A Rare Presentation of Endocarditis in Adult-onset Still's Disease in Diagnosis of Fever of Unknown Origin

To the Editor:

Adult-onset Still's disease (AOSD) was first described by Bywaters in 1971, with descriptions of 14 patients¹. Differentiation between microbial infections and rheumatic diseases such as AOSD remains difficult in many cases. Heart involvement in AOSD is uncommon and valvular involvement is extremely rare. We describe a case of AOSD in a 39-year-old woman who presented with fever, endocarditis, and hyperferritinemia.

Our patient was admitted to the emergency service with fever and chest pain. One week before she had had a sore throat, so she was given amoxicillin-clavulanate 2 × 1000 mg/day for 1 week. On examination, tachycardia and apical 2/6 systolic murmur were detected. Cardiac enzymes were normal. Laboratory tests (Table 1) showed acute-phase inflammation and leukocytosis. Cardiomegaly was seen on chest radiography. Echocardiography (ECO) showed mitral stenosis, 1.7 cm pericardial effusion, second-degree mitral insufficiency, and second- and third-degree aortic insufficiency. She had a fever of 38.7°C, and blood cultures were obtained. In transesophageal ECO, 0.6 × 0.5-cm diameter vegetation on aortic valve was seen. The diagnosis was culture-negative infective endocarditis, and she was treated with ceftriaxone and gentamicin. However, 5 days later she had persistent fever. Blood cultures were repeated and cefazolin was begun in place of ceftriaxone. Transesophageal ECO was repeated, but a ring abscess was not detected. Left-side pleural effusion was seen on chest

radiograph. Pleural fluid was exudative and nonspecific, and tuberculosis cultures and Ziehl-Neelsen staining were negative. Proteinuria was detected on urine examination. Abdominal ultrasonography revealed no pathology. The therapy was changed to ampicillin-sulbactam and gentamicin. After the third day of this therapy, the fever did not repeat, but on the 20th day, fever returned. Blood cultures remained sterile. Left-side pleural effusion and collapse and consolidation areas were found by thorax computerized tomography. The patient's renal measures and hepatic function tests were impaired. Blood urea nitrogen was 48 mg/dl, serum creatinine 1.6 mg/dl, potassium 2.7 mEq/l. Gentamicin was discontinued. Renal function test results improved with parenteral fluid and electrolyte replacement. Transesophageal ECO was repeated and showed that 0.3 × 0.3-cm diameter vegetation on the aortic valve was persisting. Ferritin was 10,938 ng/ml. An atypical cardiac manifestation of AOSD was suspected and the fever resolved with naproxen. After we ruled out infective endocarditis, 60 mg/day steroid was started. The fever, pleural and pericardial effusions, and proteinuria disappeared; hyperferritinemia and elevated liver enzymes became normal. After discharge from hospital, the patient had no complaints and her biochemical markers were normal.

Clinical and laboratory manifestations of AOSD are significant for arthralgia, arthritis, fever of 39°C or higher, sore throat, rash, myalgia, weight loss > 10%, lymphadenopathy, splenomegaly and abdominal pain, elevated erythrocyte sedimentation rate, leukocytosis, anemia, and markedly elevated ferritin levels². Cardiac involvement is rare in AOSD. However, pericarditis is the most common manifestation of cardiac involvement^{3,4}. Ikeue, *et al*⁵ reported a case of severe AOSD presenting with pleuropericarditis. Both pleural and pericardial fluids were exudative and sterile. These findings were similar with our case. Endocarditis and pericardial tamponade is an unusual manifestation of AOSD that can simulate infective endocarditis. There are only a few cases in the literature^{3,4,6,7,8,9}. Zenagui and De Coninck⁹ described a case of AOSD mimicking acute bacterial endocarditis. Their patient had fever, sore throat, rash and arthritis, vegetation involving the aortic leaflet detected in transesophageal ECO, high erythrocyte sedimentation rate (ESR) and ferritin. Sarau, *et al*⁷ reported a case of noninfective endocarditis of the native tricuspid valve in a patient with AOSD. Our case had fever, vegetation on aortic leaflet, high ESR, and leukocytosis. These are compatible with bacterial endocarditis. However, the fever and the vegetation continued despite the appropriate antibiotic regimen.

The last classification of the disease was described by Yamaguchi, *et al*¹⁰. The major criteria are fever at 39°C or more for at least 1 week, arthralgia for at least 2 weeks, typical rash, and leukocytosis ($10 \times 10^9/l$ or greater, with at least 80% neutrophils). The minor criteria are sore throat, lymphadenopathy and/or splenomegaly, liver dysfunction, and negative rheumatoid factor (RF) and antinuclear antibody (ANA). The presence of 5 or more criteria, including at least 2 major and excluding infections, malignancies, and other rheumatological disorders, leads to the diagnosis of AOSD and has diagnostic sensitivity of 96.2% and specificity of 92.1%¹⁰. In our patient, there were 2 major (fever and leukocytosis) and 3 minor (sore throat, liver dysfunction, negative RF and ANA) criteria. In addition, the ferritin level was very high. These findings led us to consider AOSD.

These patients undergo variable diagnostic procedures, and unnecessary diagnostic studies may be performed. Invasive treatment alternatives may be used because of misdiagnosis. The multisystemic involvement of the disease may complicate the clinical decision. The components and complications of the disease can mimic every clinical condition. AOSD can present with cardiac and other systemic involvement without classical features as a first clinical manifestation, and this may confuse the clinician. In cases of culture-negative endocarditis with continuous fever and hyperferritinemia, AOSD should be considered in the differential diagnosis of fever of unknown origin.

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Table 1. Laboratory investigation results.

Result	Normal Range	Initial Result	Followup
Blood count			
WBC ($\times 10^3/mm^3$)	4–9	14.8	
Hemoglobin, g/dl	12–15	10.7	
Biochemical measures			
Aspartate aminotransferase, IU/l	< 40	60	391
Alanine aminotransferase, IU/l	< 40	77	356
Gamma-glutamyl transpeptidase, IU/l	< 45	56	56
Alkaline phosphatase, IU/l	21–85	82	82
Iron, µg/dl	31–144	11	—
TIBC, µg/dl	135–526	282	—
Saturation of iron, %	20–30	4	—
Transferrin, µg/dl	94–368	197	—
Ferritin, µg/dl	5–148	814	10938
Viral serology			
Hepatitis B	Negative	Negative	—
Hepatitis C	Negative	Negative	—
Epstein-Barr	Negative	Negative	—
Cytomegalovirus	Negative	Negative	—
Bacterial examination			
Blood culture		Sterile	Sterile
Urine culture		Sterile	Sterile
Brucella agglutination		Negative	—
Salmonella agglutination		Negative	—
Plasmodium		Negative	—
Immune markers			
Rheumatoid factor	Negative	Negative	—
Antinuclear antibody	Negative	Negative	—
Anticardiolipin antibodies	Negative	Negative	—
pANCA	Negative	Negative	—
C-reactive protein, mg/dl	< 6	37.4	—
Erythrocyte sedimentation rate, mm/h	< 20	101	—

WBC: white blood cells, TIBC: total iron binding capacity; pANCA: perinuclear antineutrophil cytoplasmic autoantibodies.

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