

Primary Treatment of Kawasaki Disease with Corticosteroids

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ABSTRACT

Kawasaki disease (KD), is the leading cause of acquired heart disease in children in the developed world. The use of aspirin and intravenous immunoglobulin as the initial therapy in KD is the standard of care, as they reduce the incidence of coronary artery aneurysms, the major cardiac morbidity from this disease. The place of corticosteroids in the initial therapy is; however, controversial. We describe the course of a one-year-old child with Kawasaki disease who was treated with aspirin and corticosteroids as the initial therapy, and discuss pertinent issues.

Keywords: Coronary aneurysms, Corticosteroid, Kawasaki disease, Management, Outcome

CASE REPORT

A one-year-old male child presented to the pediatric emergency with the chief complaint of high grade fever for eight days, rash with edema over bilateral hands and feet for five days and irritability for five days. Patient had been on treatment from a local doctor in the form of paracetamol and oral cephalexin, with no response to this treatment. On examination, child had a temperature of 101°F, was toxic, and had tachycardia and tachypnea. He had a maculopapular rash with edema over bilateral hands and feet, bilateral non-exudative bulbar conjunctival injection, and a strawberry tongue. There was no lymphadenopathy or other rash on the body. Systemic examination did not reveal any other significant findings. A provisional diagnosis of atypical Kawasaki disease was made. Investigations did not reveal any alternate aetiology.

On day two of admission, an echocardiographic examination by a paediatric cardiologist revealed an aneurysm (internal diameter, 3.5 mm) in the left main coronary artery. Treatment with IVIG and high dose aspirin was planned, but could not be done due to resource constraints. IVIG was not available in the hospital and the patient was unable to afford the same. Due to the exigency, and given the availability of methylprednisolone in the hospital, patient was given

IV methylprednisolone (dose: 30 mg/Kg/day for 3 days) and aspirin (dose: 100 mg/Kg/day divided in 4 equal doses for 14 days). The child started responding by day 6 of hospital stay; fever subsided, toxicity decreased and edema and rash started clearing. The tachycardia also settled.

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) done on day 14 of hospital stay showed improvement (ESR, 44 mm FHR; CRP, 5.6 mg/dl as compared to 76 and 12.8 mg/dl, respectively on day 1). The edema and rash over hands and feet had subsided completely and replaced by dry, peeling skin. He was discharged on the same day on oral aspirin (dose: 5 mg/kg/day) and advised to be under regular follow up. Patient has now been under follow up for 31 months. His ESR, CRP and total leucocyte count normalized by 1 month of discharge. Echocardiography done after 1st month [Table/Fig-1], 6th month and 9th month reveal no increase in the size of aneurysm or appearance of new lesions. He continues to be on aspirin, has been gaining weight and is healthy. There have not been any recurrences of the disease so far.

DISCUSSION

The use of aspirin and intravenous immunoglobulin (IVIG) is the recommended initial therapy in KD [1]. As the pathology of KD consists of an immune-mediated panvasculitis of small and medium-sized muscular arteries, corticosteroids with their well-known and strong anti-inflammatory properties are expected to be of benefit. The available literature is contradictory [2-4], even though the recent RAISE study has provided evidence for advantage of corticosteroids plus intravenous immunoglobulin in high-risk patients with Kawasaki disease [5].

This may well be due to different modes of using steroids in KD, some use it as 'rescue therapy' (administered in children who fail initial IVIG therapy), whereas others address 'primary therapy' (corticosteroids administration as a component of first-line therapy, which may or may not include IVIG) [6]. The differences between these studies could also have been due to the differing dose of aspirin (30 mg/kg vs 80-100 mg/kg) or steroids (prednisolone 2 mg/kg/thrice-a-day vs IV methylprednisolone 30 mg/Kg once-a-day), or even IVIG (1 g/Kg/day for 2 days vs 2 g/Kg once). However, none of the previous studies has used the regimen, which we had to use due to pressing circumstances. Due to resource-constraints, in this patient, we could only use aspirin and corticosteroids, and follow-up showed presence of a small-sized coronary aneurysm (AHA criteria) [1].



[Table/Fig-1]: Echocardiography done one month after diagnosis shows an aneurysm of internal diameter=3.5mm in the left main coronary artery

A recent trial studied the effect of the addition of intravenous methylprednisolone to conventional therapy with IVIG and aspirin [7]. Patients who received steroids had a shorter duration of fever and shorter hospital stays, as well as a lower mean ESR and median CRP 6 weeks after the onset of illness [4]. Although, no difference in coronary outcomes was noted. Children receiving corticosteroids and IVIG, compared with those who receive IVIG alone, have been shown to have reduced levels of cytokines, including interleukin-2 (IL-2), IL-6, IL-8, and IL-10 within 24 hours of IVIG administration [7]. However, as per the most recent guidelines for Kawasaki disease, the usefulness of steroids in the initial treatment of Kawasaki disease is not well-established (evidence level C) [1].

The most compelling evidence for steroid use in KD comes from the meta-analysis by Wooditch, et al., [2]. They performed a meta-analysis of 862 children and found a significant reduction in the incidence of coronary artery aneurysms among patients who received corticosteroids and aspirin with/without IVIG, compared with aspirin alone or with IVIG. Newer studies are now testing steroid plus IVIG-aspirin combination in those not responding to the initial therapy or those likely to have more resistant disease [4,5,8].

The standard treatment of Kawasaki disease in the acute stage has been intravenous immunoglobulin and high dose aspirin therapy. IVIG has been shown to reduce the prevalence of coronary disease from 20-25% in children treated with aspirin alone to 2-4% in those treated with IVIG and aspirin within the acute stage of treatment [1]. The cost of IVIG in the Indian setting is prohibitive, to say the least. Methylprednisolone is relatively less costly. If definitive benefit or even equivalence between initial aspirin plus corticosteroid and

the standard regimen can be conclusively demonstrated in large RCTs, the use of corticosteroids may be justified.

CONCLUSION

The purpose of the present report is to inform the pediatricians regarding the role of corticosteroids in the treatment of Kawasaki disease.

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