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CASE REPORT
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Incomplete Kawasaki Disease in an Infant with Cholangitis Post Kasai Surgery for Biliary Atresia

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ABSTRACT

Kawasaki's disease (KD) is a systemic vasculitis often seen with viral and bacterial infections. Cholangitis is a known complication in biliary atresia patients post Kasai Portoenterostomy (KP). However KD, in a biliary atresia patient post KP has not been previously reported. A 1 years old girl who had previously undergone a KP for BA, presented with cholangitis which was presumed to be caused by a previous enterobacter infection that she had 2 months ago. However, on treating the cholangitis, the patient developed fever again after ten days which persisted even after changing the antibiotics. By this time she also displayed three of five characteristic features of KD in form of fever, strawberry tongue and cervical adenopathy. Investigations showed high ESR, high CRP, thrombocythemia and dilated coronary vessels on echocardiography. Treatment with intravenous immunoglobulin (IVIG) and steroids caused the symptoms to subside.

Key words. Coronary dilatation. Hepatoportoenterostomy. Infection. Cholangiopathy.

INTRODUCTION

Kawasaki s disease (KD) is an acute febrile, usually self-limiting illness of infancy and childhood which is associated with vasculitis affecting medium sized vessels. It mainly affects children under the age of five years who comprise about 75% of the cases.[1,2] Biliary atresia (BA) is characterized by obliteration or discontinuity of the extrahepatic biliary system, resulting in obstruction to bile flow. BA is corrected by Kasai Portoenterostomy (KP) and liver transplantation is reserved only for failed cases of KP. Early surgical correction with KP leads to best chance for long term survival of patients with their native liver. Early postoperative complications include: cholangitis, bleeding, leak from anastomosis, prolonged ileus, and intestinal obstruction. Late complications include: cholestasis, recurrent cholangitis, portal hypertension, ascites, hepato-pulmonary syndrome, and formation of bile lakes in the liver. In most cases of BA, biliary cirrhosis invariably develops even in those who have a successful surgically corrected KP. Though cholangitis is a common complication in patients with operated BA, KD has never been reported in patients with BA. We present a child with BA who had undergone KP and then developed cholangitis and subsequently developed KD.

CASE REPORT

A 1 year old girl, a known case of BA, who underwent a KP at 2 months of age in June 2011 presented with fever, clay coloured stools and upper respiratory symptoms for 10 days in April 2012. She had been treated for enterobacter septicemia and pneumonia in March 2012 with meropenem and amikacin for 14 days. She was asymptomatic for 15 days in between when again she presented with present symptoms. On examination, her weight was 7 kg. She had jaundice, hepatosplenomegaly with dilated veins over abdomen and bilateral wheeze. Investigations revealed hemoglobin of 11 gm%, white blood cell (WBC) count of 18,500 cell/cumm, platelet count of 268,000 cells/cumm, bilirubin of 4.5 mg/dL and SGOT 117 IU/L, SGPT 130 IU/L. Urine examination was normal. Ultrasound of abdomen showed hepatosplenomegaly with portal collaterals suggestive of portal hypertension. Her current blood culture did not grow any organism. Respiratory panel for various micro-organisms could not be done due to non-

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availability and non-affordability. She was treated with the same antibiotics as used previously in view of her previous enterobacter infection along with ursdeoxycholic acid and multivitamins for suspected cholangitis. She responded to the same and became afebrile in next 5 days. She remained afebrile for 5 days and again developed fever, leukocytosis and strawberry tongue with enlarged cervical nodes. Her blood culture was still sterile. Urine examination showed 8-10 pus cells/hpf. Urine culture did not grow any organism suggestive of sterile pyuria. Antibiotics were changed to ciprofloxacin and cotrimoxazole and fluconazole was also added, however she had no response. In view of increasing platelets (505,000 cells/cumm), high CRP (232 mg/dL) and high ESR (120 mm at end of 1 h) along with clinical features, she was suspected to have incomplete KD. She had no conjunctivitis, edema or rash. Her WBC count was 23,500 cells/cumm. An echocardiography on Day 5 of fever showed left coronary ectasia (1.4 cm). She was subsequently treated with intravenous immunoglobulin and fever subsided within 24 h, leucocyte count and platelets normalized, CRP, ESR started decreasing. Aspirin was not started in view of portal hypertension and underlying liver disease. She was continued on ciprofloxacin and cotrimoxazole for 6 weeks. On follow-up, echocardiography, in June 2012, there was persistence of the coronary artery ectasia (1.4 cm) and intermittent fever. She was subsequently treated with prednisolone (1 mg/kg/day) which was tapered in next 21 days. Her echocardiography in July 2012 showed decrease in coronary dimensions (1.2 cm) and her fever disappeared.

DISCUSSION

The specific cause of the KD is unknown though viruses, bacteria and allergens have been implicated. Endemic instances of the disease have been found to be associated with the HLA B51 serotype. KD shows a male to female ratio of around 3:2.[2] Children of Asian descent especially Japanese and Korean are more susceptible to it. The diagnosis of KD is made when the patient is suffering from a high grade fever which does not respond well to antibiotics or antipyretics for more than five days, rash on the trunk, erythema of lips or oral cavity, cracking of lips, strawberry tongue, conjunctival inflammation, enlarged cervical lymph nodes and erythema of palm and soles.[3,4] Myocarditis, diarrhea, pericarditis, arthritis, valvulitis, aseptic meningitis, pneumonitis, lymphadenitis, and hepatitis may be present and are manifested by the presence of inflammatory cells in the affected tissues.[5] Untreated patients develop cardiac symptoms such as coronary artery aneurysm.[6] While coronary artery aneurysm is a late complication of KD, a study by Kato, *et al.* consisting of 598 patients of which 146 patients demonstrated coronary artery aneurysm using coronary arteriography in the acute phase of the disease. The arteriograms were taken at 22 days to 3 months of onset with a mean of 34 days after onset. Giant aneurysms(> 8 mm) were seen in 4 patients.[7] Hepatobiliary dysfunctions such as elevated liver enzymes, cholangitis, hypoalbuminemia, hepatomegaly, cholestasis, jaundice and hydrops of the gall bladder are known complications of KD while reduction in portal vein flow in patient of KD post liver transplant has been reported.[8] Acute hepatitis is known to rarely occur in the atypical form of KD in children though cases of classical KD with acute hepatitis have been described Grech V, *et al.*, and Andrea Taddio, *et al*.[9-11] Acute febrile hepatitis associated with elevation in ESR and CRP can prove useful tools in the early diagnosis of KD.[9,12] The exact pathogenesis of hepatic dysfunction in KD is still not known but it is attributed to a combination of vasculitis, inflammation, use of non-steroidal anti-inflammatory antipyretics, toxin mediated damage and congestive heart failure secondary to myocarditis.[13-15] Vasculitis was seen in 6 of 37 KD patients autopsied and is suspected to be the potential cause of liver abnormalities.[16] Hydrops of the gall bladder was hypothesized to occur secondary to enlarged lymph nodes in the porta hepatis by some but this has not been observed during surgery.[17] Liver biopsy of a KD patient with hepatomegaly but normal LFT, described by Edwards, *et al.,* showed selective destruction of the of the biliary ductular epithelial cells by polymorphonuclear leukocytes with sparing of the hepatocytes. It was postulated that this selective destruction extended to the distal biliary system as hydrops of the gall bladder was seen. However, vasculitis was not demonstrated in the portal area. Giant mitochondria were also seen on electron microscopy.[18] As giant mitochondria probably occur as a result of oxidative damage, the liver abnormalities could be associated with the oxidative stress in a KD patient.[19]

KD associated with cholangitis have been published in two separate case reports.[17,19] However, KD in association with cholangitis in a biliary atresia patients post KP has not been reported. Post-KP cholangitis is characterized by pyrexia, abdominal pain with or without jaundice, an increase in liver function tests and it may be associated with clay coloured stools and a positive blood culture. Cholangitis is most common in the first year post KP with an overall incidence of 40-93%.[20] Our patient presented with fever, jaundice, clay stools, hepatosplenomegaly and portal hypertension. She was treated with antibiotics for cholangitis and became afebrile, but subsequently developed clinical features of KD which responded to IVIG therapy. While KD may have bacterial or viral triggers, a specific etiological agent was not determined. One must also consider the possibility of a hypersensitivity reaction second-

ary to the use of antibiotics to treat the suspected cholangitis. While our patient did not fulfill criteria for classical Kawasaki disease she could be classified as having incomplete KD along with cholangitis. Resolution of the fever following IVIG therapy and the development of coronary aneurysm further supports the diagnosis of KD. We report this case for the rarity of association and also to highlight that fever in a patient with biliary atresia post KP may not be only cholangitis and especially in the case of persistent fever, other infections and vasculitis should be kept in mind.

Limitation of the case report: Our patient had an incomplete KD along with cholangitis. We could not prove it to be classical Kawasaki disease. However defervescence of fever with IVIG is suggestive of response to treatment KD > We could not rule out other infections in the patient due to cost issues.

DECLARATION OF CONFLICT OF INTEREST

None declared.

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REFERENCES

1. Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H. A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. *Pediatrics* 1974; 54: 271-6.
2. Lin YT, Manlhiot C, Ching JC, Han RK, Nield LE, Dillenburg R, Pepelassis D, et al. *Repeated systematic surveillance of Kawasaki disease in Ontario from* 1995 to 2006. Pediatr Int 2010; 52: 699-706.
3. Baker AL, Lu M, Minich LL, Atz AM, Klein GL, Korsin R, Lambert L, et al. Associated symptoms in the ten days before diagnosis of Kawasaki disease. *J Pediatr* 2009; 154: 592-5.
4. Newburger JW, Fulton DR. Kawasaki disease. *Curr Opin Pediatr* 2004; 16: 508-14.
5. Fujiwara H, Fujiwara T, Kao TC, Ohshio G, Hamashima Y. Pathology of Kawasaki disease in the healed stage. Relationships between Typical and Atypical Cases of Kawasaki Disease. *Pathol Int* 1986; 36: 857-67.
6. Suzuki A, Kamiya T, Kuwahara N, Ono Y, Kohata T, Takahashi O, Kimura K, et al. Coronary arterial lesions of Kawasaki disease: cardiac catheterization findings of 1100 cases. *Pediatr Cardiol* 1986; 7: 3-9.
7. Kato H, Sugimura T, Akagi T, Sato N, Hashino K, Maeno Y, Kazue T, et al. Long-term consequences of Kawasaki disease. *Circulation* 1996; 94: 1379-85.
8. Wakiya T, Urahashi T, Ihara Y, Sanada Y, Yamada N, Okada N, Hakamada K, et al. Decreased portal vein flow during Kawasaki disease in a liver transplant patient. *Pediatr Int* 2013; 55: 119-22.
9. Taddio A, Pellegrin MC, Centenari C, Filippeschi IP, Ventura A, Maggiore G. Acute febrile cholestatic jaundice in children: keep in mind Kawasaki disease. *J Pediatr Gastroenterol Nutr* 2012; 55: 380-3.
10. Grech V, Buttigieg T, Portelli A, Kotes S, Attard G, Huhn P, Gauci C, et al. Kawasaki disease presenting as hepatitis. *Ann Trop Paediatr* 2007; 27: 303-6.
11. Sève P, Stankovic K, Smail A, Durand DV, Marchand G, Broussolle C. Adult Kawasaki disease: report of two cases and literature review. *Semin Arthritis Rheum* 2005; 34: 785-92.
12. Jafari SA, Kiani MA, Ahanchian H, Khakshour A, Partovi S, Kianifar HR, Saeidi M. Kawasaki Disease Presenting as Acute Clinical Hepatitis. *Int J Pediatr* 2013; 1: 51-3.
13. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. *Br J Anaesth* 2000; 85: 599-610.
14. Ohshio G, Furukawa F, Fujiwara H, Hamashima Y. Hepatomegaly and splenomegaly in Kawasaki disease. *Pediatr Pathol* 1985; 4: 257-64.
15. Bertino JS, Willis ED, Reed MD, Speck WT. Salicylate hepatitis: a complication of the treatment of Kawasaki s disease. *Am J Health Syst Pharm* 1981; 38: 1171-2.
16. Amano S, Hozama F, Hamashima Y. Pathology of Kawasaki disease. II. Distribution and incidence of the vascular lesions. *Jpn Circ J* 1979; 43: 741-8.
17. Edwards KM, Glick AD, Greene HL. Intrahepatic cholangitis associated with mucocutaneous lymph node syndrome. *J Pediatr Gastroenterol Nutr* 1985; 4: 140-2.
18. ElAdawy M, Dominguez SR, Anderson MS, Glodé MP. Abnormal liver panel in acute Kawasaki disease. *Pediatr Infect Dis J* 2011; 30: 141.
19. Bader-Meunier B, Hadchouel M, Fabre M, Arnoud MD, Dommergues JP. Intrahepatic bile duct damage in children with Kawasaki disease. *J Pediatr* 1992; 120: 750-2.
20. Gear JH, Meyers KE, Steele M. Kawasaki disease manifesting with acute cholangitis. A case report. *S Afr Med J* 1992: 81: 31-3.
21. van Heurn LE, Saing H, Tam PK. Cholangitis after hepatic portoenterostomy for biliary atresia: a multivariate analysis of risk factors. *J Pediatr* 2003; 142: 566-71.

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