ANSWER TO PHOTO QUIZ (PAGE 320)

A MEDICAL CAUSE FOR FIFTY SHADES OF GREY

DIAGNOSIS

The wide local excision performed 20 years ago turned out to be because of melanoma. CT imaging showed right axillary lymphadenopathy, diffuse metastases in liver, adrenal glands, lungs and bones. Histological exam of an axillary lymph node biopsy revealed the diagnosis of metastatic melanoma. Mutation analysis revealed a BRAF V600E mutation, and the patient started on the BRAF inhibitor vemurafenib (960 mg twice daily) in September 2015.

The blue-grey discoloration of the skin, most pronounced in sun-exposed area, is called diffuse melanosis cutis. It is a rare symptom of metastatic melanoma, often accompanied with melanuria (77%).[1] Patients with melanosis cutis have a poor prognosis with a life expectancy that seldom exceeds 3-4 months.[1] The pathophysiological mechanisms are not certain; the hypothesis is that melanin precursors and melanin are released from melanoma metastases resulting in deposition of melanin in tissues leading to skin discoloration and melanuria.[1]

To our knowledge this is the third case reporting on a patient with diffuse melanosis cutis in the setting of BRAF V600E metastatic melanoma[2,3] and the second patient to be treated with a BRAF inhibitor.[3]

The described patient is still alive ten months after presentation with diffuse melanosis cutis. The best response to vemurafenib, assessed on CT scan, was stable disease with some lesions showing signs of regression and some lesions showing minimal growth. To our knowledge, there is no mention in the literature as to whether a change in discoloration of the skin and urine can be used as an outcome measure for response to treatment. The patient's skin and urine colour were documented with follow-up photographs, but the colour did not change during treatment. In the case described by Minocha et al.[3] the patient developed progressive disease after five months of dabrafenib after which he was treated with two cycles of ipilimumab 3 mg/kg with an 15-month interval. The treatment effects in these two cases are comparable with the median progression-free survival of six months seen with BRAF inhibitor treatment in metastatic melanoma in general.[4] The course of our patient clearly demonstrates that with the use of the currently available, novel-targeted therapies, melanosis cutis may no longer be the dismal prognostic indicator it was in the past. Therapy for this entity should be similar to the therapy given for metastatic melanoma in general.

REFERENCES

1. Sebaratnam DF, Venugopal SS, Frew JW, et al. Diffuse melanosis cutis: a systematic review of the literature. J Am Acad Dermatol. 2013;68:482-8.
2. Sebaratnam DF, Martin LK, Venugopal SS, et al. Diffuse melanosis cutis in the setting of BRAF(V600E) metastatic melanoma. Int J Dermatol. 2014;53:1409-11.
3. Minocha R, Kefford R, Uribe P, Sebaratnam DF, Fernandez-Penas P. Diffuse melanosis cutis in the setting of BRAF(V600E) mutant melanoma and treatment with targeted therapies. Australas J Dermatol. 2015;56:128-30.
4. Ugurel S, Rohmel J, Ascierto PA, et al. Survival of patients with advanced metastatic melanoma: The impact of novel therapies. Eur J Cancer. 2016;53:125-34.