Vitiligo in a Patient with Metastatic Melanoma from Nigeria

***Nashabaru IM, *Yusuf SM, Sani RN ** Ahmad AM,**

*Division of Dermatology, Department of Medicine, Aminu Kano Teaching Hospital, Kano Nigeria.

** Department of Pathology, Aminu Kano Teaching Hospital, Kano Nigeria.

Corresponding Author: Shehu M Yusuf, E-Mail: shehumy@yahoo.com

ABSTRACT

The association of vitiligo and melanoma has been reported by many investigators. Patients with co-existing vitiligo and melanoma express identical antigens on both melanocytes and melanoma cells. Immune response to these antigens is responsible for delayed progression, improvement and subsequent regression of melanoma. Thus,this association portends long term survival even in patients with metastatic disease.We here present a 55year old man with melanoma for five years who apparently started noticing regression in the lesion with the appearance of vitiligo.

INTRODUCTION

Melanoma is a malignant neoplasm of melanocytes that has been reported in virtually all races, it is most common in Caucasians. It is potentially fatal, especially when metastasis has occurred.[1]Areas of depigmentation (vitiligo) are rarely associated with melanoma.[2] The mechanisms for this association is not fully understood,however, immune responses directed against shared melanoma/melanocyte antigens and those directed against tumor-specific antigens has been proposed.[3] The appearance of hypopigmentation is often viewed as a good prognostic sign in melanoma, and has even been associated with some regression of the primary lesion.[4]

CASE REPORT

55year old farmer presented to our facility with a four year history of progressive discoloration of skin the right heel. This was preceded by a year history of papule that appeared on the inner aspect of the affected heel. The papule grew slowly into a large dark painless nodule over a period of months. A tiny white spot was noticed at the summit of the nodule few months later. About the same time some nodules were felt at the groin on the same side. As the white patch enlarges over the proceeding months, the nodule seemed to regress though very slowly.

Physical examination revealed a depigmented patch involving the right heel. Within the patch were two partially pigmented contagious nodules on the medial side of the heel. The nodules were non tender, firm and not freely mobile. The right inguinal lymph nodes were enlarged. Review of other systems was not contributory.

Punch biopsy taken from one of the nodules (fig 2) revealed sheets of melanocytes having round to ovoid pleomorphic nuclei with prominent nucleoli and moderate to abundant eosinophilic cytoplasm. The lesional cells show cytoplasmic and nuclear staining with Melan A and S100 immunohistochemical stains (fig 3). Based on the physical, histological and immunohistochemical stain findings the diagnosis of co-existing vitiligo and Melanoma was made. Considering that the lesion had started to regress on its own, the patient was put under observation.

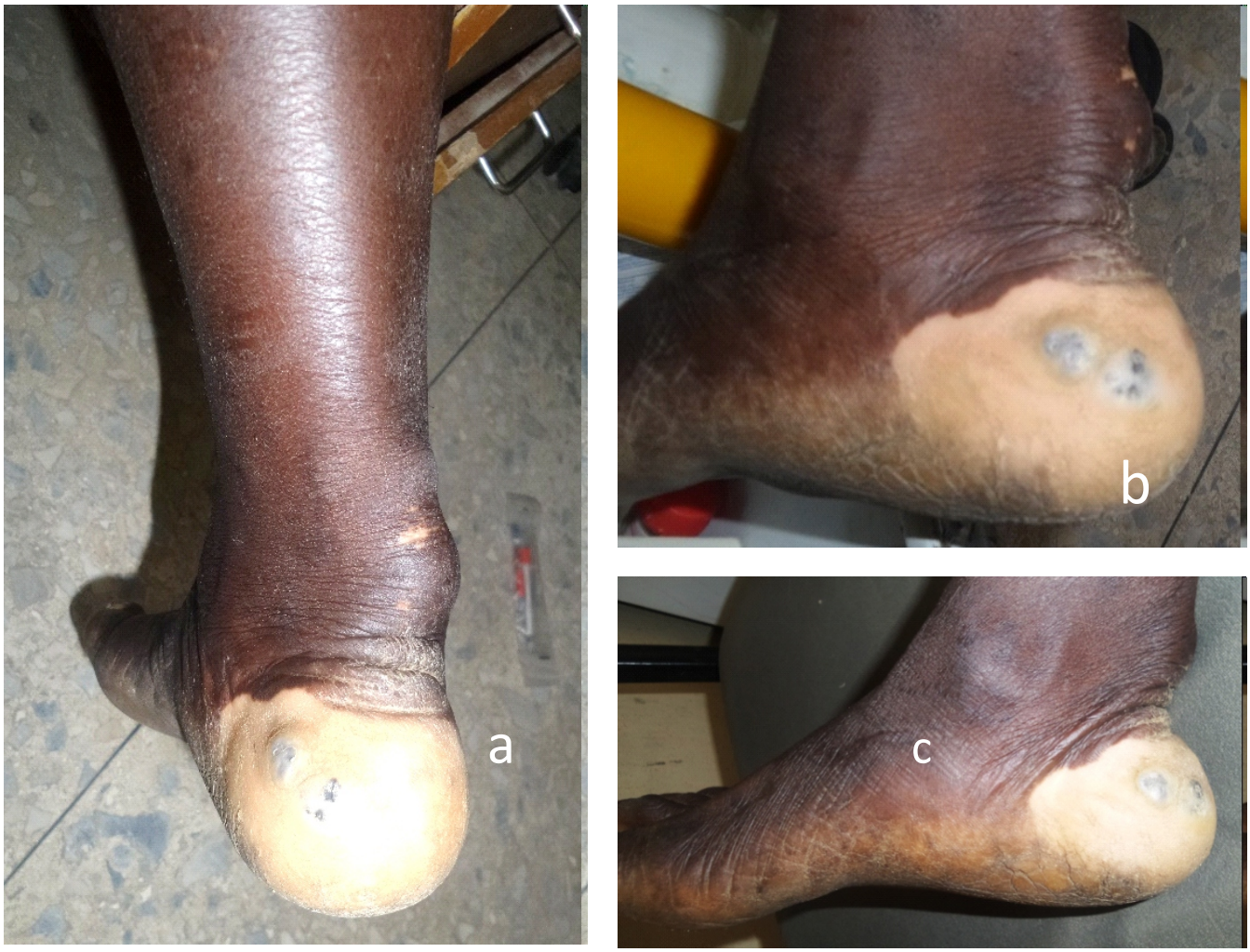

Figure 1 (a, b & c): Showing two discrete partially pigmented nodules surrounded by a large depigmented patch involving the right heel.

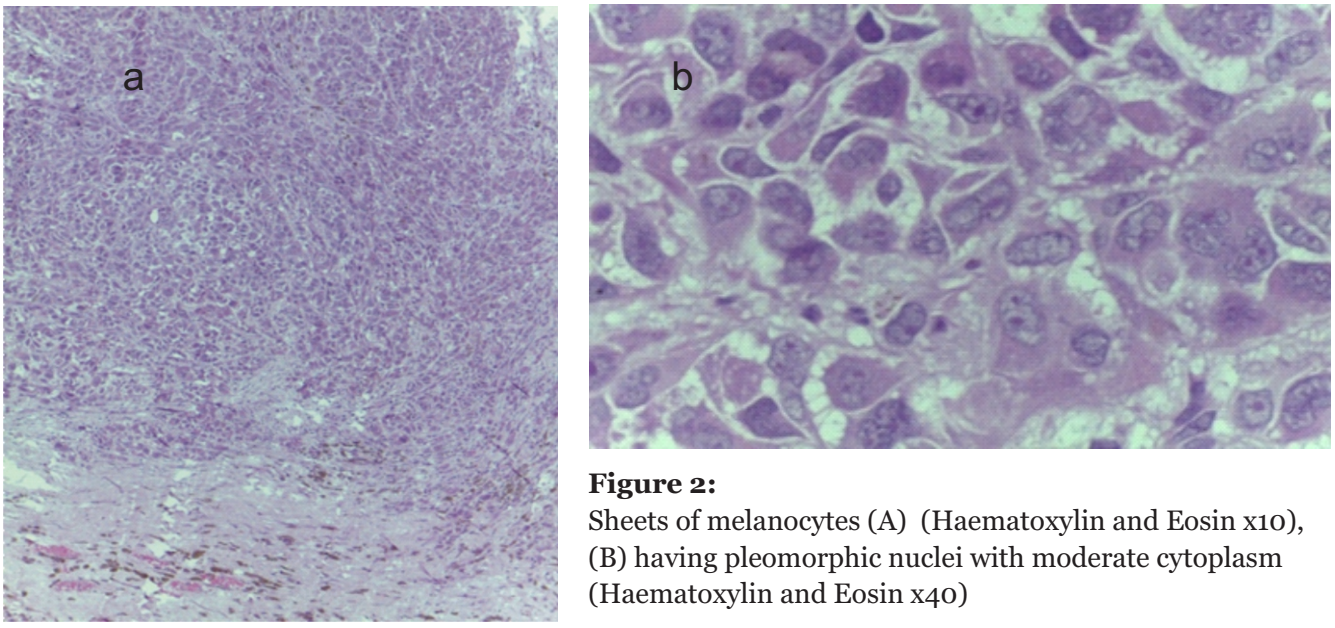

Figure 2:
Sheets of melanocytes (A) (Haematoxylin and Eosin x10), (B) having pleomorphic nuclei with moderate cytoplasm (Haematoxylin and Eosin x40)

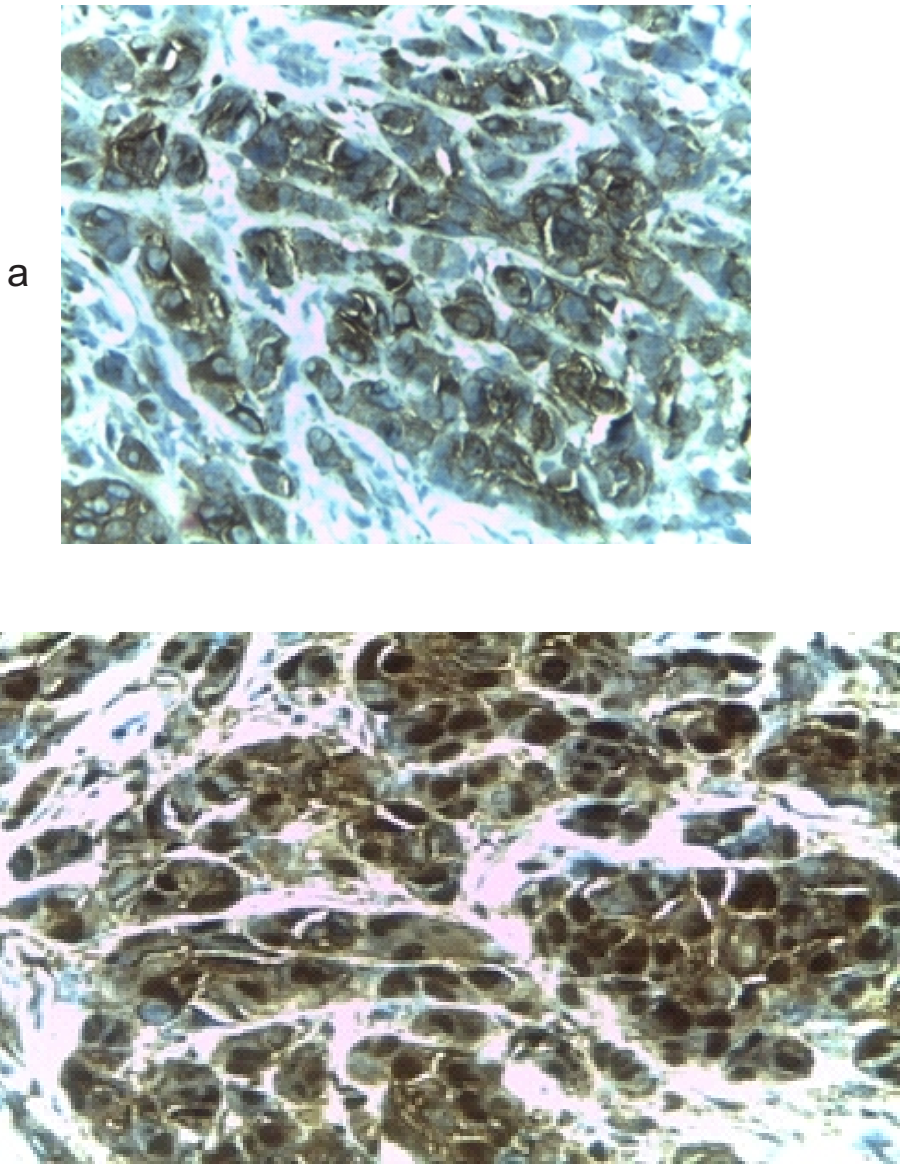

Figure 3: Imunohistochemical staining with **(A)** Melan A showing cytoplasmic and **(B)** nuclear staining patterns with S100 antibodies

DISCUSSION

Since the first report of the coexistence of vitiligo and melanoma forty years ago,[3] there has been several case reports, small patient series and a few cohort studies. Consequently, the reported incidence of melanoma associated depigmentation (MAD) or vitiligo ranges widely between 1.4- 20 %.[5,6]

Although the risk for patient with melanoma developing vitiligo was as high as 7 to 10 fold higher than general population, the risk is 0.3 fold for melanoma evolving in a cohort of patients with vitiligo.[7]

In some patients with melanoma, vitiligo was reported to have occurred spontaneously or sequel to melanoma therapy. As was the situation in the index case, vitiligo patches can appear around the site of the primary lesion.[8] It was also reported at sites distant from the primary tumour and around metastatic lesions.[8,9]

Melanoma is considered a highly immunogenic tumour, known to stimulate both humoral and cell mediated immune responses to both membrane and cytoplasmic antigens.[9] Melanoma cells express antigens, including Melanosomal membrane proteins (MMP), on both melanoma cells as well as normal melanocytes, but not other cell types. These antigens are thought to play a central role in the development of tumour immunity and autoimmune

mechanisms that leads to melanoma associated depigmentation or vitiligo.[2] Furthermore, Hartmann et al demonstrated T cells with identical receptors in both the tumour as well as the peri-tumour depigmented lesion.[10] The appearance of vitiligo has been documented to coincide with primary tumour regression and is thought to result from the immune response to these identical antigen expressed by both melanocyte and melanoma cell.[11] These T cells induce secretion of IL 2 and IFN gamma, both of which are used in immunotherapy for melanoma.[12] This explains the increased incidence of vitiligo among patients receiving immunotherapies that drive T-cell response to melanoma.[13]

Despite recent advances in the treatment of melanoma, the prognosis of patients still remain very poor. Patients with metastatic disease have survival rates of 6 % and median survival of 7.5%.[13]

REFERENCES

1. Naveh HP, Rao UNM, Butterfield LH. Melanoma-associated leukoderma - immunology in black and white? Pigment Cell Melanoma Res. 2013;26(6):796–04.
2. González R, Torres-López E. Immunological Basis of Melanoma-Associated Vitiligo-Like Depigmentation. Actas Dermo-Sifiliográficas. 2014;105(2):122–7.
3. Lindelöf B,Hedblad MA, Sigurgeirsson B. On the association between vitiligo and malignant melanoma, ActaDermVenereol. 1998; 78:483-4
4. Nordlund JJ, Kirkwood JM, Forget BM. Vitiligo in patients with metastatic melanoma: a good prognostic sign? J Am AcadDermatol 1983; 9: 689 -96
5. Milton GW, McCarthy WH, Carlton A. Malignant melanoma and vitiligo.Aust J Dermatol 1971; 12: 131 - 42.
6. Klaus SN, Lerner AB, Bystryn JC. Malignant melanoma and vitiligo. J Invest Dermatol 1971;73: 491-4
7. Schallreuter KU, Levenig C, Berger J. Vitiligo and cutaneous melanoma: a case study. Dermatologica.1991; 183: 239 -45.
8. Rubegni P, Nami N, Risulo M, Tataranno D, Fimiani M. Melanoma with halo. Clin Exp. Dermatol. 2009;34(6):749–50
9. Arpaia N, Cassano N, Vena GA. Regressing cutaneous malignant melanoma and vitiligo-like depigmentation.Int J Dermatol. 2006 ;45(8):952–6.
10. Hartmann A, Bedenk C, Keikavoussi P, Becker JC, Hamm H, Bröcker E-B. Vitiligo and melanoma-associated hypopigmentation (MAH):shared and discriminative features. J der Dtsch Dermatologischen Gesellschaft 2008;6(12):1053–9.
11. Ram M, Shoenfeld Y. Harnessing Autoimmunity (Vitiligo) to Treat Melanoma: A Myth or Reality? Ann N Y Acad Sci. 2007;1110(1):410–25.
12. Cui J, Bystryn JC. Melanoma and vitiligo are associated with antibody responses to similar antigens on pigment cells. Arch Dermatol 1995; 131: 314 -8.
13. . Barth A, Wanek LA, Morton DL. Prognostic factors in 1,521 melanoma patients with distant metastases. J Am Coll Surg. 1995;181:193-201.