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Case Report

Treatment of refractory erythroderma with apremilast

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Abstract Erythroderma is an exfoliative dermatitis with erythema involving more than 90% of body surface area. It has many causes which should be ruled out to confirm diagnosis. Apremilast is an inhibitor of phosphodiesterase 4 (PDE-4) which targets intracellularly cascade for anti-inflammatory effect. Here, we present a case of 55years old male in erythroderma with history of psoriasis who did not respond to conventional treatment of psoriatic erythroderma with phototherapy, methotrexate and acetretin but underwent almost complete remission after apremilast treatment.

Key words
Erythroderma; Psoriasis; Apremilast.

Introduction

Erythroderma is the term used to describe intense and widespread reddening of skin with or without scaling which may result from inflammatory conditions such as psoriasis, eczema, pityriasis rubra pilaris, systemic infections, drug hypersensitivity, ichthyosiform disorders, metabolic disorders and malignancy.[1] Initial management for severe cases includes fluid resuscitation, empirical antibiotics, supportive treatments and diligent diagnostic evaluation.[2]

Psoriasis is the most common form of erythroderma and accounts for 25% of all cases. When associated with psoriasis the erythrodermic variant presents less than 1.5% of cases and manifests with well-defined erythematous plaques having silvery scales. This condition is less responsive to conventional therapies, however, biological therapy has shown promising results in management of erythrodermic psoriasis.[3]

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Apremilast is an inhibitor of phosphodiesterase 4 (PDE-4) that raises levels of cyclic adenosine monophosphate (cAMP). Increased cAMP results in reduced proinflamatory cytokines, tumor necrosis factor alpha (TNF-alpha), Interleukins i.e. IL-23 and IL-17, as well as increased anti-inflammatory IL-10.[4]

Case report

A 55-year-old married male presented with erythroderma. He had red plaques with silvery scales on scalp and back of chest and abdomen for the last 2 months. 15 days ago erythema appeared on body and involved more than 90% of skin on trunk and limbs with few areas of sparing on back and abdomen. He also had swelling of both feet and hands. No history of photosensitivity, fever, weight loss, lumps and bumps and also no history of drug intake, any contact with irritant, there was thick hyperkeratotic palms and soles with subungal keratosis. Histopathology showed hyperkeratosis, hypogranulosis and acanthosis.

During his admission, the treatment started was methotrexate 15mg/wk, acetretin 25mg twice a day, phototherapy thrice a week, tab prednisolone 50mg and bland emollients.

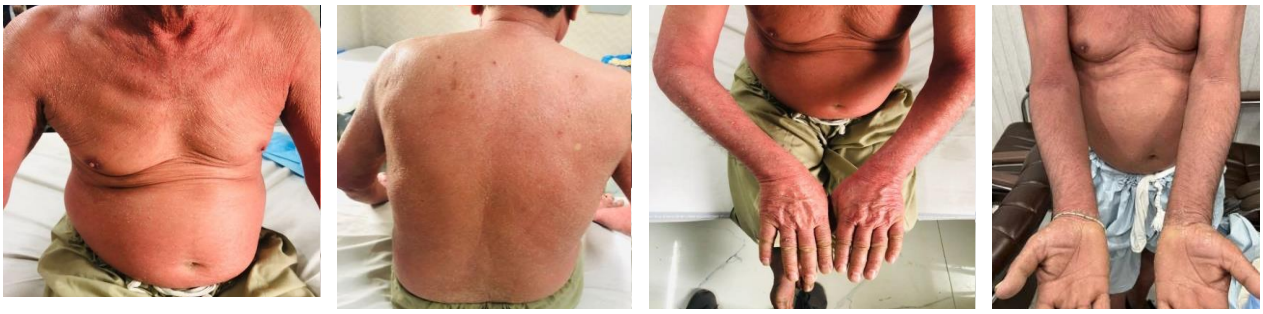

Figure 1 (a) erythema on front of chest and abdomen; (b) erythema on back with few spared areas; (c) hyperkeratosis of nails; (d) palmar hyperkeratosis.

Erythroderma remained recalcitrant and showed no improvement in 3 weeks with this treatment, rather the severity of erythroderma increased after phototherapy session. Then apremilast therapy was planned and complete work up was done including complete blood count (CBC), liver function test (LFT), renal function test (RFT), urine complete examination, hepatitis B and C, HIV, chest X-ray and electrocardiogram (ECG). Apremilast was started with the dose of 10mg daily till 60mg daily was achieved. Steroid was slowly tapered. Patient was monitored for any adverse effects. Erythema and scaling started to improve within 2 weeks. Palmoplantar keratoderma also improved. Tapering of steroid was without any relapse. Patient was stable and discharged after improvement. No relapse of disease after one month of follow up.

Discussion

Common causes of erythroderma are psoriasis, eczema, pityriasis rubra pilaris, cutaneous T cell lymphoma, drug induced erythroderma. Point in favour of erythrodermic psoriasis is the history of red scaly silvery plaques, palmoplantar keratoderma, subungal hyperkeratosis and typical histopathology in the patient.[5] There was also no history of any drug intake, lymphadenopathy, significant weight loss, any vesicobullous eruption, generalized itching or family history of itching. All the above discussed points lead the diagnosis towards psoriasis.

Apremilast is a PDE-4 inhobitor, by inhibiting PDE-4, apremilast prevents degradation of cyclic adenosine monophosphate (cAMP). Increased cAMP has antagonist effect on proinflamatory cytokine (TNF alpha, IL-23) and increase IL-10.[6]

Apremilast was approved by US food and drug administration (FDA) in 2014 and Europeon commission in 2015 for treatment of psoriasis and psoriatic arthritis.[7] Apremilast treats new psoriasis cases as well as recalcitrant cases of

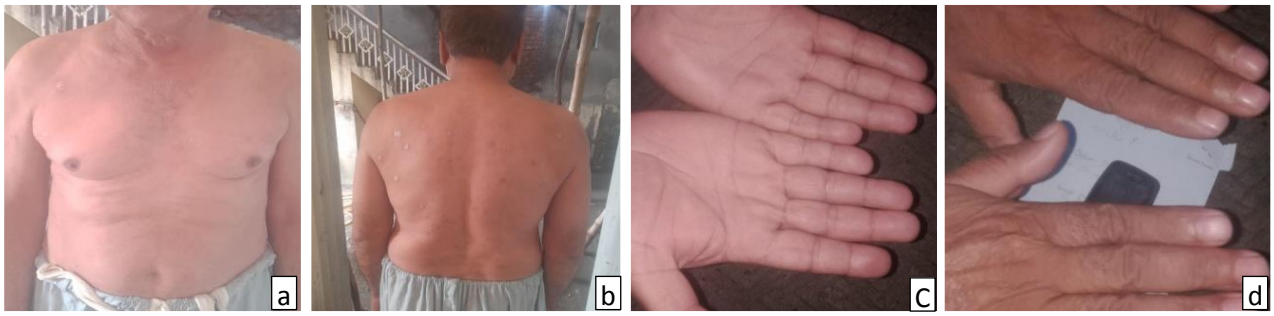

Figure 2 (a) Erythema resolved on chest & abdomen after treatment; (b) Erythema resolved on back after treatment; (c) keratoderma cleared after treatment; (d) subungal hyperkeratosis diminished after treatment.

psoriasis.[7]

Treatment guidelines recommend apremilast as second or third line treatment option for psoriasis and psoriatic erythroderma.[8]

In the treatment of psoriasis apremilast dose is as follows, start with 10mg OD then increase 10mg every day (10mg BD, 20mg OD then 20mg BD, 30mg OD then 30mg BD). After achieving 30mg BD this maximum dose is continued.[9]

Adverse effects of apremilast include diarrhea, nausea, stomach pain, vomiting, headache, upper respiratory tract infection, sneezing, fever.[10] These adverse effects can be treated symptomatically by painkillers, antibiotics and supportive medications.

In this patient no adverse effects were noted with 2.5 months of apremilast therapy, he completed his treatment without any relapse. However, more studies should be done on more number of patients to see efficacy and long term safety of apremilast in psoriatic erythroderma.

Conclusion

Apremilast proved to be a promising treatment modality for psoriatic erythroderma because of its high efficacy in treating resistant cases with short term side effects

References

1. Rothe MJ, Bernstein ML, Grant-kels JM. Life threatening erythroderma: diagnosing and treating the “red man”. *Clin Dermatol*. 2005;**23**:206-217.
2. Mistry N, Gupta A, Alva A, Sibbald G. A review of the diagnosis and Management of Erythroderma (generalized red skin). In: Advance in skin and wound care: Woltker Kluwer Health; 2015.p.228-36. www.woundcarejournal.com. [PubMed]
3. Caher JC, Crowley JJ. Use of biologic agents in combination with other therapies for the treatment of psoriasis. *Am J Clin Dermatol*. 2014;**15(6)**:467-78. Doi: 10.1007/s40257-014-0097-1. [PMC free article][PubMed][CrossRef][google Scholar]
4. Tiago Torres, Luis Puig. Apremilast: a novel oral treatment for psoriasis and psoriatic arthritis. Am J Clin Dermatol. 2018;**19(1)**: 23-32.
5. Nicolla Balato, Luisa DI Costanzo and Anna Balato. Differential diagnosis of psoriasis. *J Rheumatol Supp*. 2009:**83**:24-5. DOI://doi.org/10.3899/jrheum.090216
6. Carlo pincelli, pater H Schafer, Lars E French, Matthias Augustin, james G Krueger. Mechanism of underlying the clinical effects of apremilast for psoriasis. *J Drug Dermatol.* 2018:**17(8)**:835-40.
7. Celgene Corporation Oral Otezla (apremilast) approved by U.S Food and Drug Administration for the treatment of patients with moderate to severe plaque psoriasis. Sep 23, 2014. http://ir.celgene.com/releasedetail.cfm. accessed July 6,2015.
8. F. Amatore, A P Villani, M tauber, M Viguire, B Guillot. French guidelines on the use of systemic treatments for moderate to severe psoriasis in adults. *J Eur Acad Dermatol Venereol*. 2019;**33(3)**:464-83.
9. Celgene corporation. Product monograph 2017: otezle(apremilast) tablets 10mgmg, 20 mg, and 30 mg. available from: http://media.celgene.com/content/uploads/sites/23/otezla-product-monograph-english.pdf
10. Annia Langley, Jannifer Beecker. Management of common side effects of apremilast. *J Cut Med Surg*. 2017;**22(4)**: 415-21.