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CASE REPORT

# Risankizumab-Aggravated Crusted Scabies in a Patient with Down Syndrome

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## ABSTRACT

Risankizumab, an interleukin (IL)-23 antagonist, is a highly effective treatment for moderate to severe psoriasis. Crusted scabies (CS) is a rare and severe form of scabies, occurring mainly in immunosuppressed patients and/or neurologically or mentally ill patients. A young girl with Down syndrome was diagnosed with a hyperkeratotic form of psoriasis. As treatment with topical dermocorticosteroids, UVB-phototherapy and acitretin for 6 weeks did not improve the lesions, two injections of risankizumab were administered. Following these injections, the lesions became rapidly even more severely crusted, and new lesions appeared on the extremities and the face of the patient. There was histological evidence of a high charge of scabies, leading to a diagnosis of CS. The patient was hospitalized and successfully treated by local permethrine and systemic ivermectine. This case suggests that even though anti-IL23 antagonists display an excellent overall safety profile, a particular caution for infections should still be respected in patients with underlying risk factors.

**Keywords:** Cutaneous parasitic infections; Crusted scabies; Down syndrome; Immunosuppression; Interleukin-17; Interleukin-23; Psoriasis; Risankizumab

**Key Summary Points**

Crusted scabies is a rare disease affecting mainly fragile patients.

The immune response against crusted scabies requires T-helper (Th)2 and Th17 cells.

Practitioners should consider crusted scabies when confronted with hyperkeratotic and scaly nail or skin lesions with or without pruritus.

Crusted scabies is a complication of biotherapies, affecting directly or indirectly the interleukin (IL)-17 pathway.

Anti-IL23 and anti-IL17 antagonists should be used with caution in patients with Down syndrome.

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## INTRODUCTION

Crusted scabies (CS) or hyperkeratotic scabies is rather exceptional and poorly known to general practitioners and even to dermatologists [1]. Its rarity and clinical heterogeneity make the diagnosis difficult [2]. Risk factors for CS are immunocompromised patients in general and/or individuals suffering from neurologically or mentally debilitating diseases [1–4]. Patients with Down syndrome are even at higher risk to develop CS as they present immune alterations altering their anti-infectious defense lines [5]. Classes of immunosuppressive drugs constituting a specific risk factor for CS are not clearly established. Cases of CS during biotherapies have only been rarely reported in the literature.

A young patient with Down syndrome with scabies, misdiagnosed and treated as psoriasis, presented a severe aggravation and extension of the scabies infestation resulting in CS following unjustified injections of risankizumab, an anti-interleukin (IL)-23 antagonist.

This case report was written after receiving oral and written consent from the patient and patient's mother, and was compliant with the University Hospital ethical guidelines. Written informed consent was also obtained from the patient and the patient's mother for the publication of the patient's clinical pictures.

## CASE PRESENTATION

A 26-year-old woman with Down syndrome presented at the Emergency Department with a severe inflammatory and ichthyosiform dermatosis affecting her face and extremities (Fig. 1).

The patient lives alone with her mother and was not attending any specialized institution. She had been consulting a dermatologist for 2 years for psoriasis-like lesions. Initially her hands presented various degrees of hyperkeratosis and pachyonychia on the nails; however, progressively hyperkeratotic ichthyosis-like lesions appeared on the fingers and the limbs. These lesions were non-pruritic and no scratch lesions were identified. She had never previously presented any dermatological problems and had a completely normal skin. Her mother had a longstanding history of psoriasis limited to the elbows. The clinical aspects and the genetic history orientated to a diagnosis of psoriasis. The patient was initially treated with clobetasol propionate 0.05% ointment (once daily) for several weeks, without any clinical improvement, then treated with betamethasone combined with calcipotriol ointment (once daily) for several weeks. As this last topical treatment did not improve the patient's lesions, it was decided to use UVB-phototherapy (3 times per week for a total of 30 sessions) while continuing the use of topical steroids with creams containing 10% urea. There were still no clinical improvements, so the topical dermocorticosteroids were stopped and oral acitretin (20 mg/day) was administered for 8 weeks in combination with a keratolytic cream (10% urea) (once daily). Again, there was no clinical improvement of the lesions, leading the dermatologist to switch to a biotherapy. Two injections of risankizumab were administered with a 15-day interval between injections. In the weeks following the last injection, the patient's skin condition deteriorated progressively, and new profuse crusted lesions appeared on previously non-involved skin areas, prompting the visit to the Emergency Department. At admission, the entire tegument was hyperkeratotic with an ichtyosiform appearance, with an important involvement of the scalp and the extension regions of the limbs. She also had multiple and painful skin fissures in the flexural areas (Fig. 1). There were no systemic signs or no fever, and lymphadenopathies were not identified. A skin biopsy was performed and revealed an epidermal infiltration of a large number of *Sarcoptes scabiei*, leading to a final diagnosis of CS (Fig. 2). A blood sample revealed hyperleukocytosis (14.000/mm$^3$) with a predominant increase of neutrophils (86%) as well as a severe inflammatory syndrome (C-reactive protein 124 mg/L), probably linked to a bacterial superinfection of the fissured lesions. Her mother also presented signs of pruritic scabies infestation at presentation as well did an uncle living in the same house. The origin of the infestation was unclear, particularly as the


**Fig. 1** Severe hyperkeratotic, crusted, scaling and fissuring crusted scabies of the hands (**a**), lower extremities (**b**) and face (**c**) at admission

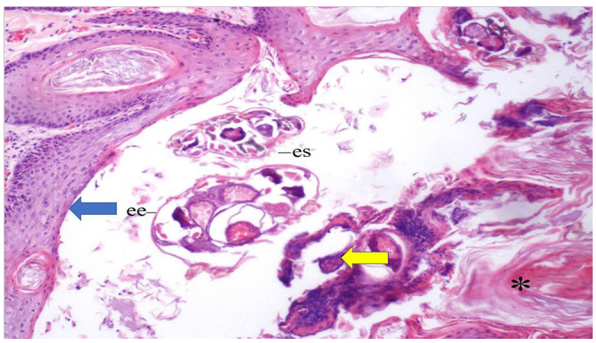


**Fig. 2** High load of scabies in the skin biopsy. *es* Triangular needles, *ee* scabies exosqueleton. Asterisk indicates hyperkeratosis, yellow arrow denotes eggs, blue arrow denote the epidermis

patient did not attend any institution. Due to the severity of the dermatosis and the Down syndrome the patient was hospitalized. The anti-parasitic treatment scheme was based on the published recommendations for CS [6]. A tube of 30 g of permethrin (50 mg/gr) cream was applied in the evening for 8 h, from day 1 to (and including) day 7, with a repetition of the application twice a week for a duration of 4 weeks. The local treatment was combined with ivermectin tablets (0.2 mg/kg) on days 1, 2, 8, 9, 15, 22 and 29. The patient also received supportive pain medication (paracetamol 4 × 500 mg/day when needed) and local keratolytic care (urea cream 15%, 1–2/day). After 1 week of hospitalization, the patient's inflammatory syndrome regressed rapidly and her skin condition improved progressively. One month after discharge there were no signs of recurrent disease (Fig. 3).

## DISCUSSION

Crusted scabies or hyperkeratotic scabies is a rare variant of *Sarcoptes scabies* var. hominis infestation [1]. In such infestations, the mites colonize the stratum corneum by the thousands [4, 7]. CS preferentially develops in individuals with cellular immunity deficiency (organ transplant recipients, bone marrow recipients, persons with human immunodeficiency virus [HIV], lymphomas, etc…) and debilitated individuals (dementia, Down syndrome, quadriplegic, etc…) [1–5]. Debilitation or the inability to scratch may furthermore lead to an uncontrollable proliferation of the parasites


**Fig. 3** Aspect of the face (**a**), hands (**b**) and lower limbs (**c**) 1 month after hospitalization

[1, 2, 5]. Several studies identified a T-helper (Th)1/Th2-cell imbalance with a deficiency in the Th2 response in CS [8]. In classical scabies, the parasitic proliferation is controlled by both cellular and humoral immunity. In CS, there is no control of the parasitic proliferation despite high levels of immunoglobulins E and blood hypereosinophilia [2]. Skin biopsies of CS patients have revealed an absence of B lymphocytes or specific antibodies but a large quantity of T lymphocytes (T cells) with a high CD8+/CD4+ ratio [7], suggesting an important role of CD8+ T cells against CS. This ratio is reversed in cases of classic scabies, for which the count for CD4+ T-cells is fourfold higher than that for CD8+ T-cells [7]. The precise role of the cytotoxic T cells in CS is not yet clear. They may have a direct effect on the keratinocytes and may partially explain the inflammatory response.

The clinical manifestations of CS are highly polymorphous, with the most common being diffuse, thickened squamous-crusted lesions with palmoplantar hyperkeratosis and nail deformities [1]. Unlike classic scabies, pruritus is not always a symptom [3, 4]. The usual locations are the extremities and scalp, but the disease can spread over the entire skin [3, 4]. A frequent complication is a bacterial infection of the skin cracks [2, 3]. Psoriasis is a common misdiagnosis, particularly in the absence of itch [2, 4, 7].

In addition to their various anatomical and physiological alterations, patients with Down syndrome present modifications of their innate and adaptive immunity with a moderate lymphopenia, impaired T-cell proliferation, impaired neutrophil chemotaxis and a poor humoral response, resulting in an increase in the frequency and severity of infections and autoimmune and hematological pathologies [9]. CS is not uncommon in individuals with Down syndrome, although the exact mechanisms for the increased propensity are still not fully known [5]. It is possible that the mental deficit of these patients also contributes to CS due to an altered interpretation of itching if present [5, 9]. In addition, patients with Down syndrome often live in institutions with other debilitated residents, which are typical environments favoring scabies epidemics [7].

CS is also observed in kidney transplant and HIV-positive patients [10]. More recently, a dozen cases of CS have been described in

patients using anti-tumor necrosis factor alpha therapies; including etanercept [11], adalimumab [6, 12] and infliximab [13]. One case was described in a patient on ipilimumab, an anti-T-cell CTLA-4 antibody, for the treatment of melanoma [14]. IL-23 leads to downstream IL-17 and IL-22 production, inducing chemokines that will attract neutrophils and macrophages to the infested sites [15]. Indeed, very high levels of IL-17 have been measured in the skin of CS patients [16]. Therefore, by blocking IL-23, risankizumab decreases the activation of Th17 cells and the production of IL-17 [17], decreasing the activation of the chemotaxic and stimulatory system of neutrophils and macrophages, an important defense line against CS. The long-term use of topical corticosteroids probably maintained the scabies infection, but no aggravation nor extension, indicative of CS, was ever observed. Furthermore, as the use of topical corticosteroids as interrupted at least 2 months before the injections, it seems more likely that the transformation of scabies into CS was linked to the injections rather than to any other drug the patient had used.

## CONCLUSION

In conclusion, the Down syndrome initially facilitated the scabies infestation. Chronicity was probably linked to the longstanding use of topical corticosteroids. Finally, the risankizumab-linked IL-23 and downstream IL-17 blockade transformed the scabies infestation into severe CS. Specific caution should be paid for infections when using biologicals affecting directly or indirectly the IL-17 pathway in patients with Down syndrome.

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***Authorship Contributions.*** Yseult Senterre and Arjen F. Nikkels both contributed equally to the design, case report, medical care, and interpretation of results.

***Disclosures.*** Yseult Senterre, Gaëlle Jouret and Patrick Collins have nothing to disclose. Arjen F. Nikkels is a member of the journal's Editorial Board.

***Compliance with Ethics Guidelines.*** This case report was written after receiving oral and written consent from the patient and patient's mother, and was compliant with the University Hospital ethical guidelines. Written informed consent was also obtained from the patient and the patient's mother for the publication of the patient's clinical pictures.

***Data Availability.*** Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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