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Adult Kawasaki's disease with myocarditis, splenomegaly, and highly elevated serum ferritin levels

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Kawasaki's disease is a disease of unknown cause. The characteristic clinical features of Kawasaki's disease are fever ≥ 102°F for ≥ 5 days accompanied by a bilateral bulbar conjunctivitis/conjunctival suffusion, erythematous rash, cervical adenopathy, pharyngeal erythema, and swelling of the dorsum of the hands/feet. Kawasaki's disease primarily affects children and is rare in adults. In children, Kawasaki's disease is more likely to be associated with aseptic meningitis, coronary artery aneurysms, and thrombocytosis. In adult Kawasaki's disease, unilateral cervical adenopathy, arthritis, conjunctival suffusion/conjunctivitis, and elevated serum transaminases (serum glutamic oxaloacetic transaminase [SGOT]/serum glutamate pyruvate transaminase [SGPT]) are more likely. Kawasaki's disease in adults may be mimicked by other acute infections with fever and rash, that is, group A streptococcal scarlet fever, toxic shock syndrome (TSS), and Rocky Mountain Spotted Fever (RMSF). Because there are no specific tests for Kawasaki's disease, diagnosis is based on clinical criteria and the syndromic approach. In addition to rash and fever, scarlet fever is characterized by circumoral pallor, oropharyngeal edema, Pastia's lines, and peripheral eosinophilia, but not conjunctival suffusion, splenomegaly, swelling of the dorsum of the hands/feet, thrombocytosis, or an elevated SGOT/SGPT. In TSS, in addition to rash and fever, there is conjunctival suffusion, oropharyngeal erythema, and edema of the dorsum of the hands/feet, an elevated SGOT/SGPT, and thrombocytopenia. Patients with TSS do not have cervical adenopathy or splenomegaly. RMSF presents with fever and a maculopapular rash that becomes petechial, first appearing on the wrists/ankles after 3 to 5 days. RMSF is accompanied by a prominent headache, periorbital edema, conjunctival suffusion, splenomegaly, thrombocytopenia, an elevated SGOT/SGPT, swelling of the dorsum of the hands/feet, but not oropharyngeal erythema.

We present a case of adult Kawasaki's disease with myocarditis and splenomegaly. The patient's myocarditis rapidly resolved, and he did not develop coronary artery aneurysms. In addition to splenomegaly, this case of adult Kawasaki's disease is remarkable because the patient had highly elevated serum ferritin levels of 944-1303 ng/mL; (normal < 189 ng/mL). To the best of our knowledge, this is the first report of adult Kawasaki's disease with highly elevated serum ferritin levels. This is also the first report of splenomegaly in adult Kawasaki's disease. We conclude that Kawasaki's disease should be considered in the differential diagnosis in adult patients with rash/fever for ≥ 5 days with conjunctival suffusion, cervical adenopathy, swelling of the dorsum of the hands/feet, thrombocytosis and otherwise unexplained highly elevated ferritin levels. (Heart Lung® 2010;39:164–172.)

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0147-9563/$ – see front matter

doi:10.1016/j.hrtlng.2009.06.007

Kawasaki's disease occurs primarily in children. The etiology of Kawasaki's disease is unclear, but it causes vasculitis and affects the myocardium, upper respiratory tract, pancreas, and kidneys. Dr Kawasaki was the first to recognize the characteristic clinical features of the disease, that is, bilateral (non-exudative) conjunctivitis with limbal sparing, pharyngeal erythema with cracking of lips/strawberry tongue, erythema, swelling of the

hands/feet, and erythematous rash, followed by periungual desquamation and bilateral cervical lymphadenopathy.[1] Before Dr Kawasaki's clinical description, the disease was recognized in autopsy by coronary aneurysms, thrombosis, and myocardial infarction. The disease was termed "infantile periarteritis nodosa."[2,3]

In children, seasonality (ie, peak incidence in winter/spring) and clustering of cases suggest an infectious cause yet to be identified. Kawasaki's disease is not seen in children aged less than 3 months and is rarely seen in adults, which supports the presence of an infectious agent for which passive maternal immunity is protective. After childhood, most adults have developed protective immunity. This theory is widely accepted.[2]

Many pathogens have been associated with Kawasaki's disease, for example, *Rickettsial sp.*, *Propriobacterium acnes*, *Leptospira*, *Streptococcus sanguis*, retrovirus, Epstein-Barr virus, cytomegalovirus, toxic shock syndrome (TSS), coronavirus, human Boca virus, and *Coxiella burnetti*,[3-8] but the evidence to support their causality is lacking/unconfirmed.

Human immunodeficiency virus (HIV) is the most frequently reported infectious disease associated with Kawasaki's disease in the rare cases in adults.[9] It has been hypothesized that Kawasaki's disease in adults is more commonly associated with HIV because the disease may be caused by a pathogen acquired in childhood and then reactivates in adulthood because of HIV-related immunodeficiency.[4-7]

It has been shown that there is infiltration of IgA plasma cells in Kawasaki's disease with CD8 T lymphocytes/CK8 macrophages present in inflammatory infiltrates of the affected tissues, and intra-cytoplasmic RNA inclusion bodies in ciliated bronchial epithelium have been demonstrated in acute Kawasaki's disease and after its resolution. These findings support a potential intracellular infectious agent acquired via the respiratory route and remaining in a dormant state until it later reactivates.[10]

In adult patients, the initial differential diagnosis of Kawasaki's disease includes infectious diseases that present fever with rash, mucosal involvement, and cervical adenopathy, for example, Rocky Mountain Spotted Fever, scarlet fever, TSS, adult Still's disease, systemic lupus erythematosus, meningococcemia, *Arcanobacterium haemolyticum*, staphylococcal scalded-skin syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, parvovirus B19, roseola, rubella, measles, and dengue.[3,9,11-15]

An experienced clinician who performs a careful clinical history, physical examination, and some nonspecific laboratory tests should be able to make a presumptive diagnosis of Kawasaki's disease. A clue to the clinical diagnosis of Kawasaki's disease stems from the fact that the disease has 3 phases: The acute phase lasts for approximately 7 to 14 days, manifested by fever, conjunctival suffusion, pharyngitis, cracked lips/strawberry tongue, swelling/erythema of the dorsum of the hands/feet, and a maculopapular scarlatiniform rash or erythema multiforme type of rash. Tachycardia caused by myocarditis is common during this phase. During the subacute phase, the fever, rash, and adenopathy usually resolve, but the conjunctival suffusion persists. Periungual desquamation ensues. Thrombocytosis, which is common in this phase, occurs from days 10 to 25. Although nonspecific, Beau lines (transverse grooves in the nails) and temporary hair loss also can be seen during this phase. The convalescent phase begins when all these signs have resolved and lasts until the complete normalization of the erythrocyte sedimentation rate (ESR). Recurrence or persistence of fever can be seen with some frequency and is associated with increased risk of late coronary complications. The clinical phases described are typical of Kawasaki's disease in children, but there is no classic description of the phases in adults (Tables I and II).[3,9,15]

CASE REPORT

A 26-year-old man presented to the emergency department with fever and rash. Symptoms began 4 days before admission with fevers to 103°F. He also reported insomnia, myalgias, nausea/vomiting, and loose stools. The patient was prescribed doxycycline by his primary care physician, but he was unable to take the medication secondary to vomiting. He had mild sore throat and swelling of his hands and feet. Medical history was significant for Epstein-Barr virus infectious mononucleosis and oral herpes simplex virus. He smoked marijuana occasionally but denied intravenous drug use. He reported being sexually active and drinking alcohol socially.

On admission, his temperature was 101.7°F with a persistently elevated pulse of 140 beats/min. His blood pressure was 120/70 mm Hg and respiratory rate was 16 breaths/min. Examination of the skin revealed a diffuse, maculopapular, blanching rash of the entire body, including the palms/soles and perianal area. The rash was warm but not pruritic. There was early desquamation on the palms and face. He had multiple tattoos.

Head, eyes, ears, nose, and throat examination revealed bilateral conjunctival suffusion and

Table I
Diagnostic criteria for Kawasaki's disease

Fever > 5 d plus > 4 of these clinical findings:
- Rash[a]
- Bilateral conjunctivitis
- Cervical lymphadenopathy
- Oral erythema/cracked/fissured lips ± strawberry tongue
- Edema of dorsum of the hands/feet

[a]Later progressing to desquamation of the hands/feet.

Table II
Associated clinical features of Kawasaki's disease

CNS involvement
- Aseptic meningitis

Cardiac involvement
- Coronary artery aneurysms
- Myocarditis
- Valvular
- Myocardial infarction

GU involvement
- Urethritis
- Sterile pyuria

Musculoskeletal involvement
- Arthralgias
- Arthritis

CNS = central nervous system; GU = genitourinary.

bilateral anterior cervical lymphadenopathy. His lungs were clear to auscultation, and cardiovascular examination revealed a decreased S1, a normal S2, no murmur, and persistent tachycardia (140 beats/min). Abdominal examination revealed a soft, nontender abdomen that was nondistended with active bowel sounds. There was no organomegaly. Musculoskeletal examination revealed bilateral nonpitting edema dorsum of the hands and feet.

On admission, laboratory results included a white blood cell count of 27.8 K/mm^3 (polymorphonuclear cells = 95%, lymphocytes = 3% and monocytes = 2%). His hemoglobin was 12.4 g/dL with a hematocrit of 35.5%, and his platelet count was 315 K/mm^3 (n = 160-394U k/mm^3). Serum lactic acid was 2.9 meq/L (n = .5-2.2 meq/L). Blood urea nitrogen was 12 mg/dL, and creatinine was .5 mg/dL. The ESR was 73 mm/h (n < 20 mm/h), and C-reactive protein was 133.56 mg/L (n < 3 mg/L). His serum ferritin level was highly elevated at 944 ng/mL (n < 189 ng/mL). Except for a negative ASO titer, the patient's cytomegalovirus, HBV, parvovirus B19, Ehrlichia, fever, and Coxsackie A/B titers were negative. He was also HIV negative. The initial chest x-ray revealed no acute pulmonary disease.

Levofloxacin 500 mg was administered orally every 24 hours. The patient had bilateral leg swelling and pain. A lower-extremity venous Doppler ultrasound revealed no evidence of deep vein thrombosis. During the patient's hospital course, his rash improved with decreased erythema and desquamation of his palms/soles progressed. After infectious diseases consultation, the clinical diagnosis of Kawasaki's disease was made and the patient was administered a single infusion of intravenous immunoglobulin 2 g/kg and acetylsalicylic acid (100 mg/kg/d). An abdominal sonogram revealed gallbladder sludge and mild splenomegaly. Later, he developed an abscess in the antecubital fossa at the intravenous line site, which was subsequently drained/cultured. The abscess culture was positive for methicillin-sensitive *Staphylococcus aureus*, and he received minocycline 100 mg (orally) every 12 hours for 2 weeks. A transthoracic echocardiogram revealed myocarditis, that is, mild global hypokinesis of the left ventricle (grade I diastolic dysfunction) with an ejection fraction of 45% to 50%, and carvedilol and enalapril were administered. A repeat transthoracic echocardiogram 4 days later showed an improved ejection fraction of 50% to 55%.

On hospital day 7, the patient developed a syncopal episode and an electrocardiogram showed ventricular bigeminy. Cardiac catheterization revealed coronary arteries with no aneurysms. During his hospitalization, serum ferritin levels peaked at 1303 ng/mL (n < 189 ng/mL), and his platelet count peaked at 560 K/mm^3. His thrombocytosis lasted 28 days. The patient's highly elevated ESR remained greater than 100 mm/h during most of his hospital course but gradually decreased to normal. His persistent/prolonged relative lymphopenia also eventually resolved.

DISCUSSION

Adult Kawasaki's disease may present differently than in children. Adults more frequently present with cervical adenopathy (93% of adults vs 15% of children), hepatitis (65% of adults vs 10% of children), and arthralgia (61% of adults vs 24%-38% of children).

In contrast, adults are less frequently affected by aseptic meningitis (10% of adults vs 34% of children), thrombocytosis (55% of adults vs 100% of children), and coronary artery aneurysms (5% of adults vs 18%-25% of children). In contrast, adults are less frequently affected by meningitis (10% of adults vs 34% of children), thrombocytosis (55% of adults vs 100% of children), and coronary artery aneurysms (5% of adults vs 18%-25% of children).[1-4]

Kawasaki's disease was initially described in 1967 by Tomisaku Kawasakias a "mucocutaneous lymph node syndrome," which had been affecting infants and young children in Japan.[1] Most cases occurred between the ages of 6 months and 8 years with an incidence of 40 to 150 cases per 100,000 in those aged less than 5 years in Japan and 1:10,000 in the United Kingdom. Kawasaki's disease is most commonly found in the Asian population. In Japan, the incidence is 10 times greater than it is in Western countries. Kawasaki's disease has replaced acute rheumatic fever as the leading cause of acquired heart disease among children in developed countries. The annual incidence of Kawasaki's disease is approximately 150 per 100,000 children of Japanese descent aged less than 5 years and approximately 10 to 15 per 100,000 US children aged less than 5 years.

Kawasaki's disease usually consists of an acute phase lasting 1 to 2 weeks, followed by a chronic phase. If Kawasaki's disease is untreated, it usually resolves spontaneously after several weeks. The major pathologic feature of Kawasaki's disease is acute systemic vasculitis. Inflammation of the coronary arteries usually develops early in the acute phase until 4 weeks after onset of disease. Coronary artery biopsy specimens reveal that there is marked endothelial cell edema, proliferation, necrosis, and adhesion of polymorphonuclear leukocytes to endothelium in these lesions. Specifically, there is an acute inflammatory response with elevated levels of circulating cytokines and CD4 and CD8 cells, polyclonal hypergammaglobulinemia on serum protein electrophoresis, and circulating IgG and IgM immunocomplexes.[2-4]

Cardiac manifestations of Kawasaki's disease in the acute phase include pericarditis, myocarditis, endocarditis, inflammation of the conduction system, and coronary artery involvement. Thrombosis and infarction may occur predominantly in the first year, and these processes are associated with aneurysm formation. A large Japanese study demonstrated that 25% of patients with acute Kawasaki's disease were shown by coronary angiography to have coronary aneurysms.[3,4]

Generally, myocarditis usually occurs during the acute phase of Kawasaki's disease and usually resolves spontaneously. The presence of myocarditis does not correlate well in predicting concomitant coronary artery aneurysms. Clinically, patients may develop a pericardial effusion and an associated S3 or S4 gallop on physical examination. The presence of a pericardial effusion may manifest as low-voltage amplitude on electrocardiogram and transient left ventricular dysfunction on echocardiography. Long-term impairment of left ventricular function rarely occurs. However, if there is coronary artery disease then persistent valvular disease may coexist, particularly affecting the aortic and mitral valves.[16-18]

Long-term complications are related to the persistence of coronary artery aneurysms, seen in the chronic phase of the disease, and associated with increased risk of ischemic heart disease, thrombotic occlusions, and premature atherosclerosis. Coronary artery aneurysms occur in 20% to 25% of cases. Associated conditions with aneurysmal formation include the fever height/duration, elevated ESR, leukocytosis, and disease duration. However, none of these are absolute predictive of coronary artery aneurysm.

The natural history of coronary artery aneurysms is related to aneurysmal size. Small (<5 mm) to moderate-sized (5-8 mm) aneurysms are detected after the acute stage regress in approximately 50% of cases. However, approximately 1% of patients who recover from acute Kawasaki's disease develop giant coronary artery aneurysms (>8 mm in diameter) or coronary artery obstruction caused by thrombosis or stenosis. Giant coronary aneurysms have the lowest regression rate, highest risk of stenosis, and strongest association with myocardial infarction. Coronary artery aneurysms occur predominantly in the proximal segments and at bifurcations of the coronary arteries, and there is usually multivessel involvement. Systemic aneurysms also may occur in approximately 2% of patients, particularly in the axillary and iliac arteries.[16-18]

Salicylates and intravenous gamma globulin therapy have been shown to reduce the morbidity and incidence of coronary abnormalities from approximately 25% to less than 5% at 6 to 8 weeks after initiation of therapy. Furthermore, coronary aneurysms regress within 1 to 2 years in most patients.[1-3]

Coronary artery screening should be conducted early with echocardiography, and electrocardiography should be performed in children with suspected Kawasaki's disease to evaluate for ischemic or arrhythmic changes; this should be repeated at 10 to 14 days to look for new lesions. It is uncertain whether children who have had Kawasaki's disease are predisposed to atherosclerosis in adulthood,

Table III
Differential diagnosis of adult Kawasaki's disease

Clinical Features	Group A streptococcal scarlet fever	TSS	RMSF	Kawasaki's disease
Symptoms				
Fever	+	±	+	+
Sore throat	+	-	-	+
Acute deafness	-	-	±	±
Prominent headache	-	-	+	-
Diarrhea	-	-	-	+
Signs				
Fever > 102°F	+	±	+	+
Relative bradycardia	-	-	+	-
Hypotension/shock	-	±	-[a]	-
Periorbital edema	-	-	+	-
Conjunctival suffusion	-	+	+	+
Bilateral (non-exudative) bulbar conjunctivitis	-	-	-	+[b]
Anterior uveitis	-	-	-	+
Circumoral pallor	+	-	+	+
Erythematous oropharynx	+	+	-	+
Unilateral cervical adenopathy	-	-		
Rash				
Perineal/perianal	-	-	-	+
Ankles/wrists	-	-	+	-
Truncal/sandpaper	+	-	-	-
Hepatic tenderness/ hepatomegaly	-	-	±	-
Splenomegaly	-	-	±	±
Edema of dorsum of hands/feet	-	+	+	+
Laboratory tests				
Nares + for *Staphylococcus aureus* (TSS-1+)	-	+	-	-
Elevated ASO titers	+	-	-	-
Elevated *Rickettsia rickettsi* titers	-	-	+	-
WBC counts				
Leukocytosis	+	+	±	+
Relative lymphopenia	-	-	+	+
Eosinophilia	+	-	-	-
Thrombocytopenia	-	+	+	-
Thrombocytosis	-	-	-	+
ESR > 100 mm/h	-	-	-	+
Highly elevated ferritin levels(> 2n)	-	-	-	+
Mildly elevated SGOT/SGPT levels	-	±	±	-
EKG: nonspecific ST/T wave abnormalities	-	-	±	±
Urinalysis				
Sterile pyuria	-	-	-	+
Abdominal ultrasound				

Continued

Table III
Continued

Clinical Features	Group A streptococcal scarlet fever	TSS	RMSF	Kawasaki's disease
Hydrops of the gallbladder	-	-	-	+
TTE:				
Myocarditis				
Early	-	-	-	+
Late	-	-	+	-
Coronary artery aneurysms	-	-	-	+
Empiric therapy	β-lactam antibiotic	Anti-staphylococcal antibiotic	Doxycycline	IVIG

TSS = toxic shock syndrome; RMSF = Rocky Mountain Spotted Fever; ASO = anti-streptolyin O titers; WBC = white blood cell; ESR = erythrocyte sedimentation rate; SGOT = serum glutamic oxaloacetic transaminase; SGPT = serum glutamate pyruvate transaminase; EKG = electrocardiogram; TTE = transthoracic echocardiogram; IVIG = intravenous immunogammaglobulin.
[a]May occur late with RMSF if myocarditis or due to excessive volume replacement.
[b]With limbal sparing.

because there is an absence of prospective or retrospective long-term follow-up data.[17,18]

Coronary angiography provides adequate luminal visualization of blood vessels, but it is limited in that it cannot specifically detect intramural changes in the coronary tree. Several postmortem examinations of patients with Kawasaki's disease who have angiographically documented regression of coronary artery aneurysms revealed intimal proliferation and fibrosis not apparent on angiography. Intravascular ultrasound imaging of the coronary arteries may allow more thorough evaluation to visualize the cross-section coronary wall morphology and the healing process.

The frequency of follow-up visits for patients with a giant or medium solitary aneurysm or multiple aneurysms is based on the patient's baseline clinical condition. If noninvasive studies or clinical symptoms suggest myocardial ischemia, then radioisotope myocardial perfusion scanning, coronary angiography, or both are indicated. The specific type of study should be performed on the basis of the particular area of interest to be evaluated. As mentioned earlier, although coronary angiography may allow visualization of the intraluminal aspect of a coronary vessel, myocardial perfusion imaging may better assess the endothelial function of the coronary tree. Patients with no evidence of aneurysm or ectasia at the 1-year evaluation are not likely to benefit from further repeated echocardiography, although patients with transient coronary artery ectasia early in the illness may be followed up at 3- to 5-year intervals.[19,20]

Magnetic resonance imaging can also assess coronary morphology with low temporal resolution (20-50 ms). The 3-dimensional spatial resolution achievable is marginal for coronary arterial imaging and is not as reliable as multidetector computed tomography. However, magnetic resonance imaging has been shown to be useful in evaluating for severe proximal multivessel coronary artery disease or coronary aneurysms in selected patients with Kawasaki's disease.[21-23]

Kawasaki's disease in adults can be confused with other infectious disorders associated with a fever and rash. The most likely infectious disease disorders likely to be confused with Kawasaki's disease include group A streptococcal scarlet fever, TSS, and Rocky Mountain Spotted Fever (RMSF). As with all differential diagnostic problems, accurate presumptive clinical diagnosis rests on identifying the characteristic physical findings/nonspecific laboratory tests that are not consistent but that are characteristic of the disorder.[11-15]

In addition to fever and a diffuse rash, the cardinal findings in streptococcal scarlet fever are circumoral pallor and Pastia's lines. Nonspecific laboratory abnormalities associated with scarlet fever include eosinophilia, an elevated ASO titer, and normal liver function test results.[12]

Table IV
Differential diagnosis of thrombocytosis

Acute thrombocytosis	Chronic thrombocytosis
Infectious causes	**Infectious causes**
• Q fever	• Chronic osteomyelitis
• *Mycoplasma pneumoniae*	• Subacute bacterial endocarditis
	• Secondary syphilis
	• Abscesses
	Lung
	Renal
	Splenic
	Empyema
Noninfectious causes	**Noninfectious causes**
• Kawasaki's disease	• Rheumatoid arthritis
• Drugs	• Ulcerative colitis
Ceftriaxone	• Regional enteritis
Miconazole	• Cystic fibrosis
β-lactam/β-lactamase inhibitors/ combinations	• Coeliac disease
Carbapenems	• Post-splenectomy
Oral cephazolins	• Sickle cell disease
• Recovery from thrombocytopenia	• Essential thrombocythemia
• Hemorrhage	• Carcinomas
• Hemolytic anemias	• Lymphomas
• Iron-deficiency anemia	• MDS
	• CML
	• Wegener's granulomatosis

MDS = myelodysplastic syndrome; CML = chronic myelogenous leukemia.
Adapted from Cunha BA. The differential diagnostic approach to thrombocytosis. Infect Dis Pract 2008;32:740-2.

In contrast with scarlet fever, in TSS there is a scarlatina form rash resembling scarlet fever but also conjunctival suffusion and edema of the dorsum of the hands and feet. In TSS, the physical findings in scarlet fever are not present, but in addition, patients with TSS have increased liver function test results, no eosinophilia, and elevated ASO titer. Also, unlike scarlet fever, hypotension/shock will be present in the sickest patients with TSS. Diagnosis of TSS is made by clinical criteria. In addition, S. *aureus* of the TSS-1 toxin-producing variety may be cultured from mucosal surfaces. TSS may result from TSS-1 colonization or infection in addition to being associated with tampon use.[12,13]

RMSF presents characteristically presents with a maculopapular rash that occurs on the wrist/ankles 3 to 5 days after the onset of infection. Later, the maculopapular lesions become petechial and may extend centripetally. Typically, RMSF presents with severe headache/confusion that may suggest neurologic infection. RMSF with abdominal pain suggests an intra-abdominal infection. In addition to the typical distribution of the petechial rash, clinical findings of RMSF include conjunctival suffusion, splenomegaly, and edema of the dorsum of the hands/feet. Nonspecific laboratory tests in RMSF include a normal/slightly elevated white blood cell count, relative lymphopenia, and thrombocytopenia. Serum transaminases are usually mild to moderately transiently elevated. The ESR is not highly elevated with RMSF. Diagnosis is confirmed by demonstrating increased *Rickettsia rickettsii* titers (Tables III-V).[15]

Kawasaki's disease has no specific diagnostic tests, and the diagnosis is necessarily based on clinical criteria. Kawasaki's disease resembles scarlet fever in having a diffuse maculopapular rash. Unlike

Table V
Highly elevated serum ferritin levels[a]

Infectious causes	Noninfectious causes
Acute	**Malignancies**
• Legionnaires' disease	• Preleukemias
• WNE	• Lymphomas
	• Multiple myeloma
	• Hepatomas
	• Breast cancer
	• Colon cancer
	• Prostate cancer
	• Lung cancer
	• Liver/CNS metastases
Chronic	**Myeloproliferative disorders**
• HIV	**Myeloplastic disorders**
• TB	**Rheumatic/inflammatory disorders**
	• Rheumatoid arthritis
	• Adult Still's disease
	• SLE
	• TA
	• Kawasaki's disease
	Renal disease
	• Acute renal failure
	• Chronic renal failure
	Liver disease
	• Hemochromatosis
	• Cirrhosis
	• α1 anti-trypsin deficiency
	• CAH
	• Cholestatic jaundice
	Other
	• Sickle cell anemia
	• Multiple blood transfusions

WNE = West Nile encephalitis; HIV = human immunodeficiency virus; CNS = central nervous system; CMV = cytomegalovirus; SLE = systemic lupus erythematosus; TB = tuberculosis; TA = temporal arteritis; CAH = chronic active hepatitis.

Adapted from: Krol V, Cunha BA. Diagnostic significance of serum ferritin levels in infectious and non-infectious diseases. Infect Dis Pract 2003;27:199-200. Cunha BA. Serum ferritin levels in Legionella community-acquired pneumonia. Clin Infect Dis 2008;46:1789-91 and Cunha CB. Infectious disease differential diagnosis. In Antibiotic Essentials (9th ed) Jones & Bartlett, Sudbury, MA, 2010.

[a]Greater than 2 times normal.

scarlet fever, circumoral pallor and Pastia's lines are not present. Mild splenomegaly may occur with Kawasaki's disease. Kawasaki's disease, like scarlet fever, may have mucosal erythema/strawberry tongue and unilateral anterior cervical adenopathy. Unlike scarlet fever, edema of the hands and feet is present in Kawasaki's disease. With early Kawasaki's disease, if myocarditis is present, it is manifested as otherwise unexplained persistent tachycardia. Nonspecific laboratory tests associated with Kawasaki's disease include relative lymphopenia, mild/transiently elevated liver function test results, and thrombocytosis.[1-4] Patients with Kawasaki's disease do not have elevated ASO titers, positive S. *aureus* cultures of nares/mucosal surfaces or elevated R. *rickettsii* titers. Kawasaki's disease also differs

from scarlet fever, TSS, and RMSF in terms of therapy, that is, intravenous immunoglobulin/acetylsalicylic acid are the preferred therapies for Kawasaki's disease versus antimicrobial therapy for scarlet fever, TSS, and RMSF.[11-15] Pathologically, the involved lymph nodes in Kawasaki's disease shows prominent polymorphonuclear cell infiltration, patchy necrosis, and small-vessel thrombocytosis. Patients with adult Kawasaki's disease should be tested for HIV.[4-8]

This case is noteworthy in several respects. First, adult Kawasaki's disease is rare. In addition to the classic findings of Kawasaki's disease, the patient had splenomegaly. His laboratory abnormalities consistent with Kawasaki's disease included relative lymphopenia, highly elevated ESR/C-reactive protein, elevated liver function tests, and thrombocytosis.[24] He had no disorders associated with elevated ferritin levels.[25] His otherwise unexplained highly elevated ferritin levels persisted during most of his hospital course.

CONCLUSIONS

Kawasaki's disease should be suspected in adults with fever/rash, cervical adenopathy, thrombocytosis, and otherwise unexplained highly elevated serum ferritin levels. This diagnostic pentad for Kawasaki's disease permits rapid clinical differentiation from scarlet fever, TSS, and RMSF. To the best of our knowledge, this is the first reported case of adult Kawasaki's disease with splenomegaly and highly elevated serum ferritin levels.

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