CASE REPORT

Pityriasis rubra pilaris rapidly cleared with ixekizumab in an HIV-positive patient

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Key words: AIDS; biologics; erythroderma; HIV; ixekizumab; pityriasis rubra pilaris.

INTRODUCTION

Pityriasis rubra pilaris (PRP) is a rare inflammatory cutaneous disease of uncertain origin characterized by follicular hyperkeratosis, palmoplantar keratoderma, and red-orange papules coalescing into scaling plaques. PRP appears to follow a bimodal age distribution with the onset in either the first or fifth decade of life and may be acquired or have genetic causes.

In 1980, Griffiths established a classification scheme for 5 subtypes of PRP. In 1995, the scheme was expanded by Miralles et al to include a sixth subtype characterized by the presence of concomitant human immunodeficiency virus (HIV) infection and worse prognosis (Table I).

Immune dysregulation and potential aberrant vitamin A metabolism have been implicated in the pathogenesis of PRP. Therapies for PRP have thus often revolved around vitamin A analogs and immunosuppressants.

We describe a case of PRP in an HIV+ male for whom traditional PRP therapies were not suitable based on other comorbidities.

CASE REPORT

In June 2020, a 53-year-old HIV+ male with a 3-month history of a burning, flaking, and painful erythrodermic rash composed of follicular papules coalescing into plaques consistent with PRP presented to our office (Figs 1 and 2). Before being seen by our practice, a skin biopsy performed in the hospital had shown subtle acanthosis, spongiosis, and vacuolar interface changes with superficial perivascular lymphocytic inflammation and eosinophils. Based on these results, the rash was initially thought to be a potential drug eruption from his dolutegravir/rilpivirine therapy, which he had been on for 4 years, although he did note a recent change in the manufacturer.

He had not taken any new medication prior to the rash onset, and at the time of presentation in our office, he was taking 40 mg of prednisone daily and using topical triamcinolone acetonide after having received 3 days of 125 mg IV/day Solu-medrol in the hospital immediately. He had also completed two 6-day courses of methylprednisolone dose packs prior to hospitalization. The rash failed to improve with steroids and was worsening on his current prednisone taper. He was compliant taking his HIV medications, and his most recent HIV-specific labs drawn 5 months before showed an absolute CD4 lymphocyte count of 407 (ref = 359-1519/uL) and an undetectable viral load (<20).

His history was also significant for chronic, uncontrolled hypertriglyceridemia, as well as recently recorded aspartate transaminase and alanine transaminase elevations of 49 IU/L and 164 IU/L, respectively, making therapies such as systemic retinoids and methotrexate unappealing given their potential side effects of dyslipidemia and hepatotoxicity. The decision was made to treat with 160 mg of the humanized anti–interleukin (IL)-17A monoclonal antibody ixekizumab (Table I), administered subcutaneously.

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antibody, ixekizumab, subcutaneously (SC) at the time of presentation. Initial dosing of ixekizumab was based on the recommended dosing for moderate-to-severe plaque psoriasis.

The patient returned in 1 week and had a 50% reduction in erythema as evidenced in Fig 3. He then received 80 mg of ixekizumab SC 2 weeks after the initial dose and 1 month after starting ixekizumab had near 100% clearance (Fig 4). Today, his disease remains well controlled, and he remains on ixekizumab 80 mg SC every 4 weeks.

**DISCUSSION**

In August 2020, 3 months after our patient started on ixekizumab, Haynes et al published a single-arm trial of 12 adults with refractory PRP treated with ixekizumab for 24 weeks. This trial utilized the United States of America Food and Drug Administration–approved dosing of ixekizumab for psoriasis and followed the mean psoriasis area and severity index improvement of each patient to measure outcomes. In that trial, 11 patients completed the treatment, and 7 participants achieved a psoriasis area and severity index 75 or greater response. Notably, however, none of the 12 patients in that trial had type VI PRP.

Treating type VI PRP presents unique challenges given the often-increased severity of PRP as well as the need to consider potential adverse effects secondary to the highly active antiretroviral therapy that these patients also need. Adverse effects of many highly active antiretroviral therapy medications such as nucleoside/nucleotide reverse transcriptase...
inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors include hyperlipidemia and liver toxicity, which are also well-known side effects of systemic vitamin A analogs.\(^1\)\(^,\)\(^5\) Thus, ixekizumab presents an appealing option for patients with type VI PRP, as it is not associated with lipid or hepatic abnormalities and avoids the more widespread immunosuppression seen with other treatment options such as methotrexate, azathioprine, and cyclosporine.

Commonly known as “biologics,” monoclonal antibodies in general are an emerging therapy for PRP. A 2017 case report evaluated the cytokine levels in the lesional skin of a patient with PRP and found elevated IL-17A, IL-17F, and IL-22, ILs that some biologics target.\(^6\) A 2019 systemic review of the use of biologics for PRP refractory to first-line therapy demonstrated that biologic therapy was efficacious both as monotherapy (81.1\% [27/33] achieving >75\% improvement) and in combination with other systemic therapies (87.5\% [14/16] achieving >75\% improvement), but no definitive recommendations can be made as the review was limited to case reports and small case series.\(^7\) The review encompassed patients treated with tumor necrosis factor-alpha inhibitors, ustekinumab (an IL-12/23 inhibitor), and the IL-17A inhibitors ixekizumab and secukinumab.\(^7\) However, over 80\% of the cases were type 1 PRP, limiting generalizability to other subtypes. More recently, a 2022 retrospective cohort study by Kettering et al analyzed outcomes for 52 patients and found that patients treated with biologics had a better drug survival rate and fewer short-term adverse effects than those treated with retinoids but a lower drug survival rate than those treated with methotrexate.\(^8\)

Further research is needed to establish a more definitive treatment algorithm for all PRP subtypes. Ideally, a large randomized-controlled trial would be conducted, but the rarity of PRP makes this difficult.

**Conflicts of interest**
No conflicts of interest declare.

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