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Case Report

Kawasaki Disease in Three Months Old Infant with Two Days Fever. Case Report

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Abstract

Kawasaki disease is a multi-system vasculitis which usually occurs in children under age of five years and very rare in infants less than three months. Occasionally the diagnosis is very challenging in young infants especially in the early phase of the illness. Hence it may delay the treatment which has an impact on the prognosis. In this paper, we discuss three months old female infant presented with skin rash, lethargy and conjunctivitis, but with two days of fever. Despite early administration of intravenous immunoglobulin and methylprednisolone, followed by two weeks course of oral steroid, she developed coronary artery aneurysm. This case demonstrated diagnostic dilemma regarding differential diagnosis and treatment of Kawasaki disease. Early detection of the clinical signs despite the presentation with two days of fever was the key for starting treatment.

Keywords: *Kawasaki Disease; Infant, Coronary Artery Aneurysm*

Introduction

Kawasaki disease is a multisystem vasculitis [11], usually affecting children below age of five years [4,5,7]. It is a common cause for acquired heart diseases in children. The diagnosis is based on presence of fever for at least five days, with four features of the following: non purulent bilateral conjunctivitis, polymorphic rash, mucocutaneous changes, extremities' changes and non-tender cervical lymphadenopathy. Early treatment with intravenous immunoglobulin (IVIG) can decrease risk of coronary artery aneurysm to 5% [1], along with acetylsalicylic acid [16]. Other modalities of treatment for refractory cases are now available, including steroids [2].

Case Report

Three months old female infant previously well, admitted with two days of fever documented at home 39° Celsius. It was hardly decreasing with paracetamol, associated with lethargy, poor feeding and irritability. No history of contact with sick person. Systemic review was unremarkable. Antenatal history was not significant.

Parents are not consanguineous. She has one elder sister who is healthy and doing well. No family history of any chronic illness. No previous medical or surgical admissions. She was corresponding to her age in developing milestones. She was not on any medications

prior to admission and had no history of allergy. Her immunization history was up to date. She was on breast milk feed and milk formula, and she was thriving well.

She presented to Al Nahdah Hospital Emergency Room, Muscat, Oman, where she was sick looking, irritable and crying. Vital signs showed fever with temperature of 38.8° Celsius, tachycardia with heart rate of 160 beats/min, and blood pressure was 102/54 mmHg. There was no respiratory distress: respiratory rate of 40 breaths/min and saturation of 98% in room air. Her weight was 6.2 kg.

She was looking pale and mildly dehydrated. In the triage room, she started to develop erythematous rash all over the body. On physical assessment, there were no distinctive facial features, no significant cervical lymph nodes, no jaundice or cyanosis. Anterior fontanelle was at level and no neurological deficit detected.

Rest of systemic examination was unremarkable.

Partial septic work up was done, but lumbar puncture was differed as she was persistently febrile and tachycardic. She was started on intravenous (IV) ceftriaxone (100 mg/kg/day) with initial impression of neonatal sepsis/meningitis. At admission, investigations revealed low hemoglobin (Hb) of 9.8 g/dL, normal white blood cells (WBC) count of 7.8 x 10^9/L, normal neutrophils of 5.9 x 10^9/L with normal platelet count 405 x 10^3/uL. Urine microscopy showed high WBC count of 44/uL. Both blood and urine cultures were collected. Few hours after admission, she was still spiking fever and body rash was increasing. She developed diarrhea, which was watery but non bloody.

On second day of admission, she started to have bilateral non purulent conjunctivitis, cracked lips and red tongue. Rash was more prominent with generalized maculopapular characterization. She was still spiking fever and tachycardic.

Repeated complete blood count (CBC) showed further drop in Hb 8.4 g/dL, other parameters were normal: WBC 5.6 x 10^9/L, neutrophils 3.5 x 10^9/L and platelet 463 x 10^3/uL. C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated, 146 mg/L and 25 mm/h respectively. She had hypoalbuminemia 29 g/L and increased normal alanine aminotransferase (ALT) 10^5 U/L. Sodium (Na) was on lower side 133 mmol/L, rest of electrolytes were normal. Other differential diagnosis which was considered at this point were toxic shock syndrome and Kawasaki disease. For the earlier, she was covered with antibiotics and good hydration was provided. For Kawasaki disease, it was early to start intravenous immunoglobulins (IVIG) with total of three days of fever. But in addition to the supportive laboratory results, by the evening of the same day, she had erythema of bacillus Calmette-Guerin (BCG) scar, which is pathognomonic for Kawasaki disease. So first dose of IVIG and high dose aspirin (80 mg/kg/day in four divided doses) were started.

On third day of admission, she was still febrile. Rash was fading and she started to have skin peeling of extremities and gentilia. She had generalized body edema and her weight increased by 400 grams (6.6 kg). She had abdominal distension and liver was palpable 4 cm below costal margin. Abdominal ultrasound revealed hydrops gallbladder (Figure 1) with moderate ascites. She was still febrile with several low grade spikes of fever, had loose motions and severe nappy rash. There was slight improvement in irritability but she was not active. Edema was worsening and weight increased to 6.8 kg.

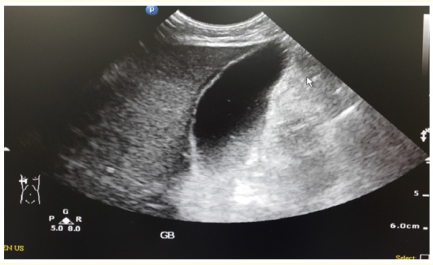

Figure 1: *Ultrasound showed hydrops gallbladder.*

Investigations were done and resulted in anemia Hb 7.8 g/dL, leukocytosis WBC 19.1 x 10^9/L, neutrophilia 13.2 x 10^9/L and normal platelet 305 x 10^3/uL. CRP dramatically increased to 215 mg/L and ESR 35 mm/h, albumin dropped to 27 g/L and ALT was still high 65 U/L. Electrocardiogram (ECG) and echocardiogram were normal. She was given IV albumin, but no much improvement.

Despite that, she continued to spike fever and had diarrhea. Mucocutaneous changes and edema were resolving gradually, and her activity started to improve. She had hepatomegaly, but no splenomegaly and no palpable lymph nodes. Blood and urine cultures were negative.

Five days later, her fever was worsening and reaching high grade 39°C and associated with lethargy. Therefore, her blood investigations were repeated and showed neutrophilic leukocytosis WBC 22.6 x 10^9/L and neutrophil 12 x 10^9/L, platelets increased to 673 x 10^3/uL. CRP decreased to 88 mg/L but ESR significantly increased to 78 mm/h. Rheumatology team was consulted and advised to start IV pulse methylprednisolone for 3 days then to continue on oral prednisolone 2 mg/kg/day. She was started on 10 mg/kg but fever was not responding, so dose increased to 30 mg/kg. After two doses of IV methylprednisolone, fever subsided and activity returned back to normal (at day 12 of admission). Diarrhea improved, and liver regressed to 2 cm. Aspirin dose decreased to antiplatelet dose (5 mg/kg/day) and oral prednisolone started. Before discharge investigations showed thrombocytosis 1212 x 10^3/uL and CRP decreased to 46 mg/L. Clinically, mucocutaneous changes and tachycardia resolved and general condition improved. She was discharged after two weeks stay in the hospital on aspirin and prednisolone for one week then tapered down. She was given close follow up appointments and she was doing well with no fever. The following table demonstrates her lab investigations during hospital stay.

Day of admission	1	2	3	5	10	11	12	15
Hb (g/dL)	9.8	8.4	8.3	7.8		8.1		8.3
WBC (x10^9/L)	7.8	5.6	13.8	19.1		22.6		23
ANC (x10^9/L)	5.9	3.5	8.8	13.2		12		12
Platelet (x10^3/uL)	405	463	411	305		673		1212
CRP (mg/L)		146		215	119		88	46
ESR (mm/h)		25		35			78	
Albumin (g/L)		29	24	27	30			30
ALT (U/L)		105	65	36	11			24

Table 1: *Blood investigations during admission.*
ANC: Absolute Neutrophil Count; ALT: Alanine Aminotransferase.

Ten days after discharge while on tapering dose of prednisolone, she was admitted again as she had occasional fever documented 38°C. Secondary Hemophagocytic Lymphohistiocytosis (HLH) and possibility of viral infections were considered. Therefore, investigations including LDH, ferritin and triglycerides in addition to EBV and CMV were collected and came normal. Other blood work up were repeated and revealed Hb 8.5 g/dL, WBC 23.8 x 10^9/L, ANC 10.9 x 10^9/L and platelets 1063 x 10^3/uL. Inflammatory markers increased further: CRP 82 mg/L and ESR 89 mm/h. In addition to the aspirin, prednisolone 2 mg/kg/day was prescribed again because of fever as recommended by rheumatology team. With that, fever improved. She continued on same dose of prednisolone until her inflammatory markers returned to normal values, then she was started on tapering dose.

One month from the initial presentation, echocardiogram showed left coronary artery dilated fusiform 6 mm aneurysmal dilatation with right coronary artery dilated fusiform 4 mm aneurysmal dilatation. Six months later, echocardiogram showed dilated coronaries (main dilations in the ostium of left main coronary artery 3 mm (Z-score 4) and distal to ostium 3.7 mm (Z-score 6). Left coronary artery

was 2.1 mm (Z-score 2). Currently she is on low dose aspirin and has regular appointment with cardiology team for follow up of echocardiogram.

Discussion

The experience of our center, Al Nahdah Hospital, Muscat, Oman, in Kawasaki disease was a total number of 12 patients (6 males and 6 females) from 2011 to 2017, including our patient in this paper. The data were retrieved from the electronic records of Al Shifa 3Plus system, electronic Health Information System in Oman. The number of patients who were below age of one year was three: 2 with typical presentation and 1 with atypical. While those who are more than one year of age were 9 patients: 6 with typical and 3 with atypical. The frequency of clinical features (See table 2) was as following: all patients had bilateral no purulent conjunctivitis and mucocutaneous changes. The frequency of rash (maculopapular, erythematous) was 66%, while extremities' changes were 58%. The least common feature was cervical lymphadenopathy. Table 3 is representing the laboratory data of the patients.

	< 1 year (No. 3)		> 1 year (No. 9)	
	Typical (2)	**Atypical (1)**	**Typical (6)**	**Atypical (3)**
Fever < 5 days at admission	1	1	2	2
Fever > 5 days at treatment	1		4	1
Conjunctivitis	2	1	6	3
Mucocutaneous changes	2	1	6	3
Rash	2		6	
Extremities changes	1		6	
cervical lymphadenopathy	1		2	3

Table 2: *Clinical features of 12 patients diagnosed with Kawasaki disease in Al Nahdah Hospital.*

Investigation	Value range (mean)
Hb (g/dL)	7.6 - 11 (9.9)
WBC x 10^9 /L	3.8 - 19.3 (12.7)
Initial platelet at admission	238 - 432 (336)
Platelet count in 2ed week	410 - 1212 (693)
CRP	60 - 216 (107)
ESR	25 - 113 (73)
albumin	21 - 35 (27)
ALT	11 - 214 (123)
Na (135 - 145 mmol/L)	Normal except in 2 patients (131-133)
Sterile pyuria	4 patients
ASO titer	Negative (not done in 2 patients)

Table 3: *laboratory investigations of12 patients diagnosed with Kawasaki disease in Al Nahdah Hospital. (Hb: hemoglobin, WBC: White Cell Count, CRP: C Reactive Protein, ESR: Erythrocyte Sedimentation Rate, ALT: Alanine Aminotransferase, Na: Sodium, ASO titer: Antistreptolysin O titer).*

All patients required one dose of IVIG, except two patients: one of them our patient in this paper and another patient required second dose because of persisting fever. Out of 12 patients, four developed coronary artery abnormalities, including our patient:

1. Prominent right coronary artery (RCA) 1.8 mm (Z score 1.35) with minimal wall thickness demonstrated at a great length, more than usual.
2. Prominent left coronary artery (LCA) 2.3 mm (Z score 1.29). Small aneurysm of the LCA bifurcation.
3. LCA fusiform aneurismal dilatation 6 mm and RCA fusiform aneurismal dilatation 3.5 - 4 mm
4. Aneurysmal dilatation of the left main artery (LMA).

All cardiac abnormalities resolved on subsequent follow up visits, except our patient.

Conclusion

The incidence of Kawasaki disease is increasing and the etiology is not yet identified. Treatment can be started even if the fever is less than five days, provided the other features of Kawasaki disease are present. It is also important to identify patients who are at high risk of developing coronary artery aneurysm, to initial other modalities of treatment at appropriate time.

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