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Giant coronary and systemic aneurysms in an infant with missed Kawasaki disease and the role of apixaban

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ABSTRACT

Infants with Kawasaki disease (KD) are at an increased risk of coronary artery aneurysms. Systemic artery aneurysms (SAA) have been sparingly reported in KD and can pose unique therapeutic challenges. In this report, we describe a nine-month-old male infant who presented with giant coronary and bilateral axillary artery aneurysms as a sequela of missed KD. He was treated with infliximab and corticosteroids, along with anticoagulation with apixaban. This case highlights the challenges involved in managing SAA in patients with KD and emphasizes the importance of anticoagulation to prevent thrombotic complications. We also discuss the use of apixaban as a potential treatment option for these patients.

1. Case report

A nine-month-old male infant of Indian parentage presented with swellings in both axillae for the past eight days. At four months of age, he experienced an acute febrile illness for 19 days, accompanied with diffuse macular rashes, non-exudative conjunctivitis, and cheilitis. The treating pediatrician diagnosed him with multi-systemic inflammatory syndrome (MIS-C) and treated him with a short course of oral steroids. On examination, the patient had bilateral pulsatile axillary swellings. Radial pulses were palpable, and systemic examination was unremarkable.

During the current admission (at nine months of age), he had thrombocytosis (650×10^9/L), leukocytosis (20.6×10^9/L), and raised inflammatory markers (ESR 45 mm/h). Axillary ultrasonography revealed bilateral hypoechoic fusiform aneurysms, measuring 18 × 12 mm in right and 29 × 15 mm in left axilla. Color Doppler demonstrated turbulent vascular flow with mild mural thickening (1.4 mm on right and 1.7 mm on left side), indicating early thrombus formation. Computerized tomography (CT) angiography confirmed the presence of axillary artery aneurysms, while other systemic arteries appeared normal [Fig. 1]. Echocardiography revealed aneurysms affecting the left main coronary artery (9 mm, Z score + 17.9), left anterior descending artery (3.5 mm, Z score + 9.4), left circumflex artery (4.2 mm), and right coronary artery (3.5 mm, Z score + 5). He was treated with intravenous infliximab (5 mg/kg) and short course of oral steroids. Upon discharge, he was prescribed low-dose aspirin, clopidogrel, and low molecular weight (LMW) heparin.

Six months later, parents expressed eagerness to explore oral substitutes for LMW heparin as they found daily subcutaneous injections challenging. Direct oral anticoagulant Apixaban (3 mg/day in two divided doses) was initiated at 15 months of age, and LMW heparin injections were discontinued. On apixaban, anti Xa levels were 0.7 IU/ml (target range 0.6–1 IU/ml). He was continued on oral apixaban along with aspirin and clopidogrel and is doing well at 24 months of age, with no bleeding tendencies. Size of axillary artery aneurysms on physical examination and CAA on echocardiogram remain unchanged.

2. Discussion

Systemic artery aneurysms (SAA) in KD are rare, with a prevalence of 0.8 to 2 % of cases [1,2]. In patients with giant CAA, the likelihood of SAA is higher (73 %) [2]. Among SAAs, axillary artery involvement is the most common, followed by common iliac and brachial arteries. Majority of these aneurysms occur in infancy, involve medium-sized vessels, and exhibit bilateral symmetrical distribution [2,3].

There is a lack of consensus on the treatment of SAAs in children with

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KD. Chu et al. successfully used intravenous prostaglandin for a ten-month-old male infant with KD associated giant CAA and bilateral axillary artery aneurysm who presented with an occluded left axillary artery [4]. In the index case, considering the potential long-term morbidity and raised inflammatory parameters, treatment with steroids and infliximab was considered prudent. We also initiated dual antiplatelet therapy along with anticoagulation.

There is limited literature on the long term outcomes of SAA in this setting. Fortunately, rupture of SAA has not been documented [4]. Zhao et al. observed that the majority of SAAs (80 %) regress to a normal size within six months. Larger SAAs (>10 mm) had a higher risk of becoming stenotic [2].

Providing long-term anticoagulation in patients poses significant challenges in clinical practice. American Heart Association's 2017 guidelines recommend usage of LMW heparin and warfarin in infants with giant CAA [5]. However, warfarin has practical problems like erratic oral absorption and need for frequent monitoring. Apixaban, a direct oral anticoagulant, has shown promising results in a Phase II trial [6]. The trial included 188 patients (29 days - 18 years) with cardiac morbidity requiring anticoagulation, randomized into Apixaban (n = 126) and Standard of Care (SOC) group (n = 62). Sixteen patients had KD(personal communication with Prof Jane C. Burns). The endpoints were determining drug safety, tolerability, and pharmacokinetics/pharmacodynamics. Serious adverse events were noted in 20.6 % and 21 % in Apixaban and SOC group respectively. Mild hematomas (6.3 %) and epistaxis (15.9 %) were more common in Apixaban group than SOC group (1.6 % and 9.7 %, respectively) [7]. The dose was calculated on weight-based pharmacokinetic studies [6].

Dummer et al. published a case series of 24 KD patients with a median age of 33.8 [22.7–49.2] years treated with DOAC for median period of 4.9 years (4.2–8.0). Six patients were initiated on DOAC prior to 18 years, the youngest being at four years. Three patients had major cardiac events, out of which only one patient with apixaban had recurrent myocardial infarction(MI). Other two patients on dabigatran and rivaroxaban had MI involving LAD and ischemic event due to distal coronary thrombosis, respectively [8]. Sagiv et al. observed two out of 16 patients with KD to experience coronary artery thrombosis after 23 and 38 months of treatment, seven and 11 years after diagnosis, respectively. The study predicted a 70 % event-free survival at 12 years after diagnosis [9]. While apixaban has significantly improved the quality of life in our case, we intend to closely monitor the child for any adverse events.

3. Conclusion

We hereby report a rare and severe complication resulting from missed KD, leading to giant coronary and axillary artery aneurysms in an infant. To the best of our knowledge, this case likely represents one of the first case reports of Apixaban use in infantile KD.

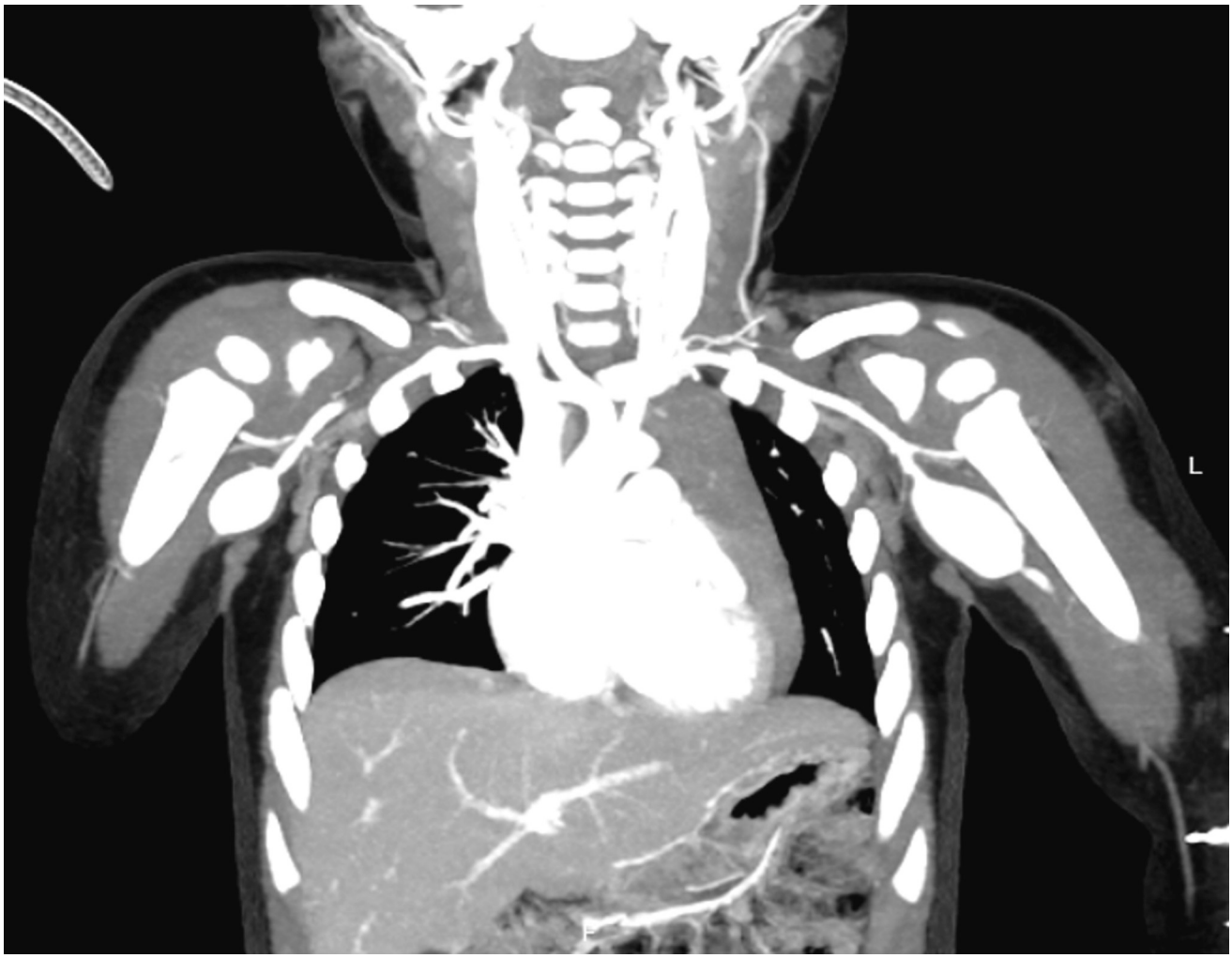

Fig. 1. MDCT angiogram with Coronal MIP reconstruction depicting bilateral fusiform aneurysms (white arrows) in right axillary artery (1.8 cm × 1.2 cm) and left axillary artery (2.9 cm × 1.5 cm) in axillary regions.

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Informed patient consent

Written informed consent will be obtained by authors from patients prior to submission of the case report.

CRediT authorship contribution statement

Neha Singh: Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Jyothi Janardhanan:** Data curation, Formal analysis, Validation. **Sudhir Kale:** Data curation, Investigation, Methodology, Validation. **Harish Kumar:** Data curation, Formal analysis, Investigation, Validation. **Chetan Ginigeri:** Data curation, Formal analysis, Validation. **Sagar Bhattad:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

No funding was received for this work.

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