**Psoriatic Erythroderma: When life-threatening complications as disseminated herpes arise: A Case Report**

Ahmad Berjawi1, Rana Attieh2, Marcella Younes2, Zeina Tannous1

*1 Department of Dermatology, Gilbert and Rose Marie Chagoury School of Medicine, Lebanese American University, Beirut, Lebanon*

*2 Department of Internal Medicine, Gilbert and Rose Marie Chagoury School of Medicine, Lebanese American University, Beirut, Lebanon*

*NB: first 3 authors contributed equally to the publication*

**Corresponding Author:**

Zeina Tannous

*Affiliation****:*** *Department of Dermatology, Gilbert and Rose Marie Chagoury School of Medicine, Lebanese American University, Beirut, Lebanon*

*Email Address:* [*Zeina.tannous@lau.edu.lb*](mailto:Zeina.tannous@lau.edu.lb)

*Mailing Address:*

LAU Medical Center – Rizk Hospital  
P.O. Box 11-3288  
Beirut, Lebanon

**Authors email Addresses:**

[Ahmad.berjawi@lau.edu](mailto:Ahmad.berjawi@lau.edu)

[Rana.attieh@lau.edu](mailto:Rana.attieh@lau.edu)

[marcellayounes@hotmail.com](mailto:marcellayounes@hotmail.com)

[Zeina.tannous@lau.edu.lb](mailto:Zeina.tannous@lau.edu.lb)

***Key words****: Erythroderma, psoriasis, disseminated herpes, ixekizumab, topical steroids*

**Introduction:**

Erythrodermic psoriasis (EP) is a rare and severe variant of psoriasis vulgaris with an estimated prevalence of 1-2.25% in psoriatic patient.1 It is the most common cause of erythroderma with around 25% of cases and has high morbidity and mortality.1 Complications with EP may arise such as tachycardia, myalgias, dehydration, fluid loss, electrolyte imbalance, and infections may occur therefore, close monitoring is needed for all patients with EP. 1 We present the case of a 49 years old with multiple comorbidities who developed erythrodermic psoriasis (EP) that was complicated with disseminated HSV-1 infection and multiple episodes of bacteremia.

**Case History/Examination:**

A 49-year-old male patient presenting to the Intensive Care Unit (ICU) hemodynamically unstable with increasing chills, worsening skin erythema, scaling, and generalized body edema.

His medical history is relevant for severe plaque Psoriasis since 2012, having failed multiple regimens of therapy, including topical steroids, methotrexate, secukinumab, and cyclosporine. Taltz (ixekizumab) was also used to control his disease, nevertheless, it was discontinued one year prior to his presentation due to local unavailability. The patient has also been suffering from liver cirrhosis due to non-alcoholic fatty liver disease (NAFLD) complicated by portal hypertension and esophageal varices that required band ligation, currently on propranolol. He also has been diagnosed with bipolar disorder, currently stable on paroxetine, mirtazapine and chlorpromazine.

The patient’s history goes back to two weeks prior to presentation, when he first presented to the dermatology clinic with severe itching and erythema involving his upper extremities. Thus, he started taking unprescribed oral prednisone which was immediately discontinued and switched to topical steroids and moisturizers. Despite that, his symptoms progressed over the next three days and the erythema increased to involve more than seventy-five percent of his body surface area (Fig 1) therefore, he was prescribed infiximab injection (5mg/kg) as a first line treatment for possible erythrodermic psoriasis. Three days later, the patient developed fever with non-resolving erythroderma. Consequently, he was admitted and started on broad spectrum antibiotics, de-escalated when skin cultures showed MSSA without a documented bacteremia. Therefore, the patient was stable enough to complete his treatment at home and be discharged on Augmentin 1 gram twice daily for 10 days. Ten days after this initial presentation, he was re-admitted for increasing chills, worsening erythema and generalized diffuse edema. He was hemodynamically stable with diffuse erythema covering more than ninety percent of his body total surface area as well as scaling without any ulcers. His labs were significant for leukocytosis and eosinophilia. The overall clinical picture was consistent with the diagnosis of erythrodermic psoriasis and a PASI score of 45.

**Methods:**

Skin biopsy revealed diffuse hypogranulosis, ectatic blood vessels, neutrophils in the stratum corneum. The presence of scattered eosinophiles in the dermis raised the possibility of a drug (mainly Inflixmib) paradoxically worsening the erythrodermic psoriasis. No evidence of direct drug toxicity in the skin such as vacuolar changes or necrotic keratoncytes were detected.

The patient was admitted to the intensive care unit, Taltz (Ixekizumab) was immediately initiated combined with topical Clobetasole propionate with a dosage of 30 mg equivalent to one entire tube per day on the affected areas. During his stay, he developed recurrent bacteremias with different organisms, resulting in hemodynamic instability and severely depressed level of consciousness requiring intubation. One week following Ixekizumab administration, disseminated vesicles, erosions, ulcers, and hemorrhagic crusts started to appear involving multiple areas and dermatomes, suggestive of disseminated herpes (Fig 2). PCR test was positive for HSV1. Intravenous acyclovir 5mg/kg every 8 hours was administered, clobetasole propionate was discontinued and Taltz (Ixekizumab) was postponed for ten days to allow further healing.

The big dilemma between immunosuppression on one hand and control of multiple concomitant infectious processes on the other, was discussed with multidisciplinary teams involving the critical care, infectious disease, dermatology and gastroenterology. He was first started on topical steroids after 1 week of Acyclovir initiation, and progressively increased to one tube daily. Following a remarkable amelioration in his herpes lesions after ten days of adequate therapy, Taltz was re-introduced. (fig 3)

**Conclusion and Results:**

At six weeks, the patient was in good clinical condition, with resolution of palmoplantar scaling and erythema, resulting in a PASI score of 9.7. Continuous improvement was observed during follow-up visits monthly, with no relapses or significant adverse events reported, oral acyclovir was continued for a total of six months.

Erythrodermic psoriasis is a serious variant of psoriasis that requires early intervention and proper management, as well as close monitoring for any possible infections that might arise. Treatment with monoclonal antibodies has started to emerge in refractory cases over the last few years, keeping in mind major complications that might arise such as disseminated HSV-1 as reported in this case. Multiple factors might have contributed such as infliximab, Ixekizumab therapy in combination with high dose of topical clobetasol.

**Discussion:**

To our knowledge, no published articles mentioned the occurrence of disseminated herpes HSV-1 in the setting of treatment of a patient with erythrodermic psoriasis on topical corticosteroids combined with Ixekizumab.

**Erythrodermic Psoriasis:**

Frequent causes of EP is the sudden withdrawal of plaque psoriasis treatment as steroids, cyclosporine or methotrexate. Its pathogenesis is not fully understood yet, though, it’s postulated that EP may be related to increased Th2 response.

According to the US National Psoriasis Foundation, the first line treatment for severe erythrodermic psoriasis is Infliximab or Cyclosporine.2 In our case, Infliximab was attempted after a previous failed course of Cyclosporine. Despite that, the patient kept deteriorating, and a possible reaction to Infliximab in addition to erythroderma couldn’t be ruled out due to the presence of eosinophils in the skin biopsy. Having had a good response to Ixekizumab previously, it was used in combination with topical Clobetasol as a mainstay of treatment and might have led to the rare occurrence of disseminated Herpes (HSV-1) infection.

**Disseminated herpes infection:**

In most immunocompetent individuals, herpes infection tends to be self-limited and has an uncomplicated course. Disseminated form of the disease is the involvement of multiple contiguous dermatomes, crossing the midline, with the possibility of visceral involvement. The occurrence of disseminated herpes infection whether with HSV-13 or varicella zoster4 in an otherwise healthy immunocompetent individual has been limited to case reports only, some of which actually seen following vaccination; for instance, the inactivated covid-19 vaccine5.

On the other hand, it is well established that some underlying factors might contribute to the disseminated infection in the settings of immunosuppression either with chemotherapeutic agents or monoclonal antibodies.

It is also remarkable to mention that the occurrence of disseminated herpes zoster has been more frequently reported than disseminated HSV-1; This was shown in a patient with AIDS and concomitant liver cirrhosis6 and in another receiving immunosuppressive therapy including mycophenolate, tacrolimus.6 It was also reported in the covid era, when treatment involved immunomodulatory agents and high doses of intravenous dexamethasone.7

Disseminated herpes HSV-1 was seen following a simple course of oral corticosteroids therapy with 60 mg of oral prednisone daily leading eventually to multi-organ involvement, 8 and in another patient receiving Infliximab for rheumatoid arthritis9. Therefore, the exposure to infliximab might have been one of the predisposing factors to the development of disseminated HSV-1 in our patient.

Our patient has been diagnosed with disseminated HSV-1 based on a positive PCR. It is essential to have a high index of suspicion in a patient with a vesicular multi-dermatomal rash and establish the diagnosis early on for adequate therapy. Differential diagnosis is broad and can include drug related hypersensitivity reactions including Stevens- Johnson, DRESS syndrome, bullous pemphigoid and small vessel vasculitis.

**Ixekizumab and topical corticosteroids:**

Ixekizumab is an injectable humanized monoclonal antibody active against interleukin 17 (IL-17A), having recently obtained the US Food and Drug Administration (FDA) approval for the management of plaque psoriasis, psoriatic arthritis and ankylosing spondylitis.10-11

UNCOVER trials 12-13 as well as data recovered from 21 clinical trials14 succeeded in showing a safety profile for the use of ixekizumab. However, one article later in 2020 documented the first case of herpes zoster infection following ixekizumab administration in an erythrodermic psoriasis patient. 15 Our case reported the occurrence of disseminated HSV-1 following Ixekizumab injection in the setting of EP.

Further studies are needed to assess the risk factors for disseminated HSV-1 infection in erythrodermic psoriasis patients.

**Conflict of interest:**

The authors declare that there is no conflict of interest.

**Funding statement:**

No funding was received for this research.

**Informed Consent statement:**

Written informed consent was obtained from patient to publish this report in accordance with the journal’s patient consent policy.

**Acknowledgment:**

None

**Key Clinical Message:**

Erythrodermic psoriasis is a serious variant of psoriasis that requires early intervention and proper management, as well as close monitoring for any possible infections that might arise. Disseminated Herpes infection should be kept in mind and treated promptly in any patient being treated with monoclonal antibodies and has new onset ulcers.

**Authorship list:**

Ahmad Berjawi: author was involved in taking care of the patient, drafting and revising the manuscript, and gave final approval for publication

Rana Attieh: author was involved in taking care of the patient, drafting and revising the manuscript, and gave final approval for publication

Marcelle Youness: author was involved in taking care of the patient, drafting and revising the manuscript, and gave final approval for publication

Zeina Tannous: author was involved in taking care of the patient, drafting and revising the manuscript, and gave final approval for publication

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