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Case Report

Atypical Presentation of Adult-Onset Still's Disease

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Abstract

Adult-onset Still's disease (AOSD) is a rare rheumatic disorder with various presentations. It is diagnosed based on the Yamaguchi criteria, besides the exclusion of infectious diseases and other rheumatic disorders and malignancies. Here, we describe a case of a young man, presenting with remittent fever, abdominal pain, and persistent nausea. Further evaluations showed elevated acute phase reactants, abnormal levels of liver transaminase, multiple lymphadenopathies, and pleural effusion. He was finally diagnosed with AOSD and responded well to corticosteroids and methotrexate. We describe the present case to alert gastroenterologists to AOSD as a rare differential diagnosis in patients with persistent gastrointestinal symptoms.

Keywords: Adult-onset, Still's disease, Persistent nausea, Abdominal pain

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Introduction

Adult-onset Still's disease (AOSD) is a rare systemic type of juvenile idiopathic arthritis caused by a severe inflammatory process with unknown etiology.[1] It is characterized by spiking fever, rash, arthritis, and extra-articular manifestations (dysphagia, odynophagia, lymphadenopathy, hepatomegaly, and splenomegaly).[2] Laboratory findings show non-specific changes including elevated inflammatory markers (erythrocyte sedimentation rate, C- reactive protein, serum ferritin, and neutrophilia). In addition, a previous study showed elevated serum adenosine deaminase (ADA) levels may be associated with Still's disease.[3]

It is diagnosed based on Yamaguchi criteria[4] after the exclusion of infections, malignancy, lymphoproliferative diseases, drug reactions, and other auto-inflammatory disorders.

Herein, we describe a young man who presented with persistent nausea, abdominal pain, and prolonged fever finally diagnosed with Still's disease. His paraclinical evaluations showed elevated serum liver transaminase, serum ferritin, lactate dehydrogenase (LDH), and exudative pleural effusion with increased ADA level. His symptoms responded well to corticosteroid therapy and methotrexate. This case is presented to point out that physicians consider gastrointestinal complaints as a rare initial presentation of AOSD.

Case Report

A 32-year-old man initially presented with a 3-month history of ambiguous periumbilical abdominal pain and persistent nausea. The abdominal pain was mild and constant but did not radiate to other sites and was not associated with bowel movement changes. The patient complained of weakness and 10 kg weight loss over 3 months. He also had a history of remittent fever, mostly in the evening for less than three hours. He did not report any night sweating, arthralgia, or skin lesions. He also denied alcohol consumption, tobacco/opium use, herbal medication use, or a history of recent travels. His medical history and family history were also unremarkable.

The patient was under symptomatic therapy, including 20 mg of pantoprazole once a day, 5 mg of domperidone three times a day, 250 mg of metronidazole three times a day, and 500 mg of naproxen twice a day. Based on the examinations, he was a young man (body mass index, 26 kg/m^2) with a blood pressure of 110/70 mm Hg, pulse rate of 82/min, respiratory rate of 12/min, and an oral temperature of 38.9°C. There was no evidence of exudate or erythema in the pharynx. A cervical lymph node examination showed a firm, mobile, non-tender cervical node (2 cm) in zone III on the right side. Moreover, axillary lymph node examinations revealed firm, mobile, non-tender nodes on both sides (maximum size, 1.9 cm). The examinations of the thorax and abdomen were unremarkable, except for mild splenomegaly. Other examinations were all normal.

During hospital admission, oral temperature measurements ranged from 36.8°C to 40°C. Table 1 summarizes the patient's laboratory data upon admission.

Considering the mildly elevated level of liver transaminase, the patient was evaluated for viral hepatitis, autoimmune hepatitis, and Wilson's disease, all of which were negative. Besides, his peripheral blood smear was

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Table 1. Laboratory findings

Hematologic					
WBC (white blood cell/μL)	21200	Coombs direct	Negative		
Lymphocyte (lymphocytes/μL) (%)	2140 (10.1%)	Coombs direct	Negative		
Neutrophil (/μL) (%)	18825 (88.8%)	PT	11		
Eosinophil (eosinophil/μL)	233 (1.1%)	PTT (s)	43		
Hemoglobin (g/dL)	8.8	INR	1.1		
MCV (fL)	78.6	ESR	75		
Platelets (platelet/μL)	335000	Reticulocyte count	Normal		
Biochemistry laboratory findings					
Cr (mg/dL)	0.7	AST (u/L)	78	CRP (mg/L)	98
Urea	76	ALT (u/L)	58	Ferritin (ug/L)	>8000
Na	134	Bili T (mg/dL)	0.87	Serum Iron (mcg/dL)	62
K	4.5	Bili D (mg/dL)	0.4	TIBC (mcg/dL)	336
Ca (mg/dL)	9	ALK.P (u/L)	287	IgG (g/L)	278 (elevated)
P (mg/dL)	3	CPK (u/L)	66		
Mg (mg/dL)	2	LDH (u/L)	742		
Rheumatologic					
Anti ds-DNA	8.4 (nl)	Anti CCP	0.8 (nl)	C-ANCA	Negative
ANA	0.4 (nl)	Rheumatoid factor	Negative	P-ANCA	Negative
Anti cardiolipin Ab (IgG)	6.6 (nl)	C3 (mg/dl)	125	Wright	Negative
Anti cardiolipin Ab (IgM)	2.8 (nl)	C4 (mg/dl)	21	2ME	Negative
Anti-B2 glycoprotein (IgM)	7.6 (nl)	SSB-LA	4.7 (nl)	Ceruloplasmin (g/l)	0.3
Lupus anticoagulant	Negative	SSA-RO	504 (nl)	Rheumatoid factor	Negative

nl: Normal; PT: Prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio; ESR: Erythrocyte sedimentation rate; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ALK.P: Alkaline phosphatase; CRP: C-reactive protein; TIBC: Total iron-binding capacity

negative for any microorganisms or abnormal cells. The stool examination was also normal, and blood culture (×3), urine culture (×2), COVID-19 polymerase chain reaction (PCR), and cerebrospinal fluid were all negative.

The purified protein derivative (PPD) skin test was non-reactive (6 mm), and the interferon-gamma release assay (IGRA) was negative. Because of persistent nausea, the patient underwent a brain computed tomography (CT), which was unremarkable. The upper gastrointestinal endoscopy revealed pangastritis. Additionally, total colonoscopy with terminal ileum intubation and magnetic resonance enterography were all normal. Abdominal/pelvic CT scan showed mild splenomegaly and non-significant lymphadenopathy in the para-aortic, aortocaval, and left iliac plexus regions (Figure 1).

During hospital admission, the patient developed sudden onset dyspnea. A lung CT scan showed moderate pleural effusion with collapse consolidation on the left side and multiple mediastinal lymph nodes (Figure 2).

Moreover, pulmonary CT angiography was negative for emboli. The pleural fluid analysis indicated exudative effusion (protein: 3400; LDH: 2311; WBC: 270; ADA: 45; tuberculosis PCR: negative), and cytology was negative. Considering the elevated ADA level and mediastinal lymphadenopathies, the patient underwent bronchoscopy, endobronchial bronchoscopic fine needle aspiration, and pleuroscopy, which did not suggest any infections or malignancies. Besides, bone marrow aspiration/biopsy (BMA/B) was normal. Enlarged neck and axillary lymph nodes were removed via excisional biopsy for a histological examination, which was negative for malignancy, granuloma, and plasma cells. On the fifth day of admission, the patient started to complain of knee and shoulder arthralgia, which partially responded to non-steroidal anti-inflammatory drugs.

Hematologic and infectious disorders were ruled out because of negative lymph node biopsy, normal BMA/B results, negative cultures, and negative serological and PCR results. Finally, a consultant rheumatologist diagnosed AOSD based on fever, arthralgia, lymphadenopathy, splenomegaly, leukocytosis, elevated LDH, and ferritin levels, and abnormal liver enzymes. Prednisolone (1 mg/kg) and methotrexate (7.5 mg/wk) were initiated for the patient. He showed a dramatic response to treatment, and his symptoms were relieved.

Discussion

In this report, we presented the case of a young man with prolonged fever, abdominal pain, and persistent nausea. He was finally diagnosed with AOSD based on the Yamaguchi criteria after the exclusion of infectious diseases, malignancies, and other rheumatic disorders.[2] Our patient met three major criteria (fever > 39°C, arthralgia, and leukocytosis with neutrophilia) and

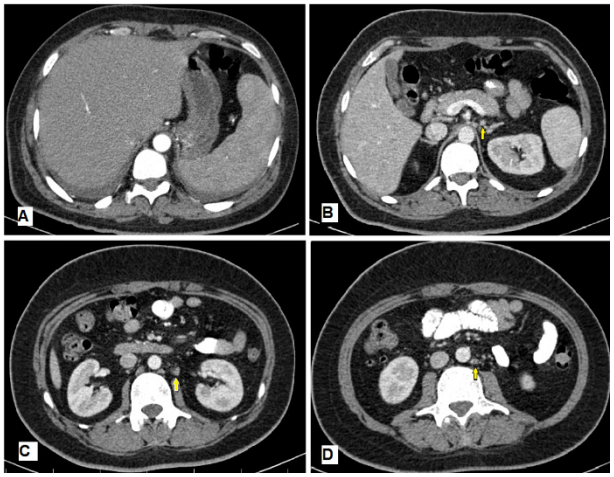

Figure 1. **(A)** Mild splenomegaly and **(B), (C), (D):** non-significant lymphadenopathies

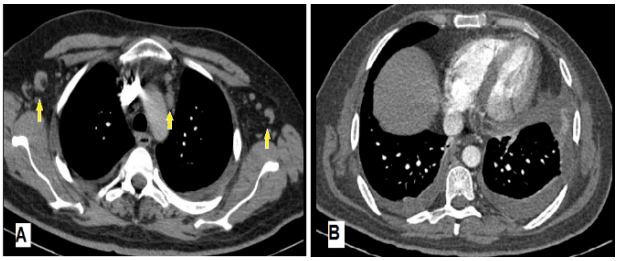

Figure 2. Chest CT scan showed **(A):** both sides axillary lymphadenopathies and multiple mediastinal pre-vascular lymph nodes enlargement **(B):** bilateral mild pleural effusion with adjacent collapse consolidation

four minor criteria (lymphadenopathy, splenomegaly, abnormal liver transaminase, and negative antinuclear antibodies [ANA] and rheumatoid factor [RF]).

Recently, Simon and colleagues presented the case of a 28-year-old man, who presented with prolonged fever, generalized arthralgia, and morning stiffness. He was diagnosed with AOSD and completely responded to prednisolone (60 mg/d) treatment.[5] Another report described the case of an 18-year-old woman, presenting with arthralgia, skin rash, fever, and lymphadenopathy. The pathological examination of lymph nodes showed a mixed pattern of lymphoid follicles and paracortical areas with a mild predominance of CD8-positive T lymphocytes.[6] However, in the present case, the pathological examination of lymph nodes showed reactive hyperplasia.

The serum ferritin level was elevated in our patient, which was associated with disease activity and relapse of AOSD. In this regard, based on a recent study conducted in Japan on 110 patients with AOSD and 46 controls, a serum ferritin level > 819 ng/mL showed sensitivity and specificity of 80% and 71%, respectively.[7] Corticosteroid is recognized as the first-line treatment for Still's disease, with a clinical response rate of 65%.[2,8] However, most of the patients do not respond to corticosteroids alone, and the addition of a disease-modifying antirheumatic drug (DMARD) is necessary. The most commonly used DMARD is methotrexate, which exhibits high efficacy against systemic and chronic AOSD. Also, treatment with biological agents may be effective for patients who are refractory to steroid and DMARD therapies.[9] Our patient was treated with a combination of prednisolone and methotrexate immediately after diagnosis and showed dramatic improvements in the clinical and laboratory findings.

We described the present case to alert gastroenterologists to AOSD as a rare differential diagnosis in patients with persistent gastrointestinal symptoms.

Competing Interests

The authors declare no conflict of interest related to this work.

Ethical Approval

Informed consent was obtained form the patient for publication of this report.

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