Multiple side effects of Efalizumab in a Saudi female with chronic persistent psoriasis followed by severe rebound after Efalizumab discontinuation

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ABSTRACT

We are reporting a case of 23-year-old Saudi female with persistent chronic plaque psoriasis who was given subcutaneous Efaluzimab 0.8 mg/kg/week for 14 weeks. During that period the patient developed multiple adverse reactions followed by severe rebound. The case is presented to highlight the importance of managing patients on Efalizumab carefully and closely.

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Psoriasis is a chronic cutaneous disease for which no curative treatment is available. Efalizumab is a humanized monoclonal immunoglobulin G-1 antibody that binds to the alpha subunit of leukocyte function-associated antigen-1 (CD11a) on the surface of T-cells that are important in the pathogenesis of psoriasis.[1] There are 2 known types of cutaneous adverse responses during Efalizumab treatment, which are a transient localized papular eruption and generalized inflammatory exacerbation (GIF).[2] We report a patient who developed multiple side effects due to Efaluzimab therapy during a period of 14 weeks from its initiation, demonstrating the importance of proper, close follow up of psoriatic patients on systemic treatment and the timing of discontinuation of specific therapy.

Case Report. A-23-year Saudi female presented with moderately severe plaque psoriasis affecting the trunk, and upper and lower extremities. She was a known case of psoriasis since the age of 3 years. During childhood, she was kept on topical treatment with acceptable response and at the age of 12 years, she was started on oral psoralen and ultraviolet light. According to the patient, the response was disappointing with periods of waxing and waning. Narrow band ultraviolet light was started at the age of 21 years, however, it worsened her condition immediately after the second session, and was discontinued. She was given acitretin 35 mg/day for 9 months, which improved her psoriasis but 4 months later the condition flared up. Methotrexate and cyclosporine were also tried, however, relapse always occured after treatment discontinuation. She was started on subcutaneous Efalizumab 0.8 mg/kg/week, in the hope of better control of the disease. During the first 3 weeks, we noticed a striking change in the morphology of psoriatic lesions having unique annular configuration with gradual clearance of psoriasis from the hands and feet, the trunk then on the face (**Figure 1**). After 6 weeks, treatment was interrupted for 2 weeks due to financial reasons, and again it was restarted with the same dose. On the 10th week, she complained of slightly painful swelling of the left ankle area with edema extending to the left leg, which resolved spontaneously after 5 days. She developed swelling of the neck for 2 days, which also resolved spontaneously. On the 12th week, she started to have diffuse erythematous scaly eruption affecting almost 60% of her skin (**Figures 2a & 2**b). So we diagnosed the patient as a case of psoriasis vulgaris with generalized inflammatory flare due to Efaluzimab. The patient was carefully observed and the drug was not discontinued because we know that it will be a temporary side effect. Fortunately by the end of the 12th week the eruption stopped progressing and some of the areas were showing clearance. By the 14th week the eruption resolved almost 85%. At that time, the patient decided to discontinue Efalizumab due to the slow response and financial reasons. So it was discontinued and a plan to start methotrexate or cyclosporine to prevent relapse of psoriasis but unfortunately the patient developed severe rebound progressing to erythroderma and was admitted to the hospital. She was kept on methotrexate with fair control of her psoriasis up to date.

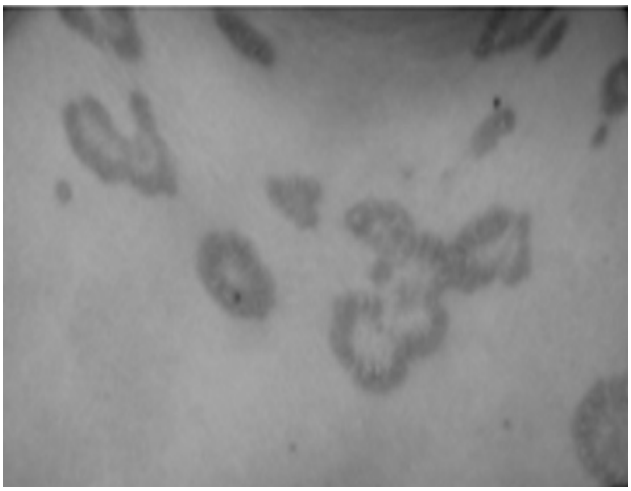

Figure 1 - Change in the morphology of psoriatic lesions from plaques to annular at the third week of treatment.

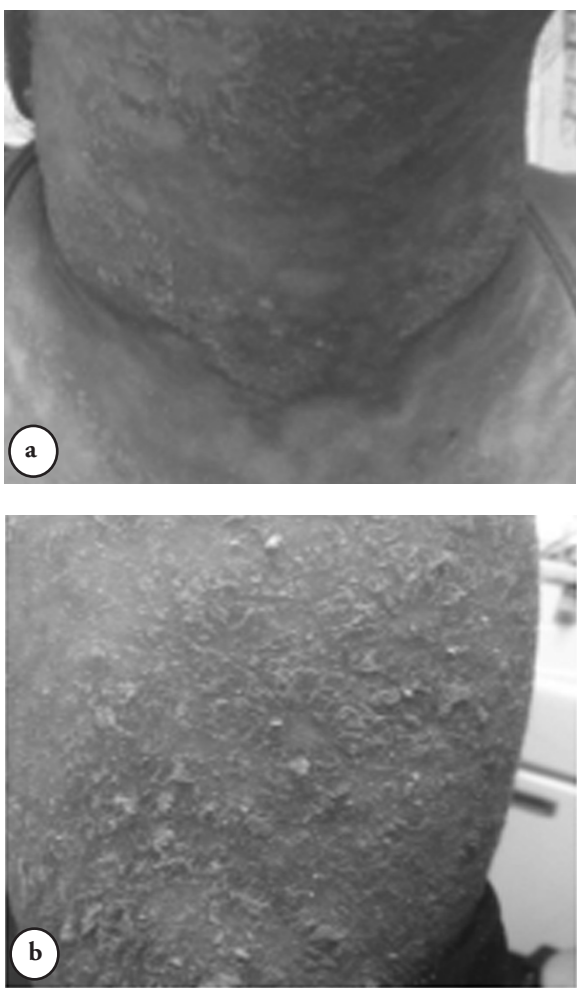

Figure 2 - Generalized inflammatory flare in the **a)** neck, and **b)** left arm at the 12th week of treatment.

Discussion. Psoriasis is a chronic cutaneous disease with variable course.[3] At present, no curative treatment is available, and the disease inevitably recurs when therapy is discontinued.[4] Investigators have observed two types of cutnaeous adverse responses during Efalizumab treatment which are a transient localized papular eruption, described as a localized mild breakthrough (LMB) and generalized inflammatory exacerbation (GIF).[2] It is estimated that approximately one-quarter to one-third of the patients may experience LMB, which is generally papular in nature, does not typically involve existing psoriatic plaques, may occur in the neck, torso or flexural areas, and often appears during the first 4-8 weeks of Efalizumab therapy.[5] In a responding patient, this eruption typically has minimal clinical impact and can be managed by "treating through" with continued Efalizumab therapy. Furthermore, the development of LMB has not been shown to be an indicator or predictor of future psoriasis adverse events.[2] The GIF is estimated to occur in 1-3% of patients. It is characterized by wide spreading erythematous, edematous lesions within existing plaques. It is typically observed in patients who do not achieve a clinically meaningful response, and are more likely to occur within 6-10 weeks of initiating Efalizumab therapy.[5] It can be managed by adding a short course of systemic psoriasis therapy to treat the flare such as cyclosporine and methotrexate. If the GIF is controlled and the underlying psoriasis is improved, the systemic therapy can be tapered off, and Efalizumab continued. If the GIF is not controlled, Efalizumab should be discontinued, or the dermatologists may choose to discontinue Efalizumab at the first sign of a GIF.[2] It is important to review patients' progress after initiation of Efalizumab therapy, which is intended to be administered continuously to provide optimal control of psoriasis symptoms. The few patients who show no response to therapy after approximately 3 months should be considered for discontinuation of Efalizumab, and initiation of alternative therapy such as cyclosporine, oral corticosteroids or methotrexate to prevent a potential psoriasis exacerbation or rebound. The incidence of rebound during the 12 weeks after Efalizumab discontinuation in multiple clinical trials was 14%, and less than 1% (0.7%) of patients experienced a serious psoriasis adverse event such as erythrodermic, pustular, or more inflammatory psoriasis.[2] Based on trial data and clinical experience, psoriasis exacerbations are manageable, and rebound may be both predictable and preventable if appropriate treatment guidelines are followed.[2] Unfortunately, in our patient, multiple adverse reactions to Efalizumab occurred including mild arthropathy of the left ankle with edema of the

left leg, swelling of the neck, transient localized papular eruption, GIF and finally severe rebound in the form of severe erythroderma.

In conclusion, it is unusual to develop such a collection of side effects in one patient during a period of 14 weeks from the initiation of Efalizumab, which might suggest that the development of multiple side effects in patients using Efalizumab can be a limiting factor in the continuation of Efalizumab therapy in psoriatic patients. It is the responsibility of the treating dermatologist to follow patients closely, and be aware of any unusual events to make a decision on discontinuing Efalizumab at the proper time to save patient from more suffering.

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