

Acral Lentigines, Is it a Paraneoplastic Syndrome?

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Abstract: We report a 34 years old gentleman who was referred to us with multiple brown spots on the palms, soles and scalp. He had those three months prior to being diagnosed with non-Hodgkin's lymphoma. His past history includes both Evan's syndrome and membranoproliferative glomerulonephritis treated by mycophenolate mofetil (MMF). On examination he had multiple brownish macules over the palms, soles and scalp. Biopsy from one of the lesions on the palms showed pigmentation of the basal cell layer with increased melanocytes. His lentigines are most likely induced by immunosuppression due to Non-Hodgkin's lymphoma.

Key words: paraneoplastic syndromes, acral lentigines, malignancy.

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Introduction

Paraneoplastic dermatosis may represent the first finding that a malignancy is lurking, if not presenting simultaneously. These interesting signs may increase the likelihood that the patients will survive, but only if recognized early on, by the curious dermatologist.⁽¹⁾

Acral lentiginos have been linked recently to malignancy.^(2,3) We present this case as a possible example of a paraneoplastic syndrome which for the first time is shown to predate malignancy.

Case Scenario

Our patient is a 44 years old gentleman of Middle Eastern origin whose Fitzpatrick's skin type is IV and who has never complained of excessive freckling or skin problems. He has Evans' syndrome which was diagnosed since childhood with recurrent episodes of hemolytic anemia. He was also diagnosed with membranoproliferative glomerulonephritis for which he was treated with mycophenolate mofetil (MMF).

Three months before he was diagnosed to have non-Hodgkin's lymphoma, he noticed brown spots spreading rapidly from his palms to his soles and finally to the scalp as seen in Fig. 1 and Fig. 2. He later sustained right femur fracture and was admitted. Since his lesions were suspicious, He was seen by an oncologist and after his extensive work up he was diagnosed with Non-Hodgkin's lymphoma after it was confirmed by bone marrow biopsy. He was started on R-CHOP chemotherapy and had already received three cycles when he was referred to us. The patient noticed that his lentiginos got darker and more numerous with chemotherapy.

On examination he had multiple brownish round macules averaging 3 mm in size on his palms, soles and scalp. They were asymptomatic and other body parts were not affected including his oral mucosa and genitalia. There was no similar illness in the family. Biopsy taken from one of the lesions over the palm showed pigmentation of the basal cell layer with increased melanocytes.

Discussion

There is a plethora of evidence linking immunosuppression and malignancy to eruptive nevi,⁽⁴⁾ but with acral lentiginos the evidence is scanty. In addition to the five cases reported as paraneoplastic,^(2,3) acral lentiginos have been reported in two patients with HIV.⁽⁵⁾ It's not clear why this happens. Many factors are incriminated. UV exposure⁽⁶⁾ and dysregulation

of certain growth factors during re-epithelialization may explain some types of eruptive nevi. But more pertinent to our case, immunosuppression seems to be the main cause.⁽⁸⁾ This could be from the chemotherapy or the disease itself, since it has been shown that some malignancies induce immunosuppression like in breast cancer.⁽⁹⁾ Finally, UV exposure has been shown to induce immunosuppression too.⁽¹⁰⁾

Only recently, five cases of Acral lentiginos were linked to malignancy. The first patients had acral lentiginos occurring simultaneously with large cell lymphoma of the small bowel before starting chemotherapy. The second patient had breast cancer and presented with acral lentiginos only after radiotherapy and surgery was performed. In The last three patients the onset of the lentiginos was either not mentioned or unknown. They had adenocarcinoma of the stomach, breast cancer and melanoma.^(2,3)

In our case, the patient had lentiginos before he was diagnosed to have non-Hodgkin's lymphoma. This maybe a true paraneoplastic syndrome presenting before malignancy, or he might have been ill from the beginning, having a silent malignancy. It's noteworthy that some authors consider true paraneoplastic syndromes only when they present after malignancy and parallel its course.⁽¹¹⁾ However, pruritus a well known cutaneous manifestation of lymphomas and leukemias are known to precede malignancy in some occasions.⁽¹²⁾

One can argue that the evidence is both thin and circumstantial. Indeed, only six cases including ours are thought to be paraneoplastic syndromes. However, the incidence of paraneoplastic syndromes is uncommon to rare.⁽¹⁾ The unique localization of lentiginos to acral sites (and scalp) points to a specific insult. Moreover the temporal relationship between lentiginos and the malignancies occurring before, during and after is crucial evidence. Our patient has skin type IV, he has never experienced widespread lentiginos before and presented with this only in his forties. Such presentation must have been the result of a new insult.

Evans syndrome is an uncommon condition defined by the combination of immune thrombocytopenia and autoimmune hemolytic anemia with a positive direct antiglobulin test in the absence of known underlying etiology.⁽¹³⁾ Non-Hodgkin's lymphoma has been associated with Evans

syndrome.⁽¹⁴⁾ Acral lentiginos are unlikely to be due to Evans syndrome in our patient since he had the syndrome since childhood. Likewise, since the patient was already on mycophenolate mofetil for two years, it's unlikely that the lentiginos are caused by it.

Nevertheless, even if acral lentiginos develop or worsen after chemotherapy, this supports the notion that immunosuppression is the common denominator between malignancy, chemotherapy/MMF and HIV. To complete the puzzle, it is helpful to know the prevalence of acral lentiginos in normal population. Besides malignancy and HIV, Acral lentiginos have been associated with PUVA⁽¹⁵⁾ and cerebral vascular accidents.⁽¹⁶⁾

In summary, the sudden eruption of lentiginos over palms, soles and scalp may signal a hidden malignancy and should alert the physician to look for silent neoplasms. However, more studies are needed to confirm this association.



Fig. (1). Lentiginos on the right palm.



Fig. (2). Lentiginos on the scalp.

References

1. Poole S, Fenske NA. Cutaneous markers of internal malignancy. II. Paraneoplastic dermatoses and environmental carcinogens. *J Am Acad Dermatol* 1993; 28:147-164.
2. Wolf R, Orion E, Davidovici B. Acral lentiginos: a new paraneoplastic syndrome. *Int J Dermatol*. 2008 Feb;47(2):168-70.
3. Wolf R, Lipozencić J, Segal Z, Davidovici B. Eruptive acral lentiginos - a new paraneoplastic sign? *Acta Dermatovenerol Croat*. 2008;16(3):130-2.
4. Martín Hernández JM, Donat Colomer J, Monteagudo Castro C, et al. [Acral eruptive nevi after chemotherapy in children with acute lymphoblastic leukemia] *An Pediatr (Barc)*. 2006 Sep;65(3):260-2.
5. Gallais V, Lacour JP, Perrin C, et al. Acral hyperpigmented macules and longitudinal melanonychia in AIDS patients. *Br J Dermatol*. 1992;126: 387-391.
6. Elder DE. Human melanocytic neoplasms and their etiologic relationship with sunlight. *J Invest Dermatol* 1989;92(Suppl):297-303S.
7. Lanschuetzer CM, Emberger M, Hametner R, et al. Pathogenic mechanisms in epidermolysis bullosa naevi. *Acta Derm Venereol* 2003;83: 332-7.
8. Happle R, Koopman RJ. [Acral nevi following chemotherapy] *Hautarzt*. 1990 Jun;41(6):331-2.
9. Kharkevich DD, Polevaia EB, Kadagidze ZG. [Tumor-induced immunosuppression in breast cancer patients] *Eksp Onkol*. 1990;12(5):53-6.
10. de Gruijl FR. UV-induced immunosuppression in the balance. *Photochem Photobiol*. 2008 Jan-Feb;84(1):2-9. Review
11. McLean DI. Toward a definition of cutaneous paraneoplastic syndrome. *Clin Dermatol*. 1993 Jan-Mar;11(1):11-3.
12. Omidvari SH, Khojasteh HN, Mohammadianpanah M, et al. Long-term pruritus as the initial and sole clinical manifestation of occult Hodgkin's disease. *Indian J Med Sci*. 2004 Jun;58(6):250-2.
13. Norton A, Roberts I. Management of Evans syndrome. *Br J Haematol*. 2006 Jan;132(2):125-37. Review.
14. Hauswirth AW, Skrabs C, Schüttinger C, Gaiger A, Lechner K, Jäger U. Autoimmune hemolytic anemias, Evans' syndromes, and pure red cell aplasia in non-Hodgkin lymphomas. *Leuk Lymphoma*. 2007 Jun;48(6):1139-49. Review.

15. Cruz A, Sánchez JL. Acral PUVA--induced pigmented macules. *Bol Asoc Med P R*. 1990 Oct;82(10):460-2.
16. Narisawa Y, Kohda H. Pigmented macules on the palms and/or soles of Japanese subjects: influences of clinical severity and duration of illness. *J Dermatol*. 1991 Jul;18(7):408-13.