CASE REPORT

Persistent serpentine supravenous hyperpigmented eruption in lepromatous leprosy after minocycline

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Accepted for publication 11 May 2015

Summary Persistent serpentine supravenous hyperpigmented eruption (PSSHE) is a peculiar patterned eruption characterised by hyperpigmented streaks following the superficial venous network on the skin. Unlike the superficial thrombophlebitis, it is characterised by underlying vessels that are patent. It has been described most commonly after injection of chemotherapeutic drugs. We describe a 40 year old man with lepromatous leprosy who developed PSSHE subsequent to starting modified multidrug therapy - multibacillary regimen in the form of minocycline and ofloxacin.

Keywords: Persistent serpentine supravenous hyperpigmented eruption (PSSHE), minocycline, leprosy

Introduction

Persistent serpentine supravenous hyperpigmented eruption (PSSHE) refers to a group of cutaneous eruptions, which begin as erythematous serpentine streaks over the veins and are soon replaced by hyperpigmentation. Its occurrence after the use of a chemotherapeutic drug and could be due to a subclinical thrombophlebitis followed by post-inflammatory hyperpigmentation.1 In lepromatous leprosy (LL), PSSHE can occur due the disease process causing phlebitis2,3 and the subsequent post-inflammatory hyperpigmentation, or it may be induced by drugs such as rifampicin.4

Case report

A 40 year old man diagnosed as a case of lepromatous leprosy (LL) was started on WHO multibacillary multidrug therapy (MB-MDT). After 24 months of therapy, his Bacillary Index (BI) was 6+ and the Morphological Index (MI) was 10%. He continued to get new lesions of
leprosy and recurrent erythema nodosum leprosum (ENL). The patient was suspected to have
drug resistance to standard MB-MDT, and was therefore prescribed clofazimine 50 mg OD,
ofloxacin 400 mg OD and minocycline 100 mg OD. In addition, oral prednisolone 40 mg/day
was started for severe ENL. After taking these drugs for 4 months, his ENL improved and
prednisolone was stopped. However, he started developing asymptomatic erythematous to
hyperpigmented streaks in a reticulate pattern over his right thigh which subsequently
involved the other leg (Figure 1).

The veins underlying the pigmented streaks were neither tender nor thrombosed.
Examination of the mucous membranes, palms and soles was unremarkable. Cardiovascular
and other systemic examination were normal. An ultrasonography Doppler study was also
normal and no superficial or deep venous involvement was observed. In addition to these
lesions on the lower limbs he was also concerned by the progressive hyperpigmentation on
his face. After 6 months of this therapy, his BI became 4+ and the MI was negative, so
minocycline was stopped and he continued on ofloxacin and clofazimine. Subsequently his
hyperpigmentation decreased and became imperceptible after a further 3 months. Based on
the clinical course, a diagnosis of PSSHE was made and the fact that it started 4 months after
starting minocycline and disappeared after stopping minocycline suggested that possibly
minocycline was the causative agent in this case.

Discussion

PSSHE is characterised by hyperpigmented streaks that follow the superficial venous network
in a linear or serpentine pattern.1,2 It may be preceded by erythema or appear as
hyperpigmented streaks without erythema. It has been most commonly reported after
intravenous use of chemotherapeutic agents such as 5-fluorouracil, docetaxel and
combinations of methotrexate, cytosine arabinoside, daunorubicin, 6-mercaptopurine,
cyclophosphamide, doxorubicin, bleomycin, vinka alkaloids and dacarbazine.1,5,6 It is
thought to result from extravasation of the cytotoxic agent after endothelial damage, causing

Figure 1. Hyperpigmented streaks in a reticulate pattern over both legs.
epidermal basal hyperpigmentation and dermal melanin incontinence. Other possible hypotheses include: a subclinical thrombophlebitis-induced post-inflammatory hyperpigmentation of the overlying skin, promotion of melanin synthesis via removal of inhibitors of tyrosinase by certain drugs or a direct stimulation of melanocytes. Histologically, it is characterised by diffuse basal layer hyperpigmentation, prominent dendritic melanocytes, rare necrotic keratinocytes and superficial perivascular lymphocytic infiltrates. PSSHE has also been reported in HIV, systemic sclerosis, systemic lupus erythematosus and rheumatoid arthritis.

There is a report of PSSHE occurring in six LL patients which was explained on the basis of occurrence of subclinical/clinical leprous thrombophlebitis and subsequent post-inflammatory hyperpigmentation; the role of drugs used in the treatment of leprosy was also hypothesised, as thrombophlebitis has been described with rifampicin. Although there are conflicting reports regarding vascular involvement in leprosy, studies have shown phlebitis and the presence of bacilli in the venous wall in multibacillary leprosy.

The occurrence of PSSHE in our case can be explained on the basis of direct involvement of the endothelial cells by *M. leprae* leading to phlebitis and subsequent minocycline induced hyperpigmentation at the site of inflammation, since the patient developed these lesions after he was started on minocycline and the lesions improved after stopping it.

Minocycline-induced hyperpigmentation may occur in up to 15% of patients. The risk factors identified in these patients are; duration of treatment, cumulative dose (high risk above 50 g), presence of previous skin alterations due to inflammation, excessive sun exposure or the concomitant intake of other pigmentary-inducing medications.

Minocycline-related pigmentary disorders usually appear after several months of treatment and have been classified into four basic clinical patterns: (i) dark blue-black macules in acne scars or at sites of previous cutaneous inflammation; (ii) localised or diffuse hyperpigmented macules distant from the site of inflammation or infection, and affecting the shins or other sun-exposed areas; (iii) diffuse brown-grey discoloration (muddy skin syndrome) with a tendency to photo-aggravation; and (iv) hyperpigmentation of the vermilion area of lower lip. However to the best of our knowledge PSSHE has not been described previously with minocycline. The various theories proposed for minocycline induced pigmentary changes include hyper-production of melanin, in inflamed or sun-exposed areas; or by direct effect on the melanocytes (Koebner’s phenomenon). Hemosiderin, lipofuscin, minocycline itself or its quinone by-product, have also been suggested since the presence of minocycline crystals has been demonstrated in up to 32% of localised pigmentation.

The main aim of presenting this case is to increase the awareness of PSSHE, a unique adverse effect of chemotherapy that can also be seen in leprosy both due to the disease process itself causing phlebitis, or induction by drugs such as rifampicin or minocycline.

References