

## BRIEF ARTICLES

## Successful Treatment of Pityriasis Rubra Pilaris with Brodalumab

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## ABSTRACT

Pityriasis Rubra Pilaris (PRP) is a rare inflammatory skin disease with highly variable clinical appearance. Treatment of PRP remains a challenge and has been mostly guided by case reports and case series. We report the first case of pityriasis rubra pilaris that is successfully treated with combination therapy of brodalumab and methotrexate.

## INTRODUCTION

Pityriasis Rubra Pilaris (PRP) is a rare papulosquamous inflammatory dermatosis of unknown etiology that may affect skin, nails, and hair. PRP is extremely rare with an estimated incidence of 1/5000 and often mistaken for erythrodermic psoriasis<sup>1</sup>. The condition mostly affects adults in their sixth or seventh decade of life with no predilection for genders and is subdivided into six different subtypes based on clinical features, age of onset and prognosis.<sup>2,3</sup> We present the case of a patient with type I (classic adult onset) PRP who achieved complete resolution after initiation with combination therapy of brodalumab and methotrexate.

## CASE REPORT

A 62-year-old gentleman with a family history of psoriasis presents with a twenty-

year history of intermittent redness and dryness of the hands, scalp, and groin that receded with over the counter medications. In the past two years, he noticed that the patches became persistent and progressively worse. The patient was diagnosed with plaque psoriasis by his previous dermatologist and failed to improve with the use of topical steroids, a topical calcineurin inhibitor, and topical vitamin D3 analogue. Despite a year on these topical treatments, the rash continued to spread predominantly to his face, trunk, and extremities, and his dermatologist decided to start systemic medications. The first combination consisted of cyclosporine and ustekinumab for three months with no visible improvement. The biologic was then changed to ixekizumab for another three months displaying only minor improvement. Finally, the dose of cyclosporine was increased from 350mg to 400mg and the patient started on guselkumab, which lead to noticeable improvement. On week nine of this regimen, cyclosporine was stopped

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when the patient developed liver toxicity that was attributed to the cyclosporine; within days of cessation, the patient developed a severe and rapid exacerbation of the skin and new onset scalp hair loss.

The patient then presented to our clinic with generalized erythematous-orange scaly patches with islands of sparing (Figure 1A). Based on his clinical presentation we diagnosed him as classic adult onset Pityriasis Rubra Pilaris (PRP).

A skin biopsy was obtained from his right upper arm. The epidermis was acanthotic with mild spongiosis. There were foci of parakeratosis accentuated around hair follicles. The parakeratosis showed both a horizontal and vertical alternating pattern. Foci of acantholysis were present. The features were consistent with pityriasis rubra pilaris with secondary spongiotic change (Figure 2).

We decided to start him on brodalumab 210mg every two weeks and on week six of treatment, we also added methotrexate 25mg every week. By week twelve of initiating brodalumab (Figure 1B), the patient displayed significant clinical improvement. Long-term remission continued through six months of combination therapy of brodalumab and methotrexate with no adverse events.

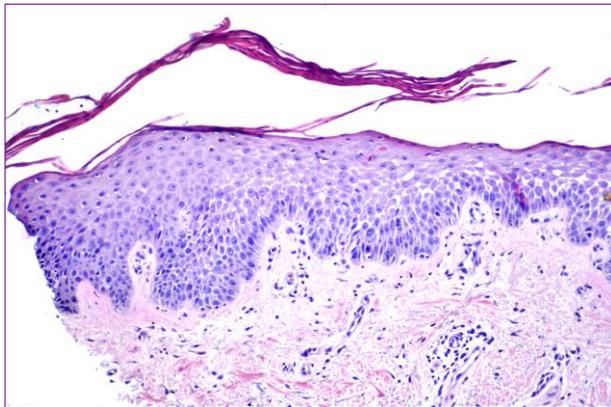
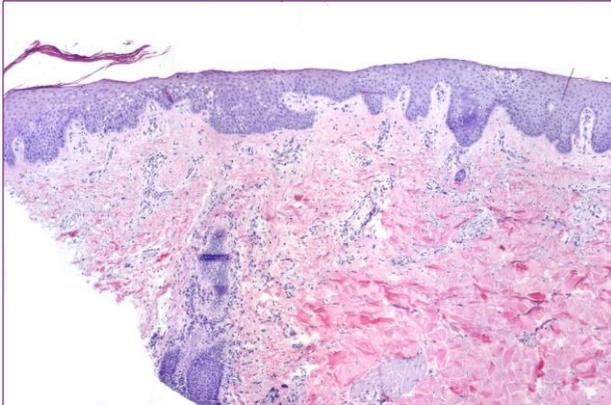
**Figure 1A.** Patient at his initial presentation to our clinic.



**Figure 1B.** Patient at 12 weeks of brodalumab treatment.



**Figure 2.** Acanthotic, mild spongiosis, with foci of parakeratosis horizontal and vertical alternating pattern



## DISCUSSION

Pityriasis Rubra Pilaris and plaque psoriasis are two distinct erythematous-squamous skin diseases that are often challenging to differentiate. Ross et al. did a multinational study of 100 patients that showed only 26% of patients were correctly diagnosed as having PRP at the time of enrollment, with the most common initial diagnoses reported as being either psoriasis or eczema.<sup>4</sup> On average, this delayed the correct diagnosis by 29 months from initial presentation.<sup>4</sup> Clinically, patients with classic adult-onset PRP typically present with a fine orange-red scaling eruption that is associated with erythroderma, palmoplantar keratoderma and a cephalocaudal progression of

coalescing plaques with islands of sparing. Complete remission is achieved spontaneously within three years of onset in 80% of cases, whereas recurrence occurs in 20% of cases.<sup>2</sup> In comparison, plaque psoriasis presents with diffuse coarse silvery scales attached to an erythematous base. PRP can also present with additional cutaneous features such as nails that are thickened, discolored, and ridged, whereas psoriasis patients display nail changes such as nail pitting, the oil drop sign, and distal onycholysis. The scalp involvement in both psoriasis and PRP may include dandruff and scaly scalp, as well as hair shedding; the atypical form of PRP is more often associated with alopecia and lesions localized to the lower extremities.<sup>5-7</sup> On histopathology, type I PRP demonstrates orthokeratosis with spotty parakeratosis, epidermal acanthosis, intact granular layer, and mild perivascular lymphohistiocytic infiltrates in the dermis. In psoriasis, the granular layer is often absent or very thin.<sup>4</sup> Thus, the time-course, clinical presentation, and histopathology are crucial for distinguishing PRP from plaque psoriasis.

We present the first case of a patient with classic adult onset PRP who failed several biologics and immunosuppressants but was able to achieve complete resolution with combination therapy of brodalumab and methotrexate. Brodalumab is a human monoclonal antibody against the interleukin-17 receptor A (IL-17A) approved in 2017 by the Food and Drug Administration for the treatment of moderate to severe plaque psoriasis. Feldmeyer et al. reported a case of biopsy proven PRP and found upregulated expression of proinflammatory cytokines including T<sub>H</sub>17 helper cells (T<sub>H</sub>17) cytokines IL-17A, IL-17F, and IL-22 and tumor necrosis factor (TNF), IL-6, IL-12, IL-23, IL-1 $\beta$ .<sup>8</sup> Analysis of the PRP patient's skin sample after treatment with ustekinumab

showed decreased levels of TH<sub>17</sub> cytokines with clinical and histopathologic improvement of the disease.<sup>8</sup> Methotrexate is a second line monotherapy for PRP that disrupts folate metabolism and downstream synthesis of thymidine. In a selection of published cases, type I PRP patients displayed a 50% treatment response rate to methotrexate alone<sup>9</sup>. Although no studies exist on the efficacy of brodalumab and methotrexate, PRP data from select published cases demonstrate biologics offer a similar or higher response rate in comparison to isotretinoin and immunosuppressants.<sup>10-12</sup> The excellent response of this patient to combination of brodalumab and methotrexate, introduces an additional biologic in the potential treatment options for pityriasis rubra pilaris.

## CONCLUSION

Treatment options for pityriasis rubra pilaris (PRP) are limited and often unsatisfactory. Brodalumab in combination with methotrexate might be a promising therapeutic agent for patient with PRP.

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