Risankizumab for the treatment of pityriasis rubra pilaris postanaplastic large cell lymphoma

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Key words: anaplastic large cell lymphoma; biologics; IL-23; lymphoma; pityriasis rubra pilaris; risankizumab.

INTRODUCTION

Pityriasis rubra pilaris (PRP) is a rare, papulosquamous, inflammatory dermatosis. There are 6 clinical subtypes of PRP, defined by age of onset, clinical presentation, and disease course. Juvenile-onset subtypes of PRP are less common, have a less favorable prognosis and are often more difficult to treat.[1]

Because of its rarity, evidence on the treatment of PRP is limited. For many years, the mainstays of management have been topical corticosteroids, systemic retinoids, methotrexate, and phototherapy. In more recent years, the trend toward biologic therapies has extended to PRP. A number of publications have reported the successful use of biologic therapies including interleukin (IL) 17 and IL-23 inhibitors.[2] Biologic therapies are still a relatively new drug class and understanding of potential adverse sequelae of their use are still evolving. Because of their inherent role in lymphocyte modulation concerns have long existed about a potential increased risk of lymphoproliferative disorders for those on biologic therapies. Available evidence varies depending on biologic and lymphoma subtype.[3] Nevertheless, a rare cohort of patients will experience both lymphoma and a dermatologic condition that is best managed with biologic therapy. Current guidelines from the Joint American Academy of Dermatology and National Psoriasis Foundation recommend a wait period of 5 years from malignancy diagnosis to use of a biologic therapy. However, they also acknowledge a lack of definitive evidence to support this recommendation, particularly for IL-12/IL-23 and IL-17 inhibitors.[4]

Abbreviations used:

ALCL:	anaplastic large cell lymphoma
IL:	interleukin
PASI:	Psoriasis Area and Severity Index
PRP:	pityriasis rubra pilaris

Here, we present a case of a patient with juvenile-onset PRP successfully treated with the IL-23a inhibitor risankizumab after developing anaplastic large cell lymphoma (ALCL).

CASE REPORT

The now 47-year-old was first diagnosed with PRP at the age of 5 years. Genetic testing in recent years was negative for the CARD14 mutation. The patient had previously been trialed on multiple treatments for PRP. Systemic therapies including acitretin, methotrexate, and cyclosporine offered inadequate response and a course of UV-B was ceased because of photosensitivity. He had also previously received multiple biologic therapies including secukinumab; to which the patient was a primary nonresponder and ustekinumab and infliximab; both of which had limited response with secondary loss of efficacy. The patient was subsequently commenced on the IL-17A inhibitor ixekizumab, achieving a Psoriasis Area and

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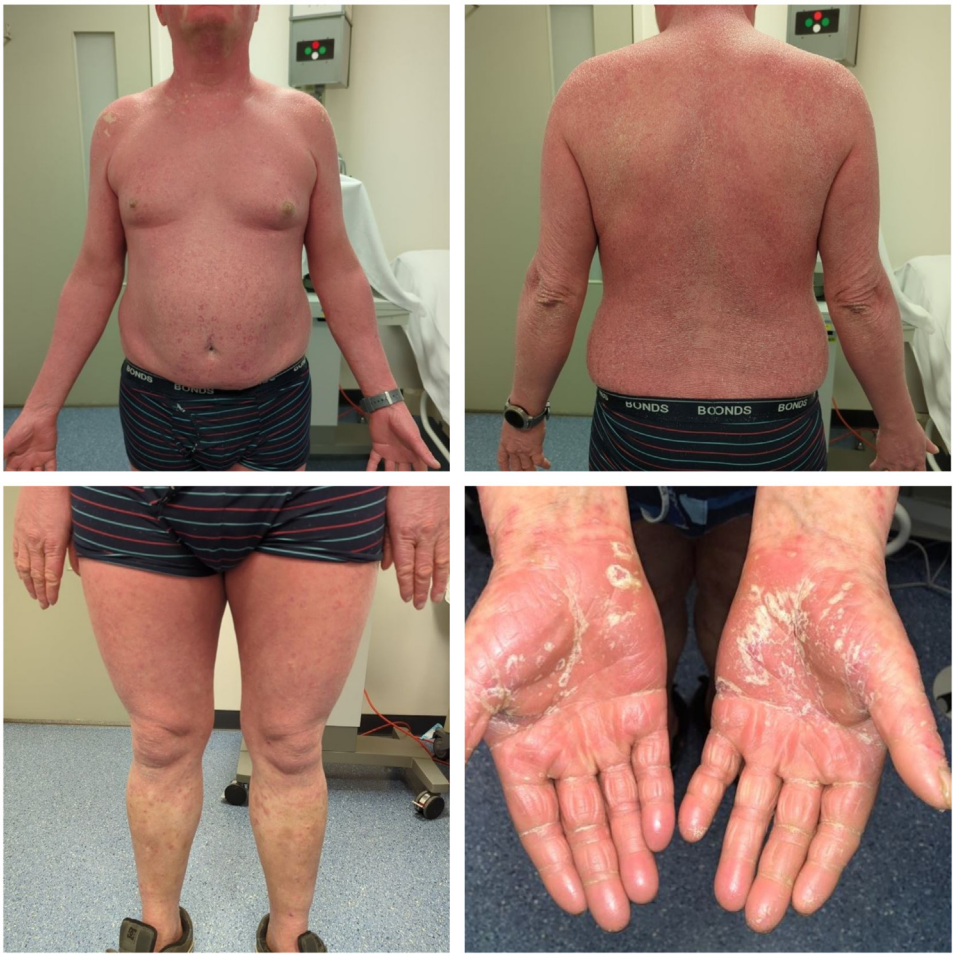

Fig 1. Patient before commencement of risankizumab.

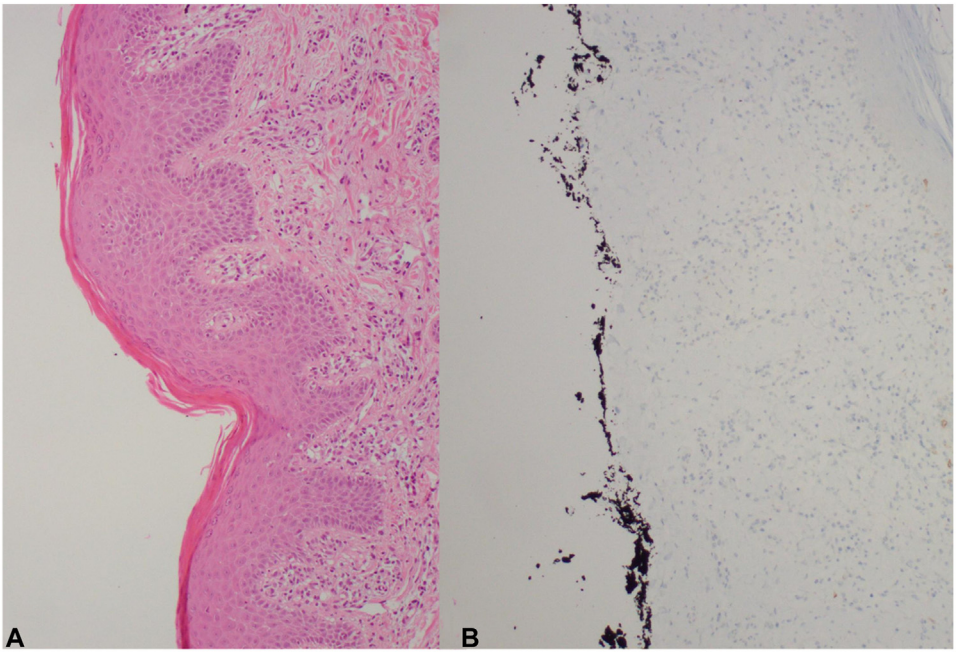

Fig 2. A, Histopathology of 2 mm shave biopsy from left arm treated with hematoxylin-eosin stain with checkerboard parakeratosis, characteristic of pityriasis rubra pilaris. **B**, Immunohistochemistry staining showing sparse CD30+ cells, not in keeping with atypical lymphoid cells.

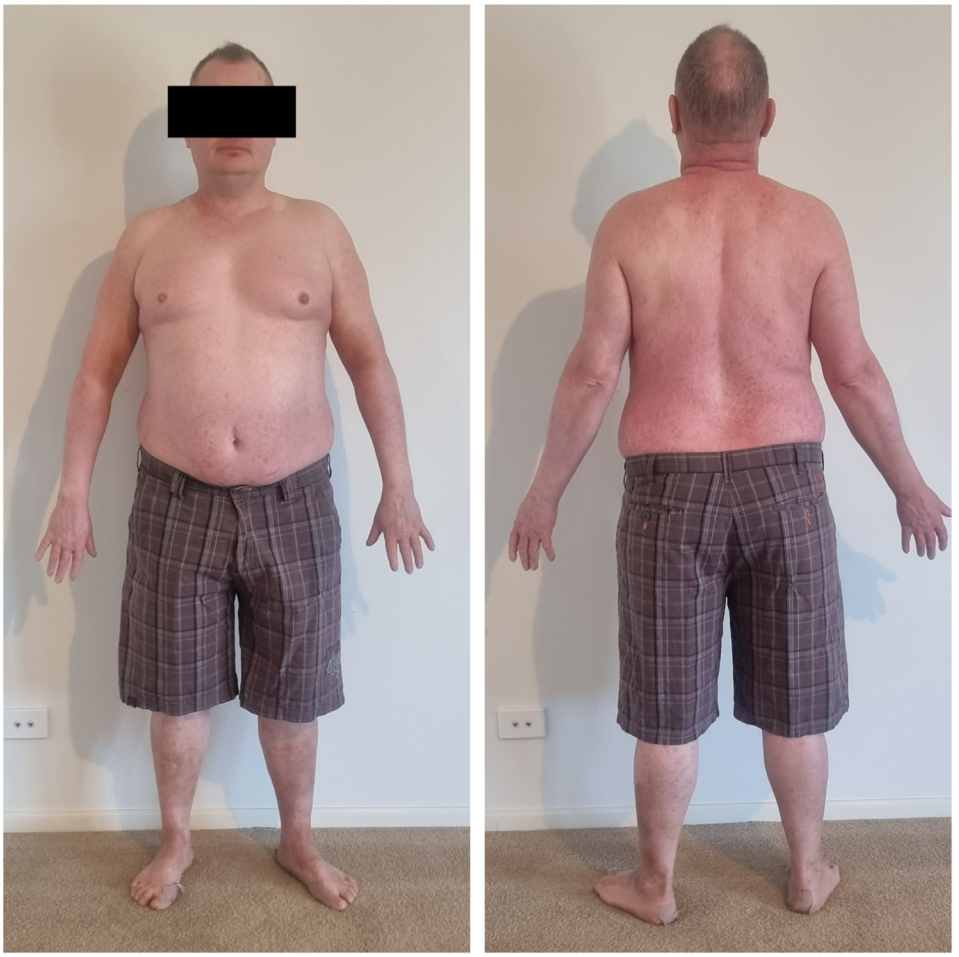

Fig 3. Patient after 9 months on risankizumab.

Severity Index (PASI)[5] of 4.5, the PASI being used to assess disease activity of his PRP.

Five years after commencing ixekizumab, the patient was diagnosed with stage 1A ALCL on left axillary lymph node biopsy after a computed tomography scan for investigation of atypical chest pain. The decision was made to cease the ixekizumab given the evolving evidence around the potential interplay between IL-17 and cutaneous T-cell lymphoma.[6]

Two months after the cessation of ixekizumab, the patient's skin began to flare. He developed characteristic hyperkeratotic follicular papules, coalescing into red-orange plaques with islands of sparing and palmoplantar keratoderma (Fig 1). The clinical morphologic features of the rash were the same as the pattern of his PRP that he had since childhood. A total of 6 punch and shave biopsies from the limbs and abdomen were performed with largely inflammatory nonspecific findings. Three of the biopsies did show mixed parakeratotic foci amidst orthokeratosis, in keeping with a diagnosis of PRP. Immunohistochemistry showed sparse staining for the CD30 receptor, excluding a cutaneous manifestation of lymphoma (Fig 2).

The patient was treated with 6 cycles of brentuximab, cyclophosphamide, and doxorubicin for his ALCL. Two months after completing chemotherapy, the patient was commenced on risankizumab, which was up-titrated to 150 mg subcutaneously every 8 weeks to treat his PRP. Before commencement, his PASI was 28.6 and his Dermatology Life Quality Index[7] was 15. At 9-month review, the patient had a PASI score of 6 and a Dermatology Life Quality Index of 2 (Fig 3). At 12 months post chemotherapy, the patient has had no recurrence of ALCL.

DISCUSSION

This case of juvenile-onset PRP in an adult patient successfully treated with singular risankizumab therapy adds to the growing body of case reports demonstrating the efficacy of risankizumab for the treatment of both juvenile and adult-onset PRP.[2,8] Because of the rarity of both non-Hodgkin lymphoma subtypes and PRP, large scale studies on safe use of biologics in these patients are near impossible to develop. Case reports

such as the one we present provide an important example of the safe use of an IL-23 inhibitor in a patient with a recent history of ALCL and challenge current guidelines. Ultimately, further research is required to better guide the balance of risk of biologic therapies in patients with a history of lymphoma.

Conflicts of interest

None disclosed.

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