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Letter

Sweet syndrome associated with interferon

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Abstract

Although still very rare, drug-related cases of Sweet syndrome have been reported. The more frequently associated medications are: tetracyclines, trimethoprim-sulphamethaxazole, azathioprine, all-trans retinoic acid, nitrofurantoin, granulocyte colony-stimulating factor, hydralazine, tripharil, lithium, oral contraceptives, furosemide, and celecoxib..

We found only one case of drug-induced Sweet syndrome secondary to pegylated interferon-alpha in combination with ribavirin reported in the literature. To our knowledge, this one is the first reported case of Sweet syndrome in association with interferon Beta 1-b therapy. Also, we would like to remark upon the atypical localization of the lesions in our patient, with a unilateral predominance on the left lower extremity and severe pain.

Case synopsis

A 43-year-old woman with newly diagnosed multiple sclerosis was started on interferon Beta-1b therapy. Four days after the first injection (subcutaneous injection in her right arm), she developed high fever and general malaise. Within 24 hours, very painful papules appeared on the legs that quickly coalesced into erythematous plaques over her left limb; she was unable to walk. Examination revealed tender, erythematous, pseudovesicular plaques on legs, with a clear predominance on the left leg, measuring between 3 and 10 cm in diameter (Figure 1). The patient remained febrile (with temperatures that spiked up to 40ºC) and her general condition deteriorated. A physical examination revealed no other symptoms.

Figure 1. Painful erythematous plaques on the thighs.

Laboratory evaluation showed an elevated white blood cell count with a neutrophil predominance, an elevated C-reactive protein

level, and elevated sedimention rate. Antinuclear antibody, rheumatoid factor, tumor markers, serum levels of C3 and C4 complement, protein electrophoresis, liver enzymes, bilirubin, creatinine kinase, lactate dehydrogenase, and electrolytes were within normal range.

A cutaneous biopsy from a plaque on the patient´s left lower extremity revealed a dense dermal infiltrate composed of neutrophils consistent with a diagnosis of Sweet syndrome (Figure 2a-b). Interferon was withdrawn .The patient was treated with prednisolone 50 mg once per day. There was significant improvement in the patient's general symptoms within 24 hours and skin lesions cleared; fever had completely disappeared in 4 days.

The dosage of oral prednisone was gradually tapered over 8 weeks. On the basis of the history, examination and complementary test, the diagnosis was Sweet syndrome associated with interferon. Interferon was withdrawn and after 7 months of follow-up there was no recurrence.

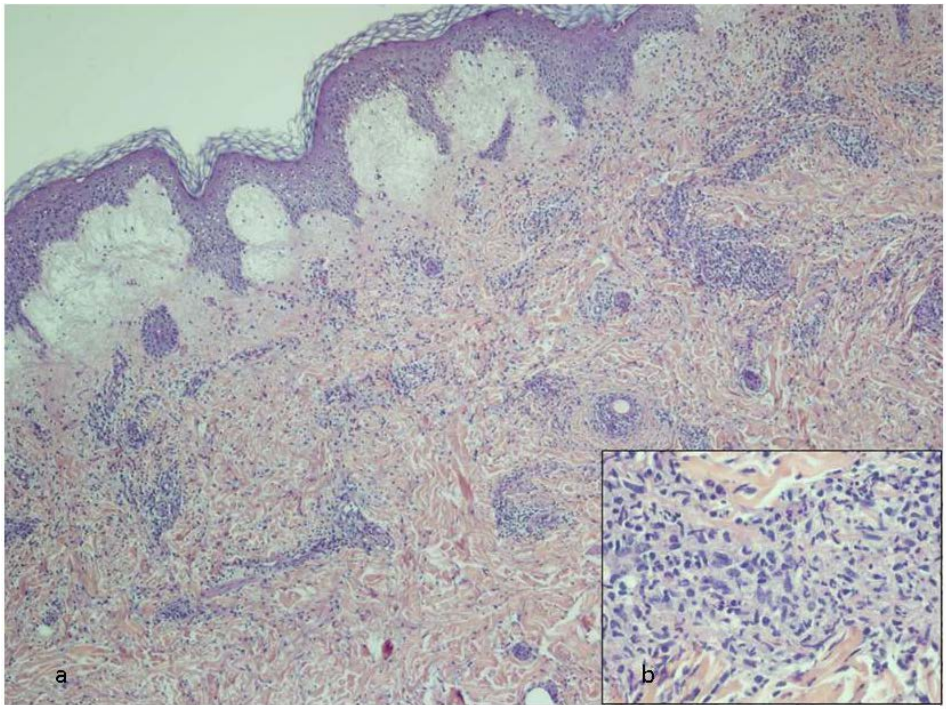

Figure 2. A. Dermal infiltrate composed of neutrophils (4x0.10). B.Neutrophils (40x0.65)

Discussion

Interferon Beta 1-b is associated with a high frequency of side effects such flu-like syndrome, headache, and local skin reactions at the site of injection. The use of interferon alfa was also associated with several cutaneous events reported in up to 20% of patients. It was proposed that upregulation of the Th1 immune response by interferon alfa may explain some adverse effects. Interferon alfa shares receptor sites and immunological effects with interferon beta, and therefore the same mechanism associated with multiple proinflammatory properties of both interferons is likely to be involved in the induction of adverse reactions [1-3].

Although still very rare, drug-related cases of Sweet syndrome have been reported. The diagnostic criteria for drug-induced Sweet syndrome have been reviewed by many authors [4]. All of these criteria are fulfilled in our patient.

The more frequent associated medications with drug induced Sweet syndrome are: tetracyclines, trimethoprim-sulphamethaxazole, azathioprine, all-trans retinoic acid, nitrofurantoin, granulocyte colony-stimulating factor, hydralazine, tripharil, lithium, oral contraceptives, furosemide, and celecoxib..

We only found one case of drug-induced Sweet syndrome secondary to pegylated interferon-alpha in combination with ribavirin reported in the literature [2]. To our knowledge, this one is the first reported case of Sweet syndrome in association with interferon Beta 1-b therapy. However, there has been described a case of idiopathic Sweet syndrome treated with interferon-alpha [5]. More studies are necessary to explain the association of interferon with Sweet syndrome. Also, we would like to point out the atypical localization of the lesions in our patient, with a unilateral predominance on the left lower extremity and very severe pain.

References

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