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INSTRUCTIVE CASE

Incomplete Kawasaki disease presenting as bilateral hip synovitis

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We report a case of a 2-year-old boy who presented with prolonged fever and a limp subsequently diagnosed and managed as incomplete Kawasaki disease (KD)[1] complicated by coronary aneurysms.

Case Report

A 2-year-old boy presented in a local Emergency Department with 7 days of fever >40.1°C temporarily relieved by antipyretics. He had occasional cough and rhinorrhoea. One day prior to onset of fever, he started limping with no history of trauma, progressing to pain in his right foot on weight-bearing with difficulty mobilising independently. His general practitioner saw him on the second day of his fever and prescribed him amoxicillin and clavulanic acid (Augmentin; Aspen Pharmacare Australia Pty, St Leonards, New South Wales, Australia). The fever persisted for a further 3 days before ceasing the antibiotics with a provisional diagnosis of viral illness.

His past medical history was unremarkable. He was born full term without complication. His immunisations were up to date and he had no known allergies. There were no infectious contacts at home; however, he attended day care.

On examination, he was febrile (40.1°C) and tachycardic (196 beats/min) returning to the normal range after antipyretics. He looked pale. He had bilateral non-purulent conjunctivitis. He had multiple palpable small cervical lymph nodes with normal ear and throat examination. He had no rashes, other adenopathy or peripheral changes of oedema or desquamation. He had normal respiratory, gastrointestinal and cardiac examination. He was in pain when weight-bearing and dragged his right foot when walking. When sitting, he had normal range of motion in his hips, knees and ankles.

He had slightly raised white cell count (WCC) of 14.8×10^9/L with neutrophilic predominance, 9×10^9/L, haemoglobin of 92 g/L and mean corpuscular volume of 78 fL. He had elevated inflammatory markers: c-reactive protein (CRP) was 134 mg/L and erythrocyte sedimentation rate (ESR) was 101 mm/h. Blood culture was sterile. His electrolytes, calcium, magnesium and phosphate, renal and liver functions were normal. Urinalysis, chest x-ray and x-rays of the right hip, tibia/fibula and femur were normal. He was diagnosed with septic arthritis and transferred to the tertiary centre for orthopaedic management.

Further investigations showed persistent anaemia and raised WCC and inflammatory markers. Rheumatologic screen was normal. An ultrasound of both hips showed bilateral small hip effusions and a bone scan was normal.

He underwent bilateral hip washout. Fluid from both joints was sent off for culture. The patient was started on intravenous flucloxacillin on admission but was changed to intravenous cephazolin for broader antibiotic coverage.

Despite this, he remained febrile for a further 3 days. The cultures of aspirates from both hips were sterile. His WCC and inflammatory markers remained elevated. He remained miserable, lethargic and unable to weight bear. His nasopharyngeal aspirate had negative PCR for influenza, parainfluenza, adenovirus, enterovirus, respiratory syncytial virus, human metapneumovirus, coronavirus, rhinovirus and bocavirus.

Medical review after 12 days of fever, raised the high likelihood of KD. Rheumatology review raised the possibility of systemic-onset juvenile idiopathic arthritis (SoJIA). Intravenous antibiotics were ceased and intravenous immunoglobulin (IVIG) and aspirin started. Cardiology review and echocardiogram revealed dilated and ectatic left coronary arteries involving the left main stem coronary artery, left anterior descending artery and circumflex.

His fever settled with IVIG treatment. WCC and inflammatory markers normalised over a few days. With ongoing limping, he was given 3 days of IV pulse methylprednisolone. He was mobilising independently and was discharged on prednisolone 1 mg/kg/day that was weaned over 3 weeks.

Aspirin was continued at a low dose cardiology follow-up showed gradual resolution of his aneurysms.

Key Points

1. Incomplete Kawasaki disease should be considered in a febrile illness >5 days not responding to appropriate treatment for a presumed cause.
2. There are various multi-systemic clinical features and laboratory findings that can be noted in cases of incomplete Kawasaki disease.
3. It is important to diagnose Kawasaki disease and start treatment early to minimise mortality and morbidity associated with coronary artery changes that are the major sequelae in Kawasaki disease.

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Discussion

KD is an acute, self-limited vasculitis that occurs predominantly in infants and young children. Its aetiology remains unknown. It is a leading cause of acquired heart disease that necessitates its prompt diagnosis and management.[1]

Classic KD is diagnosed on the presence of fever for at least 5 days and at least four of the principal features of changes in extremities, polymorphous exanthem, bilateral bulbar conjunctival injection without exudates, changes in the lips and oral cavity and unilateral cervical lymphadenopathy, more than 1.5 cm in diameter.

Cardiovascular manifestations are the leading cause of morbidity and mortality commonly involving aneurysms of the coronary arteries. Other clinical findings involve the musculoskeletal system, gastrointestinal tract, central nervous system and genitourinary tract. Treatment in the acute phase aims to reduce inflammation in the coronary artery wall and prevent coronary thrombosis. Long-term therapy is aimed at prevention of myocardial ischemia or infarction.[1]

The term 'incomplete KD' is used when the patient lacks sufficient clinical signs to complete the criteria for classic KD. Patients with fever of at least 5 days and two to three clinical features should have inflammatory markers, CRP and ESR, done. If both are raised, further supplemental tests should be performed. Positive supplementary laboratory criteria include albumin of ≤3 g/dL, anaemia for age, elevation of alanine aminotransferase, platelets after five days of ≥450 000/mm^3, WCC of ≥15 000/mm^3 and urine of ≥10 WCC/hpf. Those with at least three supplemental criteria can be treated before undergoing an echocardiogram. Those with less than three positive criteria should undergo echocardiogram and if positive, receive treatment.[1] Treatment should be given to children within 10 days of fever onset and those beyond day 10 with clinical and laboratory signs of ongoing inflammation.[1]

Our case was managed as possible incomplete KD based on 12 days of fever with clinical features of non-purulent conjunctivitis and cervical lymphadenopathy. He also had anaemia, elevated WCC, and raised inflammatory markers. He was started on treatment prior to his echocardiogram.

The presence of a limp, bilateral hip effusions with raised WCC and inflammatory markers initially directed the management towards septic arthritis however it needs to be noted that symptoms of arthritis and irritability manifested by our patient are commonly seen in patients with KD.[1,2] The persistence of fever despite 3 days of intravenous antibiotics and sterile joint fluid must lead to consideration of the diagnosis of KD.

A similar case report described a 3-year-old girl who was febrile for 4 days but afebrile for 3 days prior to her presentation with a limp. Ultrasound showed small bilateral hip effusions. She had conjunctival injection and erythematous, dry lips. Laboratory results showed raised WCC, platelets and CRP. Her echocardiogram findings were consistent with KD resulting in her treatment with IVIG and aspirin.[3]

Historically, arthritis was a common component of KD but its prevalence and symptom duration has decreased with the advent of early IVIG treatment.[4,5]

A further association of arthritis and KD is reported with patients who presented with arthritis after defervescence of fever with IVIG. Their arthritis responded to high doses of acetylsalicylic acid, ibuprofen or corticosteroids. Arthritis occurred regardless of high dose acetylsalicylic acid therapy in the subacute stage and after high dose IVIG therapy suggesting that this is a reactive arthritis due to an unknown pathogen.[6]

Systemic-onset juvenile arthritis is a differential diagnosis for this presentation. It is a multifactorial autoinflammatory condition characterised by fever for more than 2 weeks, an evanescent maculopapular rash and secondary arthritis. Cardiac complications have also been noted, most frequently myocarditis and pericarditis, but there have been case reports of coronary artery dilatation and thrombus. To differentiate KD from systemic-onset juvenile arthritis, Lefevre-Utile *et al.* suggested that the latter had mild coronary changes including limited dilatation rather than true aneurysms. In addition, children with SoJIA do not respond to IVIG therapy but rather require high dose of steroids for fever defervescence. Children with SoJIA and coronary artery abnormalities required high dose steroids, were steroid dependant and had poor prognosis.[7]

The presentation of our 2-year-old boy with fever of more than 5 days with a non-traumatic limp illustrates the importance of considering KD in paediatric patients with unexplained prolonged or a fever not responding to appropriate management for presumed cause. An early echocardiogram facilitates early treatment resulting in limiting the morbidity and mortality of cardiac complications of KD.

Multiple Choice Questions

1 What is the most important investigation to arrange for a patient with suspected KD?
   a) Full blood count
   b) Inflammatory markers
   c) Echocardiography
   d) Blood culture
   e) Electrocardiography

Answer: c. Coronary artery changes are the major sequelae in KD. Cardiac imaging is a critical investigation for this condition. Echocardiography is the ideal imaging for cardiac assessment because it is non-invasive and has a high sensitivity and specificity for the detection of abnormalities of the proximal left main coronary artery and right coronary artery.[1]

2 In which of these scenarios would you decide to treat with IVIG?
   a) Five-year-old boy with fever of 6 days, polymorphous generalised rashes for the first 2 days of fever, swelling of hands and feet, non-exudative conjunctivitis, and strawberry tongue. He has WCC of 18×10^9/L with neutrophilic predominance and platelets of 500×10^9/L
   b) Two-year-old girl with fever for 10 days, sterile blood, urine and CSF cultures and rising WCC and inflammatory markers without improvement on antibiotics and noted to have hydrops of the gallbladder on ultrasound
   c) Eight-year old with fever and cough for 8 days without improvement after 3 days of oral antibiotics, normal chest x-ray, sterile blood culture and sterile pyuria, rising WCC and CRP, platelets of 650×10^9/L
   d) Seven-year old with fever for 12 days without focus, sterile blood culture, haemoglobin of 100 g/L, WCC of 23×10^9/L, CRP of 200, ESR 90 and coronary artery aneurysm on echocardiogram
   e) All of the above

Answer: e. All of these scenarios can be diagnosed as KD, scenario (a) being the typical presentation and scenarios (b)–(d) fulfil criteria for incomplete KD.[1]

3 Apart from fever of at least 5 days and principal features, what are other clinical and laboratory findings that can be seen in KD?
   a) Extreme irritability
   b) Hydrops of the gallbladder
   c) Arthritis or arthralgia
   d) Sterile pyuria
   e) All of the above

Answer: e. This can also be seen in various cases of KD.[1]

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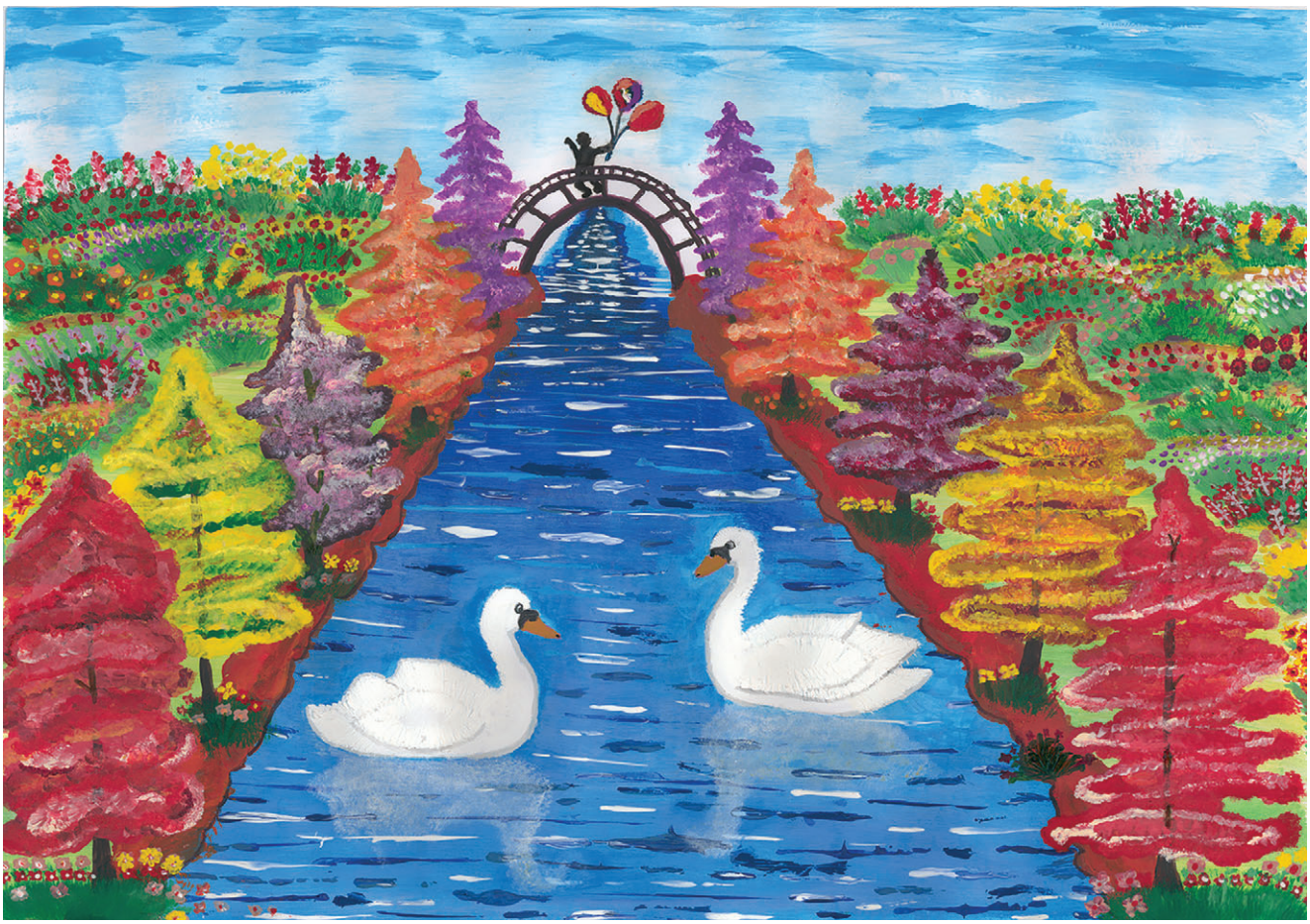

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