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REGRESSION OF CORONARY ARTERY ANEURYSM POST INTRAVENOUS IMMUNOGLOBULIN (IVIG) AND ASPIRIN TREATMENT WITHIN A MONTH IN CLASSIC KAWASAKI DISEASE IN AN INFANT

Dr. Saiprasad Onkareshwar Kavthekar*

Associate Professor, Department of Pediatrics, D.Y. Patil Medical College and Hospital, Kolhapur (416006), Maharashtra, India.

***Corresponding Author: Dr. Saiprasad Onkareshwar Kavthekar**
Associate Professor, Department of Pediatrics, D.Y. Patil Medical College, Hospital and Research Institute, D.Y. Patil Education Society (Deemed to be University), Kolhapur(416006), Maharashtra, India.

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ABSTRACT
Most cases of Kawasaki disease (KD) occur between the ages of 6 months and 8 years and is the leading cause of acquired heart disease in children. KD is generalised systemic vasculitis that affects small to medium sized blood vessels throughout the body however the coronary arteries are involved in the majority of the cases in the form aneurysms. They develop in up to 25% of untreated children however with treatment the risk is reduced to less than 5%. The fact that coronary artery aneurysms (CAA) may undergo regressions /resolutions has been reported. In some patient's regression occurs dramatically over a short period of time whereas in others it takes over years. Here I report a case where CAA regressed within a month, a very short time, after IVIG and aspirin therapy in classic KD in an infant.

INTRODUCTION
Kawasaki disease (KD) was first described in Japan in 1967 by Dr.Tomisaku Kawasaki and also termed as 'Mucocutaneous Lymph-node Syndrome', which had been affecting infants and young children in Japan.[1,2] Most cases occur between the ages of 6 months and 8 years and is now the leading cause of acquired heart disease in children in developed countries.[3]

The diagnosis of classic KD is based on the exclusion of any other disease and the presence of at least 5 days of fever and at least four of the five principle clinical features: bilateral non-purulent conjunctivitis, polymorphous skin rashes, abnormalities of the lip or oral mucosa, abnormalities of the extremities and cervical lymphadenopathy. KD is generalised systemic vasculitis that affects small to medium sized blood vessels throughout the body however the coronary arteries are involved in the majority of the cases in the form aneurysms.[3] They develop in up to 25% of untreated children however with treatment the risk is reduced to less than 5%.[4] These coronary changes may lead to myocardial infarction, ischemic heart disease or sudden death and therefore dictate the patients management after the acute phase of disease.[5]

Furthermore, regression of coronary artery aneurysms (CAA) have been reported by Glantz et al[6] in the united states and by Kato et al[7] in Japan. In some patient's regression occurs dramatically over a short period of time whereas in others it takes over years. In this case report, I report a case where CAA regressed within a month, which was a very short time after intravenous immunoglobulin (IVIG) and aspirin therapy in classic KD in an infant.

CASE
6 month male infant presented with history of fever for seven days which was moderate to high grade and unremittant in nature. Also he had history of truncal maculopapular rash on body which appeared on day 2 of illness and disappeared on 6th day. On examination baby was sick looking, febrile 102^{0}F, heart rate 120beats/minute, RR 22/minute, BP: 80/60 mm of Hg, having bilateral non purulent conjunctivitis, strawberry tongue, diffused erythema of the oropharyngeal mucosa, erythema of palms and soles, edema on feet and right sided cervical lymphadenopathy which was non tender and 2 cm in diameter. There was no hepato-splenomegaly and the cardiovascular and respiratory system examination was normal. On investigations, his complete blood count showed Haemoglobin 8.8gms/dl, TLC-16800 cells/cumm, N54%, L41%, E2%, M3%, Platelet count 730000/cumm and ESR60mm/hr and CRP was 47mg/l. His Chest X-ray was normal. The 2 D Echocardiography was done on the same day of admission and showed dilated coronaries, even after adjusted with body surface area [Left anterior descending (LAD) :2mm and Right coronary artery (RCA) :1.9mm] with single aneurysm in left main

coronary artery [LMCA aneurysm 3.2mm] and normal bi-ventricular dimensions and function. Child was treated with IVIG 2Gms / kg over 10 hours and high dose of oral Aspirin 80mg/kg/day in 4 divided doses as an anti-inflammatory dose. His fever came down to normal in next 36 hours and CRP came to normal after 72 hours. As CRP came to normal, the dose of Aspirin was tapered to 2 mg/kg day as an antiplatelet dose and continued till 1 month. Child was monitored for next 72 hours and discharged as clinical signs and symptoms improved.

2 D Echocardiology was repeated at 4 weeks after IVIG and Aspirin treatment and showed coronaries diameter were normal and regression of LMCA aneurysm [LMCA 1.8 mm, LAD 1.6mm, RCA 1.8 mm.]. The child was totally asymptomatic and his TLC, platelet count, ESR and CRP came to normal. His 2 D Echocardiography was repeated again twice, after 6 months and 1 year and which showed total resolution of coronary aneurysms and normal diameter coronaries.

DISCUSSION

KD is an acute febrile illness of childhood seen worldwide with the highest incidence occurring in Asian children, and a predilection for the coronary arteries.[8]The cardiac complications of KD are CAA, decreased coronary arterial compliance, myo-pericarditis, arrhythmias, valvular regurgitation, myocardial infarction and sudden cardiac death. The most commonest complication is CAA.[8,9] The risk factors to predict the presence of CAA include boys less than 1 year of age, fever lasting longer than 2 weeks ,elevated erythrocyte sedimentation rate persisting for more than 4 weeks and palpable axillary artery aneurysms.[8]

Patients with an acute KD should be treated with 2g/kg of IVIG and high dose of aspirin (80-100 mg/kg/day divided q6h) within 10 days of disease onset and ideally as soon as possible after diagnosis.[8] The mechanism of action of IVIG in KD is unknown, but treatment results in resolution of clinical signs in approximately 85% of patients.[8] Even strong consideration should be given to treating patients with persistent fever and / or signs of systemic inflammation who are diagnosed after the 10th day of fever. The patient with KD who has had a small solitary aneurysms should continue aspirin indefinitely. Patients with larger or numerous aneurysms may require the addition of other antiplatelet agents or anticoagulation.[8]

Overall, 50 % of CAA regress to normal lumen diameter by 1 -2 years after the illness with smaller aneurysms being more likely to regress. Giant aneurysms are less likely to regress to normal lumen diameter and are most likely to lead to stenosis and thrombosis.[8] The influence of CAA morphology on resolution is the most important factor. Fusiform CAA appear to resolve commonly than saccular ones. In Fusiform lesions there is more gradual transition from normal luminal diameter to the maximally dilated point. Whereas saccular lesions represent more abrupt change from normal to abnormal and more severe disruption of vascular wall architecture. Alternatively, there would be fusiform lesions are partially healed lesions with intimal proliferation which is already in progress.[10] This difference may be due to enhanced activity of platelet dependent growth factors in certain patients.[11] CAA in the distal segment were always associated with CAA in proximal segments. The regression process appeared to start in the distal segments of the coronary arteries and proceed centrally.[10] The right coronary artery and the circumflex branch of a dominant left coronary artery may be more prone to extensive aneurysms.(ectatic or segmented varieties), because of their courses within the atrioventricular grooves where the walls are not embedded in the myocardium.[10] The size less than 4 mm in diameter regresses spontaneously within a short time[10], where as those larger than 8 mm in diameter are often associated with a stenotic lesion.[12] Coronary artery lesions are dynamic in the late acute and early convalescent phases. The longer the time, aneurysms or stenotic lesions persist, they are less likely to resolve.[13] Takahashi M et al[10] concluded that age less than 1 year at the onset of KD, female sex, fusiform morphology and distal ones are significant factors that favor resolution of CAA. The mechanism of regression of CAA is remodeling of the vessels with fibrosis and proliferation of subendothelial tissues.[10,14] Intravascular ultrasonography has demonstrated that even regressed aneurysms are associated with marked myo-intimal thickening and abnormal functional behavior of the vessel wall.[8]

CONCLUSION

KD is generalised systemic vasculitis that affects small to medium sized blood vessels throughout the body however the coronary arteries are involved in the majority of the cases in the form aneurysms. Patients with an acute KD should be treated with 2g/kg of IVIG and high dose of aspirin (80-100 mg/kg/day divided q6h) within 10 days of disease onset or ideally as soon as possible after diagnosis and it will be helpful to regress/resolve CAA.

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