

Cyclosporine for refractory Kawasaki disease with psoriasiform eruption



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INTRODUCTION

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is a systemic inflammatory illness that most commonly occurs in children. Its classic symptoms include fever, polymorphous eruption, oral mucosal changes, erythema and swelling of the hands and feet with eventual desquamation, lymphadenopathy, and conjunctivitis.^{1,2} Cardiac sequelae, mainly coronary artery aneurysms or ectasias, occur in up to 25% of untreated patients with KD.² The cutaneous eruption has variable morphology including polymorphous, morbilliform, scarlatiniform, and may rarely present with a psoriasiform morphology.³ Approximately only 1.3% of patients with KD will develop a psoriasiform pattern.⁴ This psoriasiform eruption may develop during or after the acute phase of the disease.² Treatments for KD involve aspirin (ASA) and intravenous immune globulin (IVIG) as first-line therapies. For treatment-refractory cases, immunomodulatory treatments, including corticosteroids, infliximab, anakinra, methotrexate, and cyclosporine, have been used.^{2,5} Cyclosporine may be beneficial for the treatment of recalcitrant KD, as recent evidence has demonstrated that the calcium-nuclear factor pathway may play a role in KD pathogenesis.⁶ However, there are minimal data regarding the treatment of the associated psoriasiform eruption when traditional therapies are ineffective. We present a case of refractory KD with psoriasiform eruption in a 5-month-old infant treated with cyclosporine.

Abbreviations used:

ASA: aspirin
IVIG: intravenous immune globulin
KD: Kawasaki disease

CASE REPORT

A 5-month-old male presented with a 3-week history of fever and intermittent rashes. Physical examination revealed bilateral conjunctivitis, erythema and fissuring of the lips, swelling of the distal extremities, desquamation of the hands and feet, and onycholysis involving mostly the fingernails. Laboratory workup revealed leukocytosis, thrombocytosis, and elevated erythrocyte sedimentation rate (83 mm/h; normal, <13 mm/h) and C-reactive protein (3.5 mg/dL; normal, <1.2 mg/dL). Blood cultures were negative. An echocardiogram revealed moderate ectasia of the right coronary (z-score: 4.9) and mild ectasias of the left main coronary and the left anterior descending coronary arteries. A diagnosis of KD was made, and treatment was initiated with high-dose ASA (50 mg/kg divided into 4 times a day) and IVIG infusion (2 g/kg). He was monitored for 72 hours after infusion. He remained afebrile and was discharged home on low-dose ASA and clopidogrel therapy.

He presented 3 days later for a follow-up echocardiogram, which demonstrated a new saccular aneurysm in the first diagonal artery off the left

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anterior descending coronary and worsening of the ectasias. His conjunctivitis was persistent and desquamation was observed, with the development of a new rash on the bilateral upper extremities and cheeks, consisting of erythematous papules and plaques with fine white scales (Figs 1 and 2). A punch biopsy from his arm revealed uniform psoriasiform hyperplasia with mild spongiosis, thinning of the suprapapillary plates, hypogranulosis, hyperkeratosis with parakeratosis and neutrophils, and vascular dilation in the dermal papillae with prominent dermal and epidermal neutrophilic infiltrates (Fig 3). Histopathological features of secondary bacterial impetiginization were not present.

He was started on enoxaparin and, 7 days after the first IVIG infusion, received an additional IVIG (2 g/kg) infusion and one infliximab infusion (10 mg/kg). A repeat echocardiogram demonstrated a new aneurysm with progressive worsening of his previous ectasias. Due to his progressive cardiac disease, he was started on intravenous cyclosporine (5 mg/kg divided twice daily) and was transitioned to oral cyclosporine upon discharge from the hospital. The resolution of the psoriasiform eruption was noted within 4 weeks after starting cyclosporine. Intermittent flares of the eruption occurred when the cyclosporine dose was tapered down. These were well controlled with topical corticosteroids. Cyclosporine was weaned off without a relapse of his cutaneous and systemic disease after 6 months of therapy.

DISCUSSION

A psoriasiform eruption is a well-recognized, albeit rare, manifestation of KD. Psoriasiform eruption most commonly resembles plaque psoriasis, with a predilection for the trunk, extremities, and diaper area.⁴ It typically resolves with IVIG, ASA, and topical steroid therapy and does not adversely affect patient outcomes.⁴ In recalcitrant cases, tumor necrosis factor- α inhibitors, such as infliximab or etanercept, may be considered. Our patient had minimal and transient improvement on several treatment modalities, including topical steroids, IVIG, ASA, and infliximab. As a result of this treatment resistance, cyclosporine was utilized and was successful in treating his cutaneous eruptions and stabilizing his systemic disease. The use of cyclosporine for reducing other common symptoms and inflammation associated with KD has been studied.⁷ One study demonstrated that more than 64% of patients became afebrile following the use of cyclosporine for KD.⁸ Another study demonstrated that IVIG in combination with cyclosporine resulted in reduced coronary artery symptoms in comparison to the use of IVIG alone.⁶ The median duration of



Fig 1. Psoriasiform eruption in Kawasaki disease. Erythematous papules and plaques with a fine white scale on bilateral upper extremities.



Fig 2. Psoriasiform eruption in Kawasaki disease. Erythematous papules and plaques with a fine white scale on the bilateral cheeks, chest, and upper portion of the right arm.

psoriasiform eruption in KD in previous studies is over 8 months, suggesting that cyclosporine therapy may have decreased the duration of the psoriasiform eruption in our case as well as improved systemic symptoms⁴

The cause of psoriatic eruption in KD is currently unknown, although there are several proposed mechanisms. Since KD is an autoinflammatory condition, some studies have theorized that the release of cytokines “unmasks” psoriasis in predisposed patients. The release of cytokines may activate T-cells, causing the release of interleukin-1 α , which could subsequently lead to psoriasis due to an increase in T-cells in the skin.³ Another potential mechanism involves bacterial superantigens from *Staphylococcus aureus* or *Streptococcus pyogenes*. Superantigens can bind V β 2 receptors on T-cells, causing their activation and the production of proinflammatory cytokines, which is a process that was previously reported for psoriasis vulgaris and guttate psoriasis.^{1,3} The patient in this case report had a history of upper respiratory infections but no confirmed bacterial infections. Certain genes have

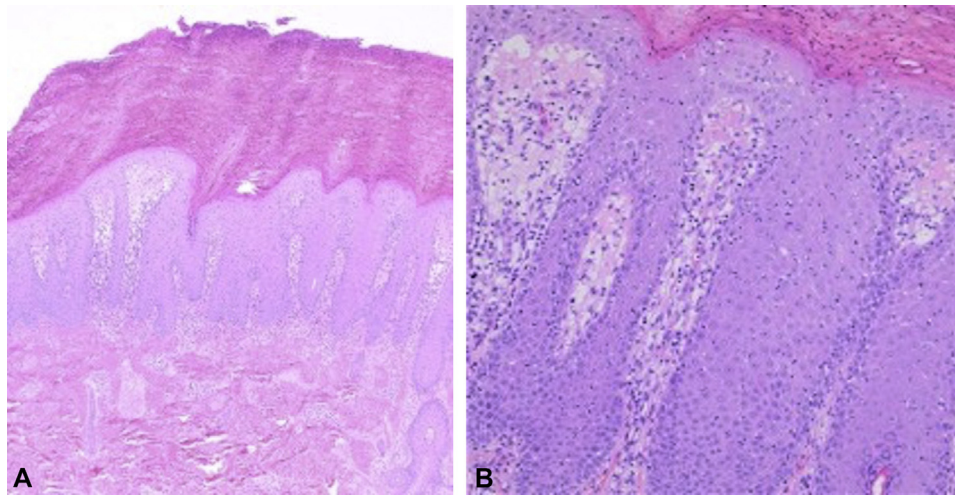


Fig 3. Punch biopsy demonstrating uniform psoriasiform hyperplasia with mild spongiosis, thinning of the suprapapillary plates, hypogranulosis, hyperkeratosis with parakeratosis and neutrophils, and vascular dilation in the dermal papillae (**A** and **B**). (Original magnifications: **A**, $\times 10$; **B**, $\times 40$.)

also been shown to confer susceptibility to the development of KD.⁶ These genes upregulate the calcium-nuclear factor pathway that plays a role in the development and activity of T-cells.⁶ Therefore, an increase in inflammatory cytokines, such as IL-2, can be seen. Cyclosporine inhibits this pathway, potentially explaining its effectiveness for mitigating the manifestations seen in patients with KD.

This patient represents a case of treatment-resistant KD with psoriasiform eruption. While the refractory systemic disease was the main indication for cyclosporine in our case, this medication proved to be successful in controlling both his systemic and cutaneous disease. This case demonstrates the benefits of cyclosporine in patients with refractory KD.

Conflicts of interest

None disclosed.

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