

## Etanercept-induced Clinical Remission of Type II Pityriasis Rubra Pilaris With Rheumatoid Arthritis

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Pityriasis rubra pilaris (PRP) is a rare papulosquamous dermatosis characterized by keratotic follicular papules, erythematous scaling, palmoplantar keratoderma and a variable degree of erythroderma. Type I PRP, the most common adult form, has a typical clinical manifestation, and remission in these patients can be achieved within 3 years. However, the rare type II PRP presents atypical features and has a long disease duration. We describe here a case of type II PRP associated with rheumatoid arthritis (RA) that achieved clinical remission with etanercept therapy.

### CASE REPORT

A 58-year-old woman visited our department with a 5-year history of scaly eruptions on her hands, feet, back and buttocks. She also reported arthralgia on both fingers and wrists lasting for 2 months.

Physical examination showed follicular keratotic papules on the back and buttocks, in addition to diffuse erythematous desquamative patches on her hands and feet (Fig. 1a and b). Swelling of her right wrist joint was also revealed. A skin biopsy on the buttock revealed alternating parakeratosis and orthokeratosis, irregular acanthosis, focal spongiosis, and lymphocytic exocytosis without Munro's microabscess or the spongiform pustule of Kogoj. The biopsy also revealed perivascular lymphocytic infiltration on the dermis (Fig. 1e). Based on these clinicopathological findings, the patient was diagnosed with PRP.

Joint space narrowing was observed on the radiocarpal and intercarpal joints of the right wrist on X-ray examination. The blood examination showed a highly positive rheumatological factor and anti-cyclic citrullinated peptide antibody, but she was negative for human leukocyte antigen B27. The erythrocyte sedimentation rate was 22 mm/h (normal range, 0–20 mm/h) and C-reactive protein was 14.4 mg/l (0–5.3 mg/l). She fulfilled the RA criteria of 2010 American College of Rheumatology/European League against Rheumatism classification.

The patient's skin lesions were initially treated with oral acitretin (10 mg/day) and topical and systemic steroid (methylprednisolone 8 mg/day) for 10 months; however, she continued to report burning and itching sensation. In the rheumatological clinic, sulfasalazine (1,000 mg/day) was started for initial 9 months, but it failed to improve the arthritis. Methotrexate (12.5 mg/week) was administered for following 14 months, but the arthritis did not resolve. Finally, the patient began to receive subcutaneous injection of 25 mg etanercept twice a week in combination with methotrexate (12.5 mg/week). Clinical remission of skin eruption and arthritis was achieved 2 months after etanercept therapy. This state was sustained for 9 months without any treatment modification (Fig. 1c and d). However, skin lesions recurred one month after cessation of etanercept treatment.

### DISCUSSION

Systemic retinoids and/or methotrexate have been used as first-line therapies for PRP, but many PRP cases are refractory to the standard treatment. Tumour necrosis factor alpha (TNF- $\alpha$ ) antagonists, including infliximab and etanercept, have been reported as effective for patients with recalcitrant PRP (1, 2). A total of 8 cases of PRP treated with etanercept have been reported (Table I) (2–6).



Fig. 1. The patient showed (a) follicular hyperkeratosis on the back and buttocks, and (b) erythematous scaling lesions on the feet. After 9 months of etanercept treatment, (c) clinical remission was maintained on back, buttocks, and (d) feet. (e) Examination of the biopsy specimen revealed alternating parakeratosis and orthokeratosis, psoriasiform hyperplasia, and superficial perivascular lymphocytic infiltration (haematoxylin-eosin staining, original magnification  $\times 200$ ).

Table I. Previously published cases and the present case of pityriasis rubra pilaris (PRP) treated with etanercept

No.	Sex/age years	Type of PRP	Treatment before etanercept	Time to remission months	Follow-up months	Initial dose	Associated disease	References
1	M/55	I	Systemic retinoids, systemic steroid Cy and topical steroid,	Unknown	7	50 mg ×2/week	None	Davis et al., 2007 (3)
2	F/16	III	Topical steroid, topical retinoids, and calcipotriene	4	6	50 mg ×2/week	None	Cox et al., 2008 (4)
3	M/37	I	Systemic retinoids and Cy	3	6	50 mg ×2/week	None	Sekin et al., 2008 (5)
4	M/59	I	Systemic retinoids, systemic steroid and Cy	1	16	50 mg/week	None	Garcovich et al., 2010 (2)
5	M/56	I	Systemic retinoids	2	15	50 mg/week	None	Garcovich et al., 2010 (2)
6	M/59	I	Systemic retinoids and Cy	2	15	50 mg/week	None	Garcovich et al., 2010 (2)
7	M/40	II	Systemic retinoids, Cy and PUVA	3	24	50 mg/week	None	Garcovich et al., 2010 (2)
8	F/30	I	Systemic retinoids and topical steroid	2	9	25 mg ×2/week	None	Guedes et al., 2011 (6)
9	F/58	II	Systemic retinoids, systemic steroids, sulfasalazine and methotrexate	2	10	25 mg ×2/week	RA	Present case

None of the cases had complications.

Cy: Cyclosporine; PUVA: psoralen plus ultraviolet A phototherapy; RA: rheumatoid arthritis.

Three of these 8 cases were treated with 50 mg of etanercept twice a week as the starting dose. The other 5 patients continuously received 50 mg once a week or 25 mg twice a week. However, there was no significant difference in the clinical remission or maintenance dose between the 2 groups. Our patient showed rapid clinical remission within 2 months of treatment with 25 mg of etanercept twice a week.

Eight cases of PRP associated with arthritis have been reported. Only one male patient was positive for rheumatoid factor, but his features were not sufficient to qualify for RA diagnosis (7). As far as we know, this is the first case of PRP associated with RA. The concurrent treatment of PRP and RA may be challenging (7). This case strongly suggests that etanercept is a proper treatment for PRP cases associated with RA. In addition, the present case is the second example of a patient with type II PRP who received etanercept for a long period (2). Our patient experienced 9 months of sustained clinical remission and relapse after drug-withdrawal, which is similar to a previous case.

While the pathogenesis of PRP is not certain, an immunological response to antigenic triggers has been proposed (8). The clinical response to etanercept in PRP patients suggests that TNF- $\alpha$ -related inflammatory reactions (e.g. interleukin-1, -6, and -8) are involved in the pathogenesis of PRP. To understand the role of etanercept in PRP treatment, further studies are needed that investigate which cytokines or immune cells change in PRP skin after anti-TNF- $\alpha$  treatment. It is not yet known whether etanercept modifies the chronic course of PRP.

In conclusion, etanercept should be considered an effective treatment option for chronic PRP, because it can induce long-term remission.

The authors declare no conflicts of interest.

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