Case report

Articular Silence: Acute Pericarditis Unveiling Still's Disease- Case Report and Literature Review

Abstract:

Adult-onset Still's Disease (AOSD) is a rare form of systemic inflammatory polyarthritis characterized by various symptoms such as prolonged fever, rash, and arthralgia. However, it can also present with pericardial effusion, often misdiagnosed as being of infectious origin, since AOSD typically manifests with fever and a biological inflammatory syndrome.

We report the case of a 54-year-old man hospitalized for dyspnea and chest pain, evolving in the context of intermittent fever related to acute pericarditis. AOSD was considered after excluding any infectious, neoplastic, or autoimmune process. Corticosteroid therapy, followed by treatment with the interleukin 1 receptor antagonist (anakinra), resulted in rapid favorable evolution.

AOSD is a rare disease with an unusual presentation and often delayed diagnosis, leading to treatment delays. This case aims to raise awareness among physicians about the multifaceted presentation of AOSD.

Keywords: Adult onset Still's disease, Flare, Pericardial evusion

Introduction

Adult-onset Still's Disease (AOSD) is a rare form of systemic inflammatory arthritis characterized by a variety of symptoms, such as prolonged fever, rash, and arthralgia. Various systems may be involved, including pharyngeal, hepatic, splenic, and lymphatic systems. Cardiac complications, especially pericardial effusions, are often misdiagnosed as being of infectious origin because the disease generally presents with fever and a biological inflammatory syndrome. Here, we describe a rare case of AOSD revealed by acute pericarditis, exploring the clinical specifics, diagnostic methods, and treatment options.

Case Report

A 54-year-old man presented to the emergency department with NYHA class III dyspnea and atypical chest pain. On clinical examination, the heart rate was elevated to 130 beats per minute and blood pressure was 103/65 mmHg. There were no signs of heart failure. The electrocardiogram (Figure 1) showed a regular sinus rhythm with PQ segment depression in the inferior territory and slight diffuse ST segment elevation concave upward without reciprocal changes. Transthoracic echocardiography revealed a moderate circumferential pericardial effusion (Figures 2 and 3). Laboratory tests indicated significant inflammatory syndrome, with negative troponin levels.

The patient was initially treated with aspirin and colchicine, but there was no clinical, biological, or echocardiographic improvement. A thorough medical history revealed intermittent fever and arthralgia. Tests for tuberculosis were negative, as well as viral serologies (HIV1 and 2, hepatitis B

and C), rheumatoid factor, and antinuclear and anti-DNA antibodies. Ferritin levels were elevated, associated with a decreased glycosylated fraction. A PET scan showed hypermetabolism in the serous membranes. The definitive diagnosis of AOSD was made according to Yamaguchi and Fautrel criteria.

Following consultation with internists, the patient was started on corticosteroid therapy. Remarkable clinical improvement was observed within a few days, with resolution of fever, inflammatory syndrome, and regression of the pericardial effusion, albeit with side effects such as weight gain, mood elevation, and hypertension. During the tapering of corticosteroids, a resurgence of the inflammatory syndrome was noted. Consequently, treatment with ANIKRA was initiated, which was well-tolerated and without signs of relapse.

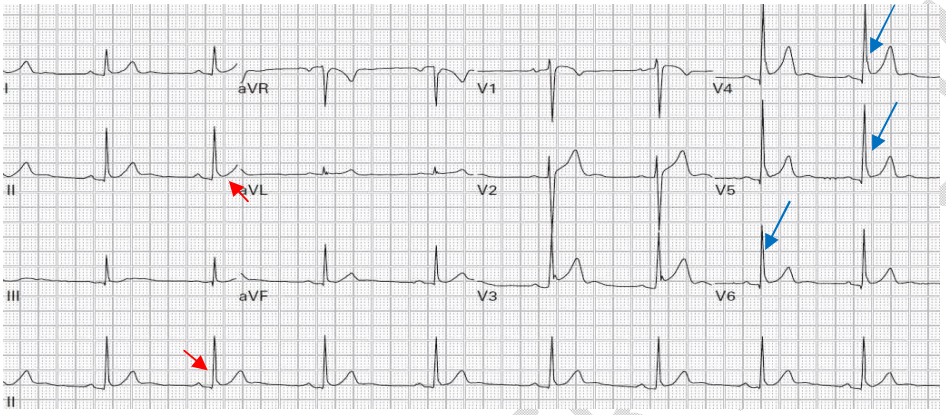
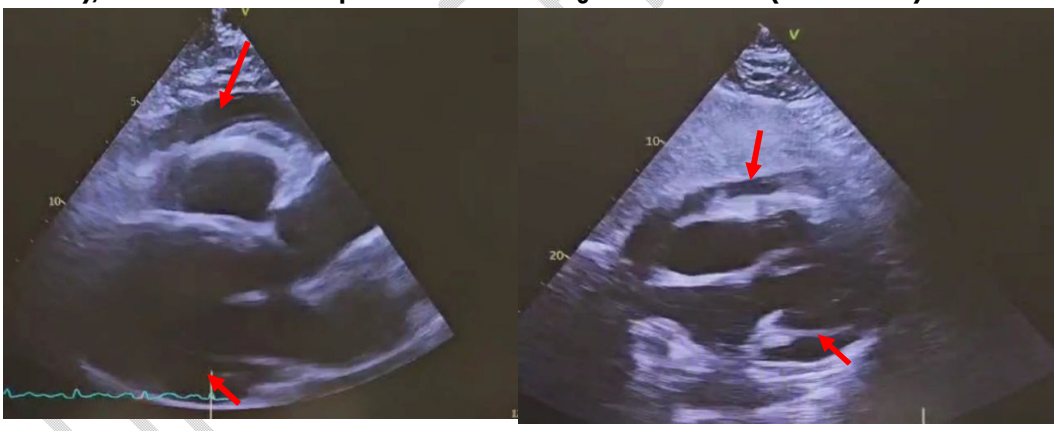


Figure 1: Surface electrocardiogram showing PQ segment depression in the inferior territory (red arrows), associated with an upward concave ST segment elevation (blue arrows).



Figures 2 and 3: Two-dimensional transthoracic echocardiography in long-axis and subcostal views showing a circumferential pericardial effusion (red arrows).

Discussion

Adult-onset Still's Disease (AOSD) was first described in children by pediatrician George Frederic Still in the late 19th century, before a similar form in adults was distinctly identified by Bywaters in the early 1970s [2]. According to studies, the average age at diagnosis ranges from 27 to 36 years, with extremes between 16 and 83 years [3].

The mechanisms responsible for AOSD are not yet fully understood. However, this pathology presents similarities with autoinflammatory diseases, including clinical symptoms such as fever, skin rashes, serous inflammations, and arthritis. Unlike autoimmune diseases, AOSD does not show specific autoantibodies or autoantigens of T lymphocytes, and it responds well to treatments blocking interleukin 1 (IL-1) [4].

While most autoinflammatory diseases are hereditary and linked to monogenic mutations, AOSD is not associated with family history, ethnic groups, or specific geographic regions. Studies have attempted to establish a link between AOSD and HLA haplotypes, without conclusive results. Various viral, bacterial, or parasitic infections and certain environmental toxic factors have been suggested as potential triggers of AOSD, though the causal link remains uncertain and based on limited observations.

Elevated levels of pro-inflammatory cytokines, such as IL-1, IL-6, IL-18, and tumor necrosis factor (TNF), have been observed in AOSD, indicating their key role in pathogenesis. Environmental danger signals could trigger an uncontrolled inflammatory response within innate immune cells (primarily macrophages and neutrophils), leading to the production and secretion of pro-inflammatory cytokines and the recruitment of adaptive immune cells.

AOSD is also strongly associated with hemophagocytic lymphohistiocytosis or macrophage activation syndrome, suggesting a common or similar pathogenesis between these conditions.

Adult-onset Still's Disease presents multiple non-specific clinical manifestations, making diagnosis difficult. Cardiac complications of AOSD require further studies. This necessity is not due to a lack of understanding of the pathophysiology but to the importance of making a prompt diagnosis. The classification criteria of Yamaguchi and the more recent criteria by Fautrel consider this disease as a diagnosis of exclusion. Physicians must first rule out more common causes such as infection, malignancy, drug reactions, or other rheumatological disorders [5, 6] (Table 1).

Table 1. Classification Criteria for AOSD

Yamaguchi	Fautrel
Major Criteria	
1. Fever ≥39°C, lasting 1 week or more 2. Arthralgia, lasting 2 weeks or more 3. Typical rash: maculopapular, non-pruritic, salmon-pink, occurring with febrile peaks 4. Leukocytosis ≥10,000/mm³ with neutrophils ≥80%	1. Febrile peaks ≥39°C 2. Arthralgia or arthritis 3. Transient or fleeting erythema 4. Pharyngitis 5. Neutrophils ≥80% 6. Glycosylated ferritin fraction ≤20%
Minor Criteria	

1. Pharyngitis or sore throat 2. Lymphadenopathy or splenomegaly 3. Abnormal liver function tests (elevated transaminases) 4. Absence of rheumatoid factor or antinuclear antibodies	1. Typical rash 2. Leukocytosis ≥10,000/mm³
Exclusion Criteria	
1. Absence of infection, particularly deep sepsis and EBV-related infection 2. Absence of neoplasia, particularly lymphoma 3. Absence of inflammatory disease, particularly polyarteritis nodosa	None
DiagnosisCriteria	
At least 5 criteria, including 2 major criteria, with no exclusion criteria	**4 major criteria or 3 major criteria and 2 minor criteria**

Pericarditis is observed in approximately 10 to 14% of patients, with 20% developing pericardial effusion and potentially presenting with cardiac tamponade. It can be accompanied by pleural effusion in 60 to 80% of cases. Pericarditis may appear during the initial flare of the disease but can recur and progress to constriction. No predictive factors for pericarditis have been identified in the context of Still's disease. The pericardial fluid is often serohematic and exudative, with pericardial biopsies typically showing non-specific acute or chronic edematous pericarditis [7].

Myocardial involvement is not uncommon and can present as rhythm disturbances, repolarization abnormalities, or intraventricular conduction issues, and in severe cases, congestive heart failure. Myocardial involvement frequently accompanies pericarditis, complicating the lesion diagnosis. Valvular involvement is rare, and only a few cases of severe pulmonary hypertension have been reported.

The diagnosis of AOSDremains complex, even with classic symptoms. Our case illustrates that pericardial effusion can be the sole symptom of an AOSD flare, and that adult-onset Still's Disease should be considered to avoid diagnostic and therapeutic delays.

Corticosteroids are the first-line treatment for AOSD. They are particularly effective in systemic forms of the disease, achieving remission in 65% of cases [8]. Although clinical efficacy is often rapid, the initial dose is generally maintained for 4 to 6 weeks before a gradual reduction. Unfortunately, 45% of patients become corticosteroid-dependent, and up to 75% develop side effects. Early introduction of corticosteroid-sparing treatments, such as methotrexate, could mitigate these risks. Methotrexate has proven effective, particularly in the articular and systemic forms of AOSD, though one-third of patients may experience mild adverse effects.

Non-steroidal anti-inflammatory drugs are not recommended as first-line treatment for AOSD due to an unfavorable benefit-risk ratio, although they may be useful in indolent rheumatologic forms [9].

Intravenous immunoglobulins have shown some benefit in AOSD refractory to NSAIDs, particularly during flares in pregnancy [10]. For refractory cases, biologic therapies are used chronologically, including TNF-α blockers, anakinra, and anti-IL-6 (tocilizumab). These treatments are generally reserved for patients refractory to first-line treatments [11].

Two distinct phenotypes can be identified:

1. **Systemic form**: Characterized by often severe initial symptoms, exposing patients to serious complications, primarily hemophagocytic lymphohistiocytosis. Anakinra, blocking the interleukin-1 pathway, appears effective for this form.
2. **Chronic articular form**: More indolent but can compromise functional prognosis in cases of destructive arthropathy. Blocking the interleukin-6 pathway seems more effective for this form.

Conclusion

This case of adult-onset Still's Disease revealed by acute pericarditis highlights the importance of a thorough diagnostic approach and well-conducted treatment. Early recognition of atypical signs and symptoms can improve the prognosis of patients with this complex systemic disease. The originality of our observation lies in the age of our patient and the mode of presentation. Our case demonstrated that corticosteroid resistance is not uncommon, necessitating the immediate initiation of anti-interleukin treatment.

Consent

Informed written consent was obtained from patient to publish his clinical data.

Ethical approval

It is not applicable.

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