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Case Report

Coronary Artery Aneurysm in a Chinese Boy with Scrub Typhus

HT **Leung**, HM **Lee**, V **Cheng**, KC **Chan**

Abstract Coronary artery aneurysm (CAA) is uncommon in children except in Kawasaki disease. Occasionally it can be seen in children with congenital disorders such as connective tissue diseases and underlying inflammatory disease. Other reported causes of CAA such as atherosclerosis, Takayasu arteritis and infections are more common in adult patients. We reported a 11-year-old Chinese boy with fever, skin rashes and hepatosplenomegaly who was diagnosed to have scrub typhus and right coronary artery aneurysm.

Key words *Coronary artery aneurysm; Kawasaki disease; Rickettsia; Scrub typhus*

Introduction

Scrub typhus is an acute febrile zoonosis, caused by an obligate, intracellular bacterium named *Orientia Tsutsugamushi*. It is vectored by the biting of the larval life stage of infected *Leptotromidium*. It is an important differential diagnosis in patients presented with pyrexia of unknown origin, especially from Endemic areas. Scrub typhus commonly presented with fever, cough, gastrointestinal disturbance, rash, eschar and lymphadenopathy.[1]

Transient right coronary artery dilatation has been reported in a 3-year-old boy with Mediterranean spotted fever, caused by Rickettsia coronii, which belonged to the same family Rickettsiaceae as *Orientia Tsutsugamushi*.[2] Although coronary artery aneurysm (CAA) has also been reported in children with Kawasaki disease (KD) together with scrub typhus,[3] it has never been reported in patient with scrub typhus alone.

We describe an 11-year-old Chinese boy who was found to have a right coronary artery aneurysm and finally diagnosed to have scrub typhus.

Case Report

In June 2020, an 11-year-old locally born Chinese boy was first admitted to our hospital with 7-day history of fever. His family reported that he had a trail walking among the bushes in Tung Chung, Lantau Island 3 weeks before admission. He could not recall being bitten by any insects. He did not travel outside Hong Kong in the past 1 year and he did not have contact with any sick people. Patient enjoyed good past health with no history of KD.

Other than the high swinging fever, he also had a dry cough, abdominal pain and reddish maculopapular rash over his trunk. On examination, his temperature was 37.7°C, blood pressure of 126/77 mmHg, pulse rate was 122 beat per minute and respiratory rate of 24 per minute. Abdominal examination revealed tenderness over the right upper quadrant, with liver palpable 3 cm below costal margin and splenic tip was palpable. There was generalised

Department of Paediatrics and Adolescent Medicine, Alice Ho Miu Ling Nethersole Hospital, 11 Chuen On Road, Tai Po, N.T., HKSAR, China

HT **Leung**（梁羲濤） *MBBS(HK)*
HM **Lee**（李孝文） *MBChB(CUHK), FHKAM(Paed), FHKCPaed*
V **Cheng**（鄭恩華） *MRCP(UK), MRCPCH(UK), FRCP(Edinburgh)*
KC **Chan**（陳國超） *MBBS(HK), FHKCPaed, FRCPaed(UK)*

Correspondence to: Dr. HT **Leung**
Email: lhtivan@gmail.com

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maculopapular rash over the trunk, which subsided one day after admission and there was no eschar found. There was no lymphadenopathy. Other examinations were unremarkable.

Complete blood count revealed thrombocytopenia with platelet count of 59 x 10^9/L (150-384 x 10^9/L), white cell count and haemoglobin level were normal. The peripheral blood smear showed atypical lymphocytes but no blast cells. Blood tests revealed deranged liver function test with elevated Alanine Aminotransferase (ALT) of 467 IU/L (<67 IU/L), Alkaline phosphatase (ALP) of 635 IU/L (160-478 IU/L), Aspartate Aminotransferase (AST) of 357 IU/L (<50 IU/L), Gamma-Glutamyl Transferase (GGT) of 355 IU/L (<95 IU/L) and total bilirubin of 21 µmol/L (<19 µmol/L). Other abnormal blood biochemistry results were as follows: C-reactive protein 40.1 mg/L (<9.9 mg/L); Erythrocyte Sedimentation Rate (ESR) 51 mm/hour (2-19 mm/hour); Other biochemical studies including creatinine, urea, calcium, phosphate, amylase, coagulation profile, ceruloplasmin, high sensitive troponin T were all unremarkable. Nasopharyngeal swab was negative for COVID-19, influenza A, influenza B, adenovirus, parainfluenza virus, enterovirus/ rhinovirus, mycoplasma pneumonia. Sputum culture, blood culture, mid-stream urine cultures were negative. Urine streptococcus antigen was negative. EBV capsid IgM and IgG antibodies were negative. Serology studies for hepatitis A, hepatitis B, hepatitis C, Dengue virus, Bartonella henselae, Malaria were all negative. Urine and saliva cytomegalovirus (CMV) polymerase chain reaction (PCR) were negative.

The first chest X-ray taken during admission was normal, but patient started to have desaturation on day 3 of admission (i.e. day 9 of fever) requiring oxygen supplement. Repeated chest X-ray showed left lower lobe consolidation. Antibiotics namely intravenous cefotaxime and oral Azithromycin were started to treat the left lower lobe pneumonia. Computed tomography (CT) of the chest, abdomen and pelvis was also done since the child also complained of worsening of abdominal pain and he showed hepatosplenomegaly, periportal oedema and bilateral basal lung consolidation and pleural effusion. However, fever was still swinging despite the antibiotics. On day 8 of admission (i.e. day 14 of fever), a soft systolic heart murmur was detected over the left lower sternal border and electrocardiograms were all along normal. Echocardiogram was performed on the next day (i.e. day 15 of fever) and a right coronary artery small-sized aneurysm measured 4.89 mm in width (z-score: +3.77) and 11.8 mm in length. (Figure 1) There was no pericardial effusion or valvular regurgitation. The ejection fraction was 74% which was

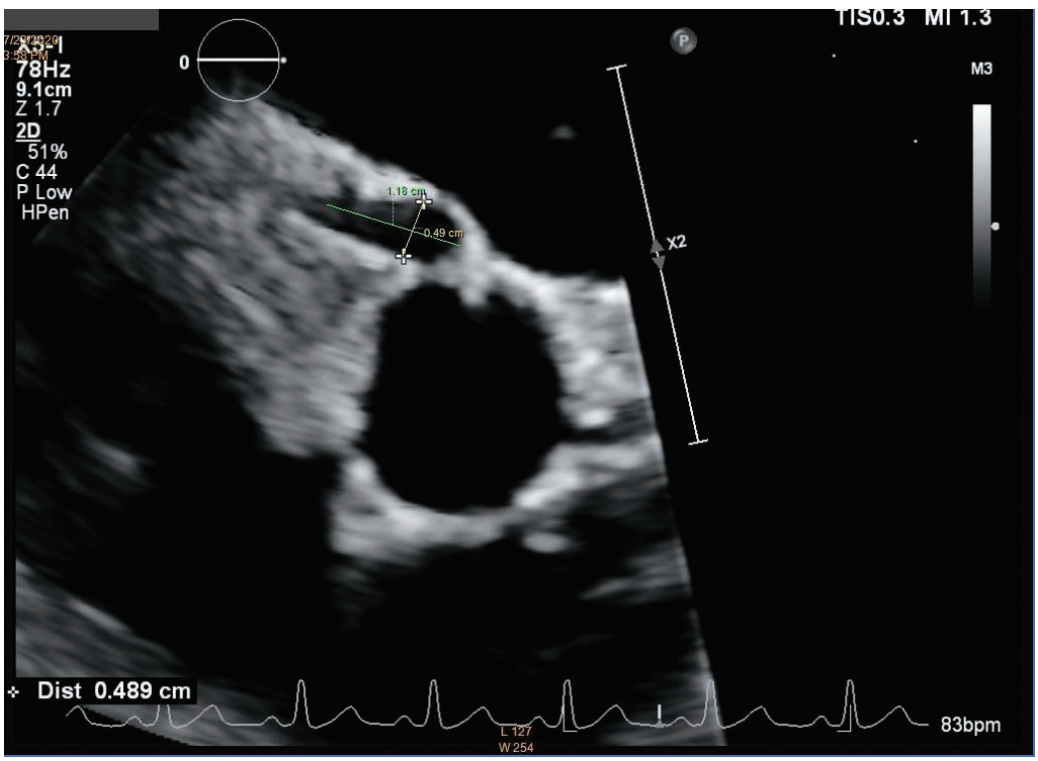

Figure 1 Echocardiogram showed right coronary aneurysm.

normal. CT coronary arteriogram also confirmed a solitary 5 mm size coronary artery aneurysm over the proximal right coronary artery (Figure 2).

At that juncture, we were unable to think of any causes for the persistent high swinging fever and the coronary artery aneurysm and giving it the benefit of doubt, we suggested treating the child as a case of atypical KD. A dose of intravenous immunoglobulin (IVIG), 2 grams per kg and high dose of oral aspirin was given and the fever became low-grade on the second day, but it never settled.

The result of Oreintia Tsutsugamuschi came back two days after the IVIG infusion. The first IgM titre of Oreintia Tsutsugamuschi was <128 and the second IgM titer taken on day 16 was 4096. Scrub typhus was finally diagnosed and oral antibiotic namely doxycycline was started, and the fever was finally settled. The child was discharged uneventfully.

Discussion

Rickettsia infections are a diverse collection of obligately intracellular Gram-negative bacteria found in ticks, lice, fleas, mites, chiggers, and mammals. It can be classified as 3 groups: typhus group, spotted fever group and others. Rickettsia is uncommon in our locality and there have only been 97 cases reported in Hong Kong between 2015 and 2019.[4]

Scrub typhus belongs to the typhus group of Rickettsia and it is caused by Orientia Tsutsugamushi. Orientia Tsutsugamushi is an obligate, intracellular bacterium causing scrub typhus. The genus Orientia belongs to the order Rickettsiales in the family of Rickettsiaceae. It can present with a wide range of symptoms, from asymptomatic to mild symptoms including fever, headache, abdominal pain and rash, to severe complications including severe pneumonia, meningitis and myocarditis.[1]

Studies showed that Rickettsia species primarily infects the endothelial cell lining of small to medium-sized blood vessels. This leads to alteration of vascular permeability and vascular inflammation, which is collectively named as 'Rickettsial vasculitis'.[5] In fact, dilated right coronary artery has been reported in a case of a 3-year-old boy suffered from Rickettsia coronii infection.[2] In the case report, author proposed that coronary ectasia may be a manifestation of rickettsial vasculitis. Similarly, our case illustrated that coronary artery aneurysm can also be one of the clinical features and complications of scrub typhus, caused by rickettsial vasculitis.

Presentation of rickettsia can also mimic KD. There were cases reported in Korea that scrub typhus presented with prolonged fever, bilateral conjunctivitis, rash and limbs erythema and oedema were initially misdiagnosed to be KD, and all of these cases had no specific findings suggestive of KD on echocardiogram.[6] On the contrary, there were cases in both Korea and Sri Lanka that scrub

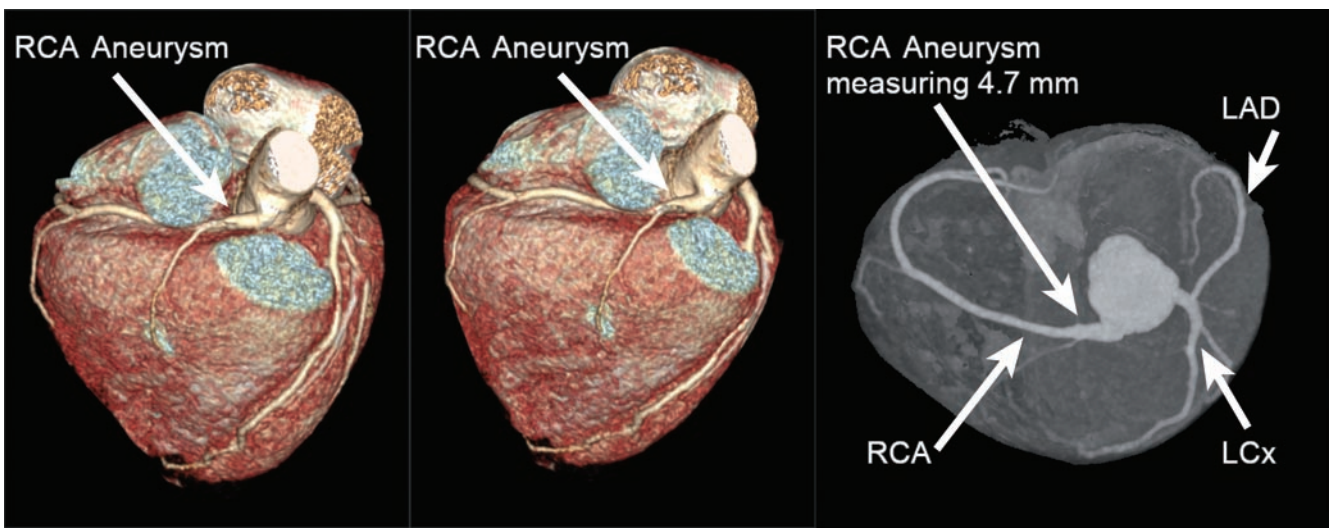

Figure 2 Computer tomography showed a right coronary aneurysm.
Abbreviations: RCA = Right coronary artery; LCx = Left circumflex artery; LAD = Left anterior descending artery

typhus can be complicated by KD, leading to coronary artery aneurysm.[3,7]

The diagnosis of KD should be based on the presence of fever for at least 5 days, and at least 4 out of 5 criteria, namely extremity changes, rash, conjunctivitis, oral mucosal changes, and cervical lymphadenopathy.[8] For our patient, he had only fulfilled two criteria of KD, i.e. prolonged fever and erythematous rash. A diagnostic algorithm was also proposed evaluate patients with suspected incomplete KD but the patient still needed to fulfill at least 3 out of 5 clinical criteria together with supportive laboratory criteria to make a diagnosis of atypical KD with the help of echocardiogram.[8]

Previous study showing that that the finding of coronary artery Z score of the right coronary artery greater or equal to 2.5 has a specificity of 98% (95% CI, 88%-100%) and sensitivity of 20% (95% CI, 14%-28%) for the diagnosis of KD,[9] especially since the serology result of Oreintia Tsutsugamuschi was not available at that time. We treated our patient as KD based on the right coronary artery aneurysm as suggested by the above study. However, the clinical pictures and the laboratory findings were unable to fulfill the diagnosis of KD and atypical KD. While KD is the most common cause of coronary artery aneurysm in children, there are still other rarer causes include trauma, congenital diseases e.g. Loeys-Dietz syndrome and vasculitis e.g. Takayasu vasculitis[10] etc. Our case reminds that physicians should consider alternative diagnosis to KD even if coronary artery aneurysm is detected in children.

In looking back on our case, the child presented with swinging fever, skin rashes, abdominal pain and hepatosplenomegaly which were typical clinical symptoms and signs of scrub typhus. Treatment of scrub typhus with doxycycline is usually straight forward once diagnosis is made. The serology results and the prompt response to treatment by doxycycline could have supported the diagnosis of scrub typhus complicated by coronary aneurysm in our case.

In conclusion, coronary aneurysm can be a manifestation of scrub typhus due to rickettsial vasculitis. Physicians should be alert that coronary artery aneurysm can appear in children with scrub typhus and echocardiogram is useful to detect CAA. Fortunately, coronary artery abnormalities are usually resolved after Rickettsia was properly treated.

Declaration of Interest

There are no conflicts of interest to declare.

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