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Tumor necrosis factor antagonist-induced psoriasis in a 3-year-old boy with Kawasaki disease

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Abstract

Tumor necrosis factor (TNF) antagonists have been known to trigger new-onset psoriasis in adult and pediatric patients. Here we report a case of TNF antagonist-induced psoriasis in a 3-year-old boy treated with infliximab for Kawasaki disease. Our patient is a 3-year-old boy with Kawasaki disease unresponsive to intravenous immunoglobulin who was then treated with one dose of infliximab. A few days later he developed psoriatic plaques on the face and extremities. The psoriatic plaques were treated with topical calcineurin inhibitors and topical corticosteroids, with marked improvement. Prior reports of TNF antagonist-induced psoriasis in the pediatric population have been in children with inflammatory bowel disease or juvenile idiopathic arthritis. To the best of our knowledge, this is the first case of TNF antagonist-induced psoriasis in a pediatric patient with Kawasaki disease, and the youngest patient to date. Although we do not fully understand the mechanism behind this phenomenon, *in vitro* studies have implicated the importance of interferon-α, a pro-inflammatory cytokine, and plasmacytoid dendritic cells. Further research is necessary to understand who is at risk for this condition and the molecular basis for this paradoxical reaction.

Keywords: pediatric, Kawasaki, TNF antagonist-induced psoriasis, infliximab

Case Synopsis

A 3-year-old boy presented to the authors a rash on his face, arms, and legs. One month prior, he had been diagnosed with Kawasaki disease after developing fever, posterior cervical lymphadenopathy, dry cracked lips, a strawberry tongue, swelling and desquamation of the hands and feet, and a rash on the abdomen. He was initially treated with intravenous immunoglobulin (IVIg) and high-dose aspirin, but his fever persisted. He received a second dose of IVIg, still without improvement, and subsequently received one dose of infliximab after which his fever resolved. Several days after receiving infliximab, he developed a rash on his face, arms, and legs.

On physical examination, he had well-demarcated, erythematous scaly plaques on his face, arms, and legs (**Figure 1**), consistent with plaque psoriasis. There was no erythema of his oropharynx or perianal erythema. He denied a sore throat or joint pains. There was no family history of psoriasis, inflammatory bowel disease, or other autoimmune disorders. A throat culture was negative for streptococcus. He was treated with tacrolimus 0.03% ointment twice daily (lesions on the face) and triamcinolone 0.025% ointment twice daily (lesions on the body). Three weeks later, the lesions had resolved leaving only post-inflammatory hyperpigmentation. To date, he has not had any recurrence.

Case Discussion

Tumor necrosis factor (TNF) antagonist-induced psoriasis is a paradoxical finding first reported in adults treated for disorders including inflammatory bowel disease (IBD), rheumatoid arthritis, ankylosing spondylitis, and Behcet disease [1,2]. In 2009, the Federal Drug Administration (FDA) mandated an

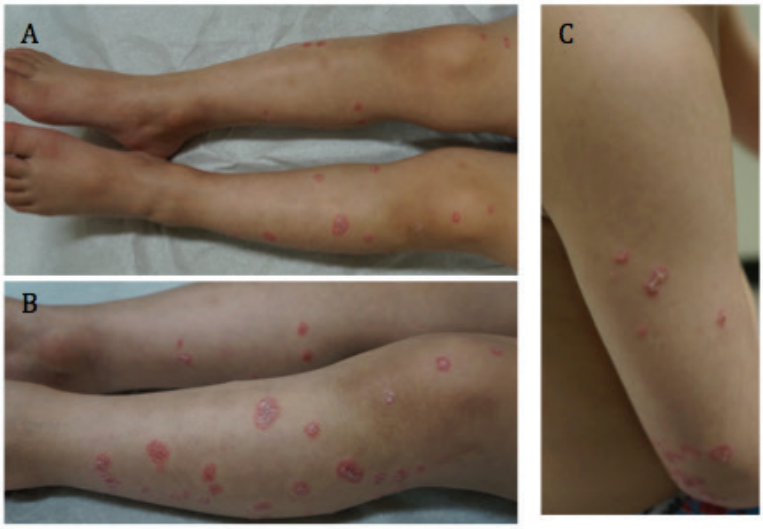

Figure 1. *Infliximab-induced psoriasis on the extremities of a 3-year-old boy. Images depictingwell-demarcated, erythematous plaques with silveryscale on the lower extremities (A, B) and upper extremity (C) of a 3-year-old boy after one infusion of infliximab for the treatment of Kawasaki Disease.*

update to the Adverse Events for TNF antagonists that included the possibility of new-onset psoriasis, especially pustular and palmoplantar psoriasis [3].

TNF antagonist-induced psoriasis in children is most commonly associated with IBD and has been noted in 10-50% of patients in two larger studies developing this phenomenon [4,5]. There are case reports associated with juvenile idiopathic arthritis (JIA) as well [6-8]. In a large retrospective study, the median age of onset of TNF antagonist-induced psoriasis was 14.6 years [4]. Whereas psoriasis can occur anywhere, scalp and preauricular involvement is frequently reported and can result in scarring alopecia [7]. The most commonly implicated medication is infliximab, although cases have occurred after exposure to adalimumab and etanercept [6-8]. Lesions have appeared after only one dose of infliximab, as with our patient, and even several years into therapy. The majority of patients do not have a family history of psoriasis.

Fortunately, most children can be managed with topical corticosteroids and continue treatment with the anti-TNF agent. In the study by Malkonen et al., only 7 of the 84 children had to discontinue therapy. None required systemic therapy or phototherapy. However, there is one report of a 12-year-old boy with CD who developed pustular psoriasis that persisted despite discontinuing infliximab and required treatment with methotrexate [9].

Current data suggests that plasmacytoid dendritic cells are abnormally found in the skin of patients with psoriasis [10]. These cells produce large amounts of interferon α, contributing to the inflammatory milieu [11]. Another study showed that CD patients with anti-TNF-induced psoriasis were more likely to have certain genetic polymorphisms in the interleukin-23 receptor [4], which is implicated in the pathogenesis of psoriasis [12].

Interestingly, there are a few case reports of children with Kawasaki disease not treated with TNF blockers developing psoriasis-like eruptions [13,14]. Haddock et al. described 11 cases of psoriasis-like eruptions in children with Kawasaki disease, of whom only 3 had been treated with infliximab [15]. The lesions most commonly resembled those of plaque psoriasis, but had more of a serous exudate or crust. We cannot, therefore, exclude the possibility that our patient's psoriatic lesions were related to the Kawasaki disease itself and not the infliximab.

Conclusion

The TNF blockers are used extensively in children with IBD and JIA. Their use will likely be expanded to other chronic pediatric disorders as our safety and efficacy data accumulates. The mainstay of treatment for Kawasaki disease is IVIg and high dose aspirin, however a double-blind trial highlighted the use of infliximab for more severe cases [16]. Further research is needed, especially at the molecular level, to fully understand why certain patients treated with TNF blockers are more susceptible to this paradoxical side effect and why some patients with Kawasaki disease in general are more likely to develop psoriasiform eruptions.

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