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CASE REPORT

Long-Standing Remission After Tildrakizumab Treatment in a Case of Refractory Type I Pityriasis Rubra Pilaris in a Breast Cancer Patient

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Abstract: Pityriasis rubra pilaris (PRP) is a rare chronic inflammatory skin disease characterised by follicular keratotic papules and perifollicular erythema coalescing into orange-red scaly plaques, and palmoplantar keratoderma. Characteristic islands of sparing are usually observed. A standardised therapeutic approach is lacking owing to the infrequent occurrence of this disease. However, anti-interleukin (IL)-17 and anti-IL-23 therapies have recently emerged as effective therapies in patients affected by PRP, with improvements in severity scores, change in severity of erythema, scaling, and thickness of lesions. Here, we report a 43-year old, female breast cancer who developed severe refractory PRP, which greatly impacted her quality of life. The patient experienced a marked improvement after treatment with tildrakizumab. Treatment was stopped after one year, and the three-year follow-up did not show relapse. In conclusion, 52- week treatment with tildrakizumab, an IL-23 antagonist, proved to be a favourable treatment option for PRP, leading to good patient adherence, improvement in quality of life, and long-term follow-up without relapse.

Keywords: pityriasis rubra pilaris, treatment, tildrakizumab, breast cancer

Pityriasis rubra pilaris (PRP) is a rare, chronic, papulosquamous inflammatory dermatosis whose pathogenesis remains unclear. It is clinically characterised by keratotic follicular papules, well-demarcated salmon-coloured scaly plaques interspersed with distinct islands of unaffected skin, and palmoplantar keratoderma.[1] Both sexes and all ages, including children, are affected, with two common peaks: the first in childhood (1–10 years of age) and the second in adulthood (50–60 years of age). According to Griffiths' classification, based on the age of onset, clinical features, prognosis, and other associated aspects, five types of PRP were distinguished.[1] The disease duration may vary from month to year. Treatment is a major therapeutic challenge owing to the lack of clinical evidence.

Case Report

A 43-year-old patient receiving tamoxifen for adjuvant treatment of oestrogen-positive breast cancer diagnosed 4 years ago presented with widespread, scaly, red-orange plaques showing keratotic follicular papules on the scalp, chest, back, and limbs. Skin lesions showed extensive coalescence with circumscribed islands sparing the trunk and the upper and lower extremities (Figure 1a and b). Mild palmoplantar keratoderma was observed. The laboratory test results did not reveal any significant abnormalities. Family history of psoriasis and PRP were negative. Skin biopsy revealed alternating orthokeratosis and parakeratosis, psoriasiform acanthosis, follicular plugging with parakeratosis at the edges of the follicular orifice, and marked acantholysis in multiple areas. The immunofluorescence analysis yielded negative results. Based on clinical and histopathological findings, the patient was diagnosed with type 1 PRP. Prior systemic treatments included oral steroids (prednisone 0.5 mg/kg/day tapered over 6 weeks) and cyclosporine (3 mg/kg/day for 4 months) without any noticeable therapeutic effect. UVB 311 nm phototherapy (24 exposures) was also performed without any clinical improvement. The Total Body Surface Area (BSA) involved was approximately 40%, with a significant impact

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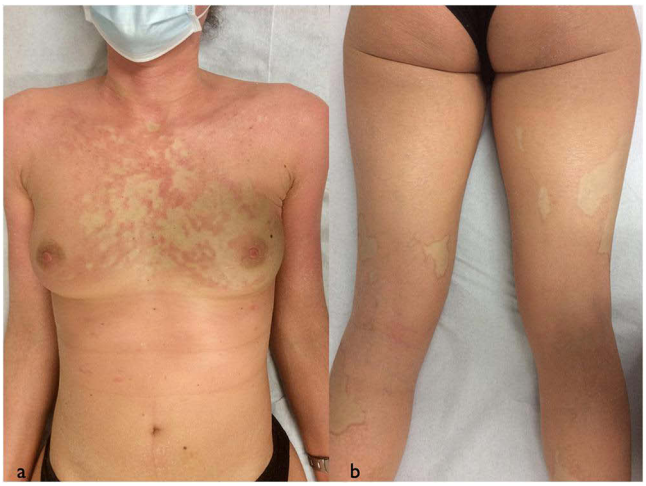

Figure 1 (**a** and **b**). Extensive skin involvement with small islands of sparing on the trunk and lower extremities before tildrakizumab treatment.

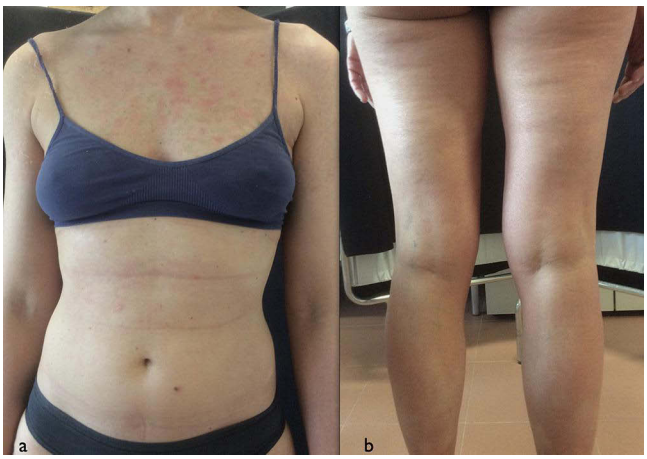

Figure 2 (**a** and **b**). Skin improvement after 16 weeks of therapy with tildrakizumab with residual patches on the pectoral area.

on the patient's quality of life (DLQI: 20) and daily functioning. Owing to the disease severity, persistent itchy symptoms, lack of efficacy of previous therapies, and cancer history, treatment with tildrakizumab was initiated. The drug was administered subcutaneously at a dose of 100 mg (weeks 0, 4, and 12-weekly thereafter). The treatment was continued at a 12-week subcutaneous dose of 100 mg.

Significant improvement was observed after 16 weeks, with residual mild palmar hyperkeratosis and erythematous skin patches in the pectoral region (Figure 2a and b). The BSA and DLQI ratings were 5% and 4, respectively. At week 28, only scattered patches were observed in the pectoral region, with BSA 4% and DLQI 4.- At week 40, a sustained therapeutic effect was observed and no adverse effects were reported. The treatment was stopped after 52 weeks. A three-year follow-up did not reveal relapse of PRP or any adverse effects. The oncologic follow-up results were negative.

Discussion

PRP is a keratinisation disorder of unknown aetiology. It has been postulated that this could be an exacerbated immune response to antigenic triggers with a preferential helper Th17 cell expression profile.[2–4] Therefore, the central role of the interleukin 23–helper T cell 17 axis has been highlighted, providing a rationale for targeting this pathway.[2,4] Proteomics and gene expression profiles have also shown dysregulation of nuclear factor κB.[3]

PRP, especially in its severe form, significantly affects the quality of life and psychosocial well-being of the affected patients. Owing to their low occurrence rates, treatment recommendations are lacking. Systemic anti-psoriatic treatments

such as retinoids and methotrexate have been used with mixed results. An increasing number of studies have highlighted the effectiveness of anti-psoriatic targeted therapies. A review of relevant studies published up to June 2023 following the PRISMA guidelines collected 10 studies with encouraging outcomes with both risankizumab and guselkumab. Among the 11 patients treated with risankizumab, 10 showed notable improvements in various disease domains, including pruritus, erythema, and the affected body surface area. All five patients treated with guselkumab exhibited improvement, with complete clearance in three of five cases.[5] However, not all PRP types seem to be responsive, having seen treatment failure in the case of type IV PRP with ustekinumab.[6] Recently, a single-arm, non-randomised trial was conducted with guselkumab in 14 adults with moderate-to-severe PRP, of whom 12 completed the trial. The primary endpoint was the mean change in the Psoriasis Area Severity Index (PASI) score at week 24. The results showed a mean improvement in the PASI score, pruritus, and Dermatology Life Quality Index scores of 61.8% ($P < 0.001$), 62.3% ($P = 0.001$), and 60.2% ($P < 0.001$), respectively. Stronger dysregulation of keratinocyte development pathways was observed in the non-responder patients.[3]

Tildrakizumab is a humanised monoclonal IgG1 antibody targeting the p19 subunit of IL-23, which results in inhibition of IL-23 signalling. It has been licenced for the treatment of moderate to severe chronic plaque psoriasis. To date, only a few cases of tildrakizumab therapy in patients with PRP have been reported, with a positive and fast response, even in the erythrodermic type.[7–10]

The key findings of this case are the treatment with tildrakizumab in a patient with breast cancer and the timing of cessation of therapy in PRP. While tildrakizumab does not carry a warning for malignancy risk, there is still limited data on safety in patients with malignancy. Interestingly, IL-23/IL-23 receptor gene expression levels were also found to be high in breast cancer tissues as well.[11] Finally, we achieved near-complete remission of PRP after 52 weeks of tildrakizumab treatment. One year treatment was sufficient to prevent relapse during a 3-year follow-up.

A consistent number of real-world clinical experiences may play a role in drug repurposing for orphan diseases such as PRP, although the possibility of spontaneous remission has to be taken into account. Additional research may help to establish more appropriate treatment schedules and ideal duration of treatment.

Ethics and Consent

Institutional approval was not required to publish the case details.

The patient was fully informed of the report's purpose and provided her consent for publication of her case and photographs.

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The authors report no conflicts of interest in this work.

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