Widespread Vitiligo After Erythroderma Caused by Nevirapine in a Patient with AIDS

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Sir,

The therapeutic options for human immunodeficiency virus (HIV) disease include several drugs, and it is now recognized that treatment with a combination of at least three drugs is the most effective. Nevirapine was the first non-nucleoside reverse transcriptase inhibitor (RTI) with a rapid and potent anti-HIV activity. It selectively inhibits the reverse transcriptase of HIV1, but not of HIV2. It has widespread tissue penetration, including the central nervous system. In addition, it has no cross-resistance or cross-reactivity with nucleoside RTIs. Nevirapine can be administered together with nucleoside RTIs and/or protease inhibitors. The most common adverse reactions to nevirapine therapy include cutaneous reactions and elevated liver enzyme concentrations. In rare cases the cutaneous reactions can be serious, including drug hypersensitivity syndrome, toxic epidermal necrolysis and Stevens-Johnson syndrome (1).

Vitiligo is a common cutaneous disorder, characterized clinically by white macules on the skin that can be localized or generalized. Loss of colour can occur by two mechanisms: a defect in the synthesis or the transfer of melanin; or a partial or complete absence of melanocytes from the epidermis (2). Vitiligo has been described in association with several drugs (3, 4) as well as with viral infections (5), including HIV infection.

CASE REPORT

A 34-year-old male patient with AIDS presented with erythroderma, high fever and hepatitis one month after initiation of nevirapine treatment (200 mg/12 h). Physical examination revealed jaundice and a confluent, macular rash involving the upper and lower extremities, trunk and face (Fig. 1a). Laboratory tests showed elevated serum total bilirubin 10.6 mg/dl (normal 0.1–1.1), aspartate aminotransferase 460 UI/l (5–31), alanine aminotransferase 866 UI/l (5–31), gamma glutamyl transpeptidase 170 UI/l (5–39) and alkaline phosphatase 408 UI/l (35–130). Cell blood count and antinuclear antibody (ANA) titres were normal. Histopathological examination of a skin lesion showed a parakeratotic epidermis with focal spongiosis, individually necrotic keratinocytes and vacuolar degeneration of the basal layer, together with moderate oedema and a perivascular mononuclear cell infiltrate with some eosinophils in the upper dermis.

Nevirapine was withdrawn and oral prednisolone (1 mg/kg/day) was given, with subsequent good clinical response; the cutaneous lesions disappeared and the liver enzymes returned to normal values after 2 weeks. However, when the dose of oral steroids was decreased to 0.3 mg/kg/day, there were two recurrences of both skin lesions and abnormal liver function tests, which required a new increase in the dose. Five months after the development of the initial lesions, the patient progressively developed widespread vitiligo involving the head and body hair, eyelashes and eyebrows (Fig. 1b). After 6 years' follow-up, there have been no changes in the extent or intensity of the vitiligo lesions.

DISCUSSION

The most commonly associated adverse reactions to nevirapine are mild cutaneous rashes, usually occurring during the first month of therapy, as well as elevated serum liver enzymes. Severe skin reactions may also occur (1, 6), but so far vitiligo is not on the list.

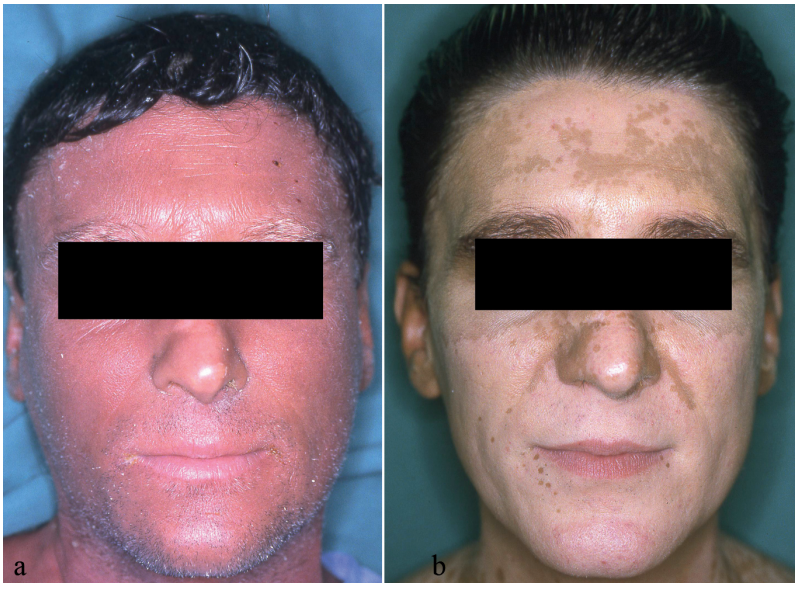

Fig. 1. (a) Initial lesions of erythroderma involving the face on December 4, 1998. (b) Vitiligo with widespread facial involvement in May 20, 1999. Cosmetic dyes are used by the patient for the hair of the head and the eyebrows.

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The pathogenesis of vitiligo has been related to a combination of mechanisms leading to melanocyte impairment and loss, including stress, drugs, infections and autoimmunity (3–5, 7). Several theories have been postulated to explain the mechanism for the development of vitiligo in HIV-infected patients: direct viral infection of melanocytes by HIV; polyclonal B-cell activation against melanocytes; production of gamma-interferon, which may be cytotoxic for melanocytes; and changes in the balance between helper and suppressor T cells (8). Thus, the development of vitiligo in HIV-infected patients may be due to an autoimmune inflammatory reaction in a genetically predisposed host (5). In accordance with these theories, the role of cell-mediated immunity for melanocytic destruction in classical vitiligo has been postulated based on the increased number of $CD8^+$ cytotoxic T cells in lesional skin as well as in peripheral blood (9), together with a decrease in $CD4^+$ T cells (10, 11), leading together to an increased $CD8^+/CD4^+$ ratio. Thus, in accordance with these data, the decreased number of $CD4^+$ peripheral T cells usually observed in patients with AIDS, which is closely correlated with disease stage, could also favour the development of vitiligo in these patients.

The onset of vitiligo after prodromal erythroderma has been reported previously (3, 9). However, to our knowledge, widespread vitiligo following erythroderma caused by nevirapine has not been reported previously. In our case hypopigmentation could be, at least partially, secondary to previous inflammation of the skin; however, as discussed previously, the vitiligo lesions were probably favoured by immune alterations associated with AIDS. We suggest that an increased $CD8^+/CD4^+$ ratio due to $CD4^+$ down-modulation could be one of the main mechanisms involved in the development of vitiligo in our patient.

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