

# A Case of Kawasaki Disease With Concomitant Leptospirosis

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## Case Report

A 7-year-old Malay girl was admitted to our institution presenting with fever for 4 days that was persistently above 38°C, with a maximum temperature of 39.9°C. This was associated with a papular and pruritic rash over her chest and limbs for 4 days, as well as a tender right neck swelling for 3 days, diarrhea, and bitemporal headaches for 2 days. This was accompanied by early morning vomiting and nausea, but no blurring of vision or other neurological deficits. She also had red eyes and a dry cough that was not accompanied by coryzal symptoms for 1 day. She initially presented to a family physician and was given 3 days of oral azithromycin. However, her right neck swelling grew in size and redness over the last 2 days prior to admission. It was reported that she did not have contact with any sick persons. However, she had travelled to South India a month ago.

On physical examination, the child was febrile with a temperature of 38.4°C, and lethargic. Her heart rate was 122 beats per minute, blood pressure was 100/60 mm Hg, and respiratory rate was 27 breaths per minute. There was no pallor or jaundice. An erythematous papular rash was noted over her trunk and limbs, but with no skin peeling. Her conjunctiva was extremely injected bilaterally without any eye discharge. Her lips were red, and she had a strawberry tongue. Her throat was mildly injected with no tonsillar enlargement or exudates. Tympanic membranes were normal bilaterally. There was a palpable right cervical lymph node, measuring 5 by 3 cm, which was tender and warm to touch with overlying erythema, causing limited lateral rotational movement of her neck. On auscultation of her chest, both her heart sounds were heard without any murmurs, and her lung fields were clear bilaterally with no adventitious sounds heard. Her abdomen was soft and nontender, with no hepatosplenomegaly. Her limbs were not edematous or erythematous.

Initial laboratory investigations were done, and the results are summarized in Tables 1 to 3.

The child was empirically covered for infection with intravenous Augmentin for 1 week. However, she remained persistently febrile, and her repeated platelet count was climbing, with high erythrocyte sedimentation rate and C-reactive protein (Table 1) on day 7 of illness—all in keeping with Kawasaki disease.<sup>1</sup> In view of this, she was treated as for Kawasaki disease with intravenous immunoglobulin 2 g/kg and high-dose oral aspirin on day 7 of illness. Leptospira serology was also done on day 7 of illness in view of her bilateral conjunctival injection that was out of proportion to her illness, and positive travel history to South India a month ago.

Subsequently, her condition improved—her fever and other symptoms subsided, and her oral intake improved. She was discharged afebrile and well on day 9 of illness and kept on low-dose oral aspirin. On cardiology review at day 14 of illness, she was afebrile, clinically well, and noted to have skin peeling distally over her fingers. The day 14 transthoracic 2D-echocardiography showed normal coronary arteries. Postdischarge, the leptospira serology was traced and turned out to be positive for IgM. She had already completed 1 week of Augmentin.

## Discussion

Kawasaki disease is an acute febrile vasculitic syndrome of early childhood, characterized by fever and signs of mucocutaneous inflammation. Although prognosis is good with treatment, if left untreated, 15% to 25%

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**Table 1.** Timeline of Blood Investigations Done.

	Day of Illness	
	Day 4	Day 7
Hemoglobin (g/dL)	11.6	11.9
White blood cell count ( $\times 10^9/L$ )	16.8	15.9
Platelet count ( $\times 10^9/L$ )	403	565
Erythrocyte sedimentation rate (mm/h)	81	84
C-reactive protein (mg/L)	126.6	171.0
Procalcitonin (mg/L)		0.30
Albumin (g/L)	32	
Total bilirubin ( $\mu\text{mol/L}$ )	7	
Direct bilirubin ( $\mu\text{mol/L}$ )	4	
Alanine transaminase (U/L)	34	
Aspartate transaminase (U/L)	29	
Alkaline phosphatase (U/L)	205	
Gamma-glutamyl transferase (U/L)	34	

**Table 2.** Timeline of Microbiological Investigations Done.

	Day of Illness	
	Day 4	Day 7
ASOT	<200 IU/mL	
Blood culture	No bacterial growth	
Urine culture	No bacterial growth	
Respiratory virus antigen	Not detected	
Leptospira serology		IgM positive
Respiratory virus multiplex polymerase chain reaction		Not detected
Cytomegalovirus serology		IgM negative
Epstein-Barr virus serology		IgM negative

**Table 3.** Timeline of Radiological Investigations Done.

	Day of Illness: Day 5
Ultrasound neck	Bilateral cervical lymph nodes noted, largest measuring $3.5 \times 1.3$ cm on the right. No evidence of liquefaction noted in the nodes. Thyroid gland appeared normal.

develop coronary artery aneurysms or ectasia, which may lead to myocardial infarction, sudden death, or ischemic heart disease.<sup>1</sup>

A diagnosis of classical Kawasaki disease can be made clinically, according to the guidelines by American Heart Association<sup>1</sup>: a fever persisting 5 days or more with at least

4 out of the following 5 features: changes in extremities, polymorphous exanthem, bilateral nonpurulent conjunctival injection, changes in the lips and oral cavity, and cervical lymphadenopathy of >1.5 cm diameter. In the presence of less than 4 of these features, a diagnosis can still be made if coronary artery disease is demonstrated on transthoracic echocardiography. A similar diagnostic guideline has been described by the Kawasaki Disease Research Committee in Japan.<sup>2</sup>

This patient fulfilled the diagnostic criteria for classical Kawasaki disease. Her laboratory findings were also in keeping with the diagnosis—elevated erythrocyte sedimentation rate, C-reactive protein, and platelet count  $>450\,000/\text{mm}^3$ . In addition, she did not respond to intravenous antibiotics, and instead responded well clinically to intravenous immunoglobulin treatment. Her other symptoms that are not described in classical presentation are also commonly found in patients with Kawasaki disease—cough, diarrhea, and vomiting.<sup>3</sup>

On the other hand, leptospirosis is a zoonosis caused by infection with pathogenic *Leptospira* species, usually due to direct or indirect contact with the urine of an infected animal. Its pathology is characterized by the development of vasculitis, endothelial damage, and inflammatory infiltrates, primarily affecting the liver, kidney, heart, and lungs.<sup>4</sup> Potential complications therefore include hepatitis, acute renal failure, pulmonary hemorrhage, pleural effusion, and myocarditis. Other rare complications that have been reported include cerebrovascular accidents,<sup>5</sup> acute acalculous cholecystitis,<sup>6</sup> aortic stenosis,<sup>7</sup> and Guillain-Barré syndrome.<sup>8</sup>

Clinical presentation of leptospirosis varies widely, although severity depends on the presence of icterus. Common presenting symptoms include headache, conjunctival suffusion, anorexia, myalgia, cough, nausea, vomiting, diarrhea, and hepatomegaly.<sup>9</sup> Leptospirosis is a possible differential diagnosis of Kawasaki disease due to its varied and possibly similar presentation. In our patient's case, she had presented with headache, conjunctival suffusion, cough, nausea, vomiting, and diarrhea, and she had recently travelled to India, which is endemic for leptospirosis. Large outbreaks of leptospirosis have been reported in Nicaragua, Brazil, India, southeast Asia, and the United States.<sup>9</sup> Kawasaki disease has been reported to have developed in patients with leptospirosis.<sup>10,11</sup> The exact mechanism is unknown due to the lack of literature on this subject. If leptospirosis is found concomitantly with Kawasaki disease, then appropriate treatment should be instituted. In our patient's case, she was treated with 1 week

of intravenous Augmentin. Treatment of leptospirosis depends on the severity and duration of symptoms. Patients who are anicteric and with flu-like symptoms require symptomatic treatment only. Patients with jaundice and symptoms of end-organ dysfunction will require hospital admission and close observation, as well as additional interventions such as renal replacement therapy depending on severity of illness.<sup>9</sup> There is insufficient evidence to show that antimicrobial therapy is beneficial—limited evidence shows that the use of antibiotics may decrease duration of illness, although the benefit for severe disease remains unclear.<sup>12</sup>

## Conclusion

There is significant overlap between the clinical presentation of Kawasaki disease and leptospirosis. We believe that this rare case further adds to the growing literature that there may be an association between Kawasaki disease and leptospirosis. Physicians who are treating patients who meet the diagnostic criteria for Kawasaki disease may consider concomitant leptospirosis, especially if other clinical features are suggestive of leptospirosis, and if there is a positive travel history to a country where leptospirosis is endemic.

## Author Contributions

CCYF: Contributed to design; contributed to analysis and interpretation; drafted manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

EHML: Contributed to analysis and interpretation; critically revised manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

KBP: Contributed to analysis and interpretation; critically revised manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

CYC: Contributed to analysis and interpretation; critically revised manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

NWHT: Contributed to design; contributed to analysis and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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