

Severe Adult-Onset Still's Disease Mimicking Systemic Infection

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Abstract

Adult-onset Still's disease (AOSD) is an uncommon entity that can mimic infection. Patients present with fever for more than 1-week, joint pain, and rash. We report a case of 22-year-old male who presented with fever, sore throat, and abdominal pain. During hospitalization, he had multiple episodes of tachycardia and tachypnea requiring mechanical ventilation. The patient had elevated white blood cell count, procalcitonin, and troponin. He was extensively investigated and diagnosed as AOSD. He responded to steroids and was discharged on day 20.

Keywords: Adult-onset Still's disease, fever, procalcitonin

INTRODUCTION

We present an unusual case of young 22-year-old male who was admitted to intensive care unit with high-grade fever and hypoxic respiratory failure requiring ventilatory support. The patient had elevated white blood cell count, procalcitonin (PCT), and troponin. Differential diagnoses were myocarditis, pneumonia, and sepsis. Despite broad-spectrum coverage, his fever never subsided prompting to extensive investigation to rule out both infectious and noninfectious etiology. This case shows how diagnosis of Still's disease is complex, time, and resource consuming and is a diagnosis of exclusion.

CASE REPORT

A 22-year-old young male presented with fever, sore throat, and generalized weakness, myalgia, and abdominal pain for 3 days. He was treated as an outpatient for the above symptoms, with no relief. He was admitted to the floors for further evaluation. On examination, he had tachycardia (heart rate: 118/min) and febrile spikes (Tmax: 102.7* F). Rest of systemic examination was unremarkable. Oral cavity examination was normal. There were no petechiae or muscle tenderness. Past history of rheumatic fever during childhood for which he was on penicillin prophylaxis and stopped seven years prior to the presenting complaints. There was no history of heart ailments in past or recurrence of joint pains. He was evaluated,

and his investigations showed leukocytosis (thin-layer chromatography: 20.3×10^3) Rest of routine blood investigations were within normal limits.

After sampling for blood cultures, he was started on intravenous antibiotics. During his stay, he became tachypneic, tachycardic and complained of chest pain. Electrocardiogram showed global ST depression and troponin I was elevated. Subsequently, he was intubated in view of respiratory distress. Two-dimensional (2D) echo showed new onset global hypokinesia which was normal at time of admission. He continued to have febrile spikes. His antimicrobials upgraded suspecting pneumonia with sepsis and myocarditis. Infective (bacterial and viral) causes were evaluated. His blood cultures, throat swab for H1N1, and diphtheria were negative. There was persistence of febrile spikes with typical rise in the evening along with upper abdominal pain and tachycardia. Repeat 2D echo normalized and troponin I decreased. Hemodynamics was maintained throughout his hospital stay. Contrast-enhanced computed tomography of the chest and abdomen was done to find infective source, which only showed bilateral basal consolidation. Baseline

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PCT level was elevated. Other infective and autoimmune causes were ruled out by doing *Leptospira*, dengue, malarial parasite, HIV, hepatitis C virus, HbsAg, scrub typhus, and *Brucella* serology. Antinuclear antibody (ANA), ANA profile, rheumatoid arthritis, C-ANCA, P-ANCA, and antistreptolysin O titers were negative. Transesophageal echocardiography was negative for any infective endocarditis. His antibiotics were upgraded to colistin as *Acinetobacter* was isolated from bronchoalveolar lavage cultures. Despite treatment with colistin, he continued to have febrile spikes with episodes of pulmonary edema. Serial PCT levels were elevated. He failed to extubation and was reintubated. Repeat computed tomography chest was consistent with prior findings. Blood was sent for septic polymerase chain reaction panel which was also negative. Bone marrow biopsy and cultures were inconclusive. C-reactive protein and serum ferritin levels (>1200) were elevated. He was initiated on steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) after which his febrile spikes subsided. His PCT levels have decreased after initiation of steroids. He was extubated on day 13. Steroids were gradually tapered, and he was discharged after 20 days [Table 1].

DISCUSSION

This case illustrates the challenges in diagnosing adult-onset Still’s disease (AOSD) due to its nonspecific symptoms and lack of diagnostic markers. It is a diagnosis of exclusion after ruling out infective and non infective causes. Most of the patients present with fever of unknown origin with complaints of fever, joint pain, or rash.^[1] Diagnosis can be made basing on clinical presentation. There are several sets of classification used for AOSD, and Yamaguchi’s disease is the sensitive of all. It includes major and minor criteria.^[2]

Major criteria include (1) fever of at least 39°C for at least a week, (2) arthralgia or arthritis for at least 2 weeks, (3) nonpruritic salmon-colored rash on the trunk or extremities, and (4) granulocytic leukocytosis (10,000/micro or greater). Minor criteria include (1) sore throat, (2) lymphadenopathy, (3) hepatomegaly or splenomegaly, (4) abnormal liver function tests, and (5) negative tests for rheumatoid factor and ANA. Diagnosis requires at least five features with two of them being major diagnostic criteria. In 2002, Fautrel *et al.* proposed a new criterion which contained two new markers, i.e., serum ferritin and glycosylated ferritin.^[3] Major criteria include (1) spiking fever $\geq 39^{\circ}\text{C}$, (2) arthralgia,

(3) transient erythema, (4) pharyngitis, (5) neutrophilic polymorphonuclear count >80%, and (6) glycosylated ferritin <20%. Minor criteria include (1) typical Still’s rash and (2) leukocytosis (10,000/mm³). For diagnosis by Fautrel criteria requires 4 major criteria or 3 major and 2 minor criteria.

AOSD is a rare systemic inflammatory disorder with unclear pathogenesis. Many factors have been implicated including genetics, infectious etiology, and immunological contributors. Recent studies have shown pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, IL-18, tumor necrosis factor (TNF), and macrophage colony-stimulating factors elevated in AOSD, thus playing a pivotal role in pathogenesis. This surge in cytokines leads to neutrophil and macrophage activation.

AOSD presenting as a mimic of infection makes it more complicated for the physician. PCT which is marker of infection and sensitive biomarker used to differentiate from noninfectious etiology can be falsely elevated adding onto the dilemma of sepsis. Serum PCT normally produced in the C-cells of the thyroid gland is a precursor of calcitonin. Its level is undetectable (<0.1 ng/ml) in healthy humans. During severe infections with systemic manifestations, serum PCT levels may increase to over 100 ng/dl. However, this can also be falsely elevated in AOSD as it is also activated by cytokines. In AOSD, there is a surge of cytokines (TNF-alpha) causing systemic inflammatory response syndrome response, and blood sampling during the surge can elevate the PCT levels.^[4] Interpretation of results can misguide us to injudicious usage of antibiotics and subject the patient to a battery of clinical investigations. The treatment of AOSD consists of NSAIDs, steroids, and antirheumatic agents.^[5] Recent understanding of disease pathogenesis has led to the development of targeted therapies. Biological agents such as IL-1 and IL-6 inhibitors and TNF inhibitors have been used.^[6] Anti-TNF agents such as infliximab, etanercept, and adalimumab had shown promising results in several studies. IL-1 inhibitors have specifically led to clinical improvement in refractory AOSD. Presently available IL-1 antagonists are anakinra, canakinumab, and riloncept. Plasma exchange and intravenous immunoglobulins are the other alternative therapies to be considered in refractory AOSD.

CONCLUSION

Our spectrum of differentials must be much broader when we encounter a patient with nonresponding unremitting febrile

Table 1: Investigations

	Day 1	Day 2	Day 3	Day 7	Day 9	Day 11	Day 12	Day 13	Day 15
WBC ($\times 10^3$)	20.3	18.6	16.0	21.2	35.1	36.7	35.2	15.1	14.8
Neutrophils (%)	86	91	85	90	93	96	91	81	85
PCT (ng/ml)			2.56		6.8	81.59	73.10		1.62

WBC: White blood cell; PCT: Procalcitonin

spikes with an elevated PCT and not rather treat as another case of sepsis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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