (10–35) AST: 345 (10–40) ALP: 1211 (40–150) GGT: 578 (5–55) was detected. PET/CT revealed the presence of multiple hepatic metastasis, lung metastasis, inguinal lymphadenopathy and multiple bone metastases. The patient accepted the proposed treatment. The patient was treated with combination chemotherapy (cisplatin/temozolomide) and palliative radiotherapy of the spinal cord. He received three cycles of chemotherapy. After the initiation of chemotherapy, he developed progressively darkening of the entire skin, darkened urine. ACTH and cortisol levels were measured ACTH: 15.7 (0–46) cortisol: 10.2 (6–18) was detected.

The patient was referred to a dermatologist. Dermatologic exam showed cutaneous metastasis characterized by black papules and nodules on his skin (Fig. 1) and diffuse skin hyperpigmentation (Fig. 2). After three cycles of chemotherapy, imaging studies showed disease progression in liver metastases and bone metastases. And he subsequently developed liver failure and four months after the onset of melanosis, the patient died.

* Corresponding author.
E-mail address: zeynep44oruc@hotmail.com (Z. Oruç).
Peer review under responsibility of Turkish Society of Medical Oncology.

http://dx.doi.org/10.1016/j.jons.2016.08.003

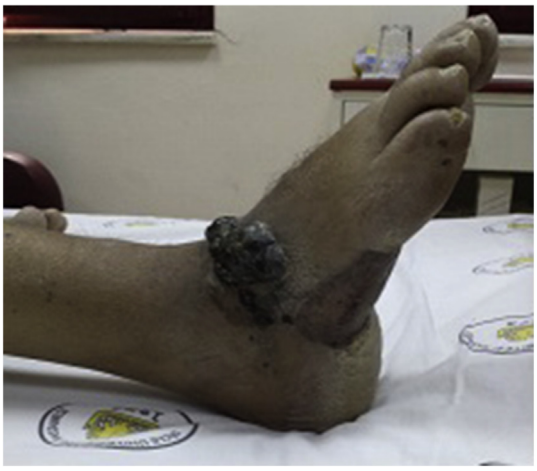

Fig. 1. Cutaneous metastasis

occurs as a result of chemotherapy, immunological response or central ischemia induced tumor lysis with the release of melanosomes into the blood circulation.[4] The release of melanosomes excretes in urine and occurs melanuri and dark urine.

In our patients as well, diffuse melanosis appeared after beginning cisplatin and temozolomide. Also, as in most case reports, our patient had common liver metastases.

The prognosis are poor in patients with diffuse cutaneous melanosis.[1] Our patient died four month after the onset of melanoma. The mean duration between diagnosis of melanoma and the onset of melanosis in these patients is less than a year. And the survival time from the onset of DMC is approximately 4 months. The patients with DCM have a poor survival results (4–5 months).[2]

DCM should be considered in the differential diagnosis list of skin discoloration after excluding other common differential diagnoses.

Conflict of interest

There is no conflict of interest.

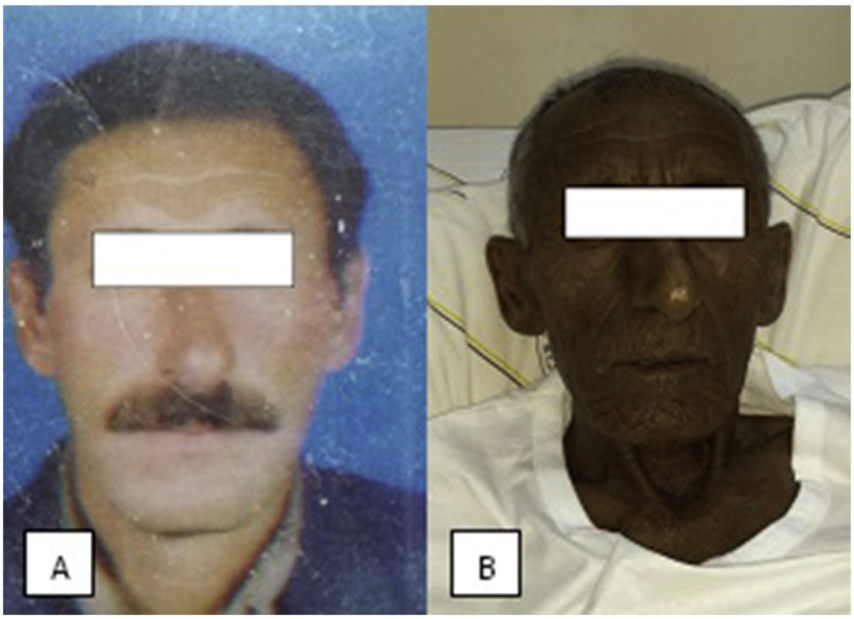

Fig. 2. Brown-gray hyperpigmentation (A: Before onset of diffuse cutaneous melanosis (DCM) B: After onset of DCM)

3. Discussion

Diffuse cutaneous melanosis (DCM) is rarely encountered condition in malign melanoma. It is often associated with liver metastases.[4] DCM also can be seen in Addison disease, porphyria cutanea tarda and hemochromatosis.[5]

The pathogenesis of diffuse cutaneous melanosis is unknown. Approximately 20% of cases with DCM in malignant melanoma have shown melanoma metastases within the pigmented skin.[6] There are a few mechanisms under discussion on this topic. Bohm et al suggested that cutaneous diffuse melanosis is linked to an excessive production of melanocytic growth factors (MSH (melanocyte stimulating hormone), Hepatocyte growth factor (HGF), Endothelin-1 (ET-1)). Excessive production of MSH (from tumor), HGF and ET-1 (from distinct site of metastasis) induce normal and malignant melanocytes resulting in enhanced proliferation, melanogenesis and melanin releasing.[7] Alternative hypotheses diffuse melanosis

References

1. Hofmann M, Kiecker F, Audring H, et al. Diffuse melanosis cutis in disseminated malignant melanoma. *Dermatology*. 2004;209:350–352.
2. Sebaratnam D, Venugopal S, Frew J, et al. Diffuse melanosis cutis: A systematic review of the literature. *J Am Acad Dermatol*. 2012;68(3):482–488.
3. Goldsmith LA, Katz SI, Gilchrest BA, et al. *Fitzpatrick's Dermatology in General Medicine*. 7 th ed 2008:1094–1198.
4. Klaus MV, Shah F. Generalized melanosis caused by melanoma of the rectum. *J Am Acad Dermatol*. 1996;35:295–297.
5. Filho T, Neto P, Reis J et al. Diffuse cutaneous melanosis in malignant melanoma. *Dermatol Online J*. 12(3):9.
6. Fields K, Milikowski C, Jewell T, Fields J. Localized diffuse melanosis associated with melanoma successfully treated with imiquimod cream 5%: A case report and review of the literature. *Cutis*. 2014 Mar;93(3):145–150.
7. Böhm M, Schiller M, Nashan D, et al. Diffuse melanosis arising from metastatic melanoma: Pathogenetic function of elevated melanocyte peptide growth factors. *J Am Acad Dermatol*. 2001;5:747–754.