A case report of Adult-onset Still’s disease as a cause of severe mitral regurgitation

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Background

Adult-onset Still’s disease (AOSD) is an uncommon systemic inflammatory disease, causing spiking fever, skin rash, and arthritis. Pericarditis and myocarditis are the most common cardiac manifestation of AOSD but valvular involvement is rarely reported.

Case summary

An 18-year-old boy presented with gradually worsening shortness of breath for 6 months. There was a history of low-grade intermittent fever and polyarthralgia affecting ankles, knees, and elbows. He was in heart failure with cardiogenic and septic shock. He was managed initially with antibiotics, inotropes, and diuretics. Echocardiography showed flail anterior mitral leaflet with severe mitral regurgitation. He remained febrile with persistent negative blood cultures. Intravenous antibiotics led to neutropenia without any response to fever and clinical status. On further workup, he was diagnosed to have AOSD, and he responded dramatically to oral steroid therapy. Later his mitral valve was replaced surgically. On follow-up, he was stable with mild exertional dyspnoea. His international normalized ratio was in therapeutic range and his follow-up echocardiography showed normally functioning mitral prosthesis. He is following rheumatology and currently on the maintenance dose of steroids.

Discussion

Adult-onset Still’s disease is a systemic illness with diagnosis is based on clinical features and exclusion of other illnesses. Adult-onset Still’s disease should be considered as a differential diagnosis in culture-negative endocarditis, especially in those with systemic features and non-responders to antibiotics.

Keywords

Case report • Adult-onset Still’s disease • Mitral regurgitation • Infective endocarditis

Learning points

• Adult-onset Still’s disease is systemic disease presenting as triad of fever, rash, and arthralgias.
• Cardiac manifestations range from pericarditis, myocarditis to endocarditis.
• Management of cardiac involvement depends on the severity.
• Adult-onset Still’s disease should be considered as differential diagnosis in culture-negative infective endocarditis.
Introduction

Adult-onset Still’s disease (AOSD) is an uncommon systemic inflammatory disease, causing spiking fever, skin rash, and arthritis. It is characterized by the presence of neutrophilic granulocytosis, raised ferritin levels, deranged liver enzymes, and absence of rheumatoid factor and antinuclear antibody test results. The exact aetiology of this illness is still unknown, and the diagnosis is based on exclusion, as there are no pathognomonic features. Pericarditis and myocarditis are the most common cardiac manifestation of AOSD, but valvular involvement is also reported. Here, we report a case of a young male who was initially diagnosed and treated as infective endocarditis, but later multisystemic involvement, lack of response to antibiotics, and further workup led to the diagnosis of AOSD.

Timeline

| First admission | Week 1  | • Admission with infective endocarditis and heart failure  
|                |        | • Diagnosed severe mitral regurgitation due to flail leaflet  
|                |        | • Intravenous diuretics  
|                |        | • Antibiotics  
|                | Week 2  | • Development of neutropenia  
|                |        | • Haemodynamically stable  
|                |        | • Negative blood cultures and positron emission tomography scan  
|                |        | • Antibiotics stopped  
|                | Week 3  | • Diagnosis of Adult-onset Still’s disease  
|                |        | • Recovery from neutropenia  
|                |        | • Started corticosteroid treatment  
|                | Week 4  | • Leucocytosis  
|                |        | • Symptomatic recovery  
|                |        | • Discharge home  
| Second admission | Week 1  | • Elective admission for surgery after 8 weeks  
|                |        | • Surgical mitral valve replacement  
|                | Week 2  | • Post-operative recovery  
|                |        | • Discharge  

Case presentation

An 18-year-old boy presented to our centre with gradually worsening shortness of breath for 6 months. For the last 5 days, he was experiencing dyspnoea at rest, along with orthopnoea and paroxysmal nocturnal dyspnoea. There was a history of low-grade intermittent fever and polyarthralgia affecting ankles, knees, and elbows. He also experienced intermittent ankle joint swelling over the past 2 months. His symptoms were associated with productive cough and a single episode of haemoptysis. On physical examination, he was tachycardic (heart rate of 105 b.p.m.) with low blood pressure (92/59 mm/Hg) and oxygen saturation was 89% on room air. His recorded body temperature was up to 39°C. Right supraclavicular lymph nodes were palpable. His apex beat was displaced and on auscultation, he had a pan-systolic murmur at the mitral area, radiating to the axilla.

Initially, he presented to the secondary level hospital and diagnosed as infective endocarditis based on history and transthoracic echocardiographic finding of possible vegetation on the mitral valve (Figure 1, Supplementary material online, Video 1). He was started on intravenous (IV) antibiotics (Vancomycin, Gentamycin, and Ceftriaxone) without significant response. He was admitted to the cardiac care unit after transfer to our centre and started on Norepinephrine 0.03 µg/kg/min initially and then titrated according to blood pressure. Furosemide IV infusion was started at 10 mg/h. His antibiotics regimen was revised, and he was given Vancomycin 1 g IV twice daily, Gentamycin 60 mg IV thrice daily, and Tazobactam–piperacillin 4.5 g IV 6 hourly.

Transoesophageal echocardiography showed Flail anterior mitral leaflet (mainly A2 segment) due to rupture chordae with severe mitral regurgitation (Figure 2, Supplementary material online, Video 2). There was no evidence of vegetation on the mitral valve. The left ventricle was severely dilated with normal systolic function (ejection fraction = 60%). The right ventricle was normal in size and function, and other valves were normal. His blood investigations revealed negative blood cultures and low white cell count with neutropenia in the first week (Table 1). He remained febrile despite being on antibiotics. All antibiotics were stopped, considering them as a possible cause of neutropenia. Bone marrow biopsy was done, which showed hypocellular bone marrow (cellularity of 40%) with trilineage haematopoeisis. There was no evidence of granuloma or malignancy. After stopping antibiotics, repeated blood cultures remained negative. His total white cell and neutrophil count started rising, and he continued to have a fever. His other investigations revealed the erythrocyte sedimentation rate (ESR) of 68 mm/h (normal range <15 mm/h) and C reactive protein (CRP) 9 mg/L (normal range <3.0 mg/L). His liver functions were deranged (alanine transaminase, aspartate transaminase, alkaline phosphatase) (Table 1). His ferritin level was

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Table 1

| Admission | First week | Second week |
|-----------|------------|-------------|
| Admission | Week 1     | Week 2      |
| Admission | Week 3     | Week 4      |

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Figure 1 Transthoracic echocardiogram (parasternal long-axis view), on left showing flail anterior mitral leaflet and on right, severe posteriorly directed jet of severe mitral regurgitation. AML, anterior mitral leaflet; MR, mitral regurgitation.
25 499.4 ng/mL (normal range 12–300 ng/mL). Other immune markers like antineutrophil cytoplasmic antibody, antinuclear antibody (ANA), and rheumatoid factor (RF) were negative. The viral panel was also negative. The infectious disease team advised doing a whole-body positron emission tomography scan, which failed to show any focus of inflammation.

Considering his presentation of polyarthralgia, fever, and lymphadenopathy, rheumatology was consulted, who, based on Yamaguchi’s criteria, labelled him as an AOSD (Table 2). He was started on prednisolone 1 mg/kg/day. He responded to steroid therapy, and his fever started settling along with markers of inflammation (white cell count, ESR, and CRP). After 4 weeks of this admission, he was discharged home with outpatient follow-up with rheumatologist and cardiac surgeon. He was electively readmitted for surgery after 8 weeks. The mitral valve was assessed intraoperatively and due to non-suitability for repair, it was replaced with a mechanical valve (ATS size 31) with total chordae preservation. The excised valve was sent for histopathological examination which showed areas of fibrosis.

### Table 1 Blood investigations during first and second admission

| Parameters                  | Normal values | First admission | Second admission |
|-----------------------------|---------------|----------------|-----------------|
|                             |               | First week     | Second week     | Third week     | Fourth week   | First week    | Second week   | At discharge  |
| White cell count (10⁹/L)    | 3.9–11        | 5.76           | 1.69            | 6.32           | 20.25         | 12.84         | 10.93         | 14.8          | 13.67         |
| Absolute neutrophil count   | 1.35–7.5      | 2.93           | 0.52            | 3.31           | 15.85         | —             | 6.28          | 11.36         | 10.85         |
| Haemoglobin (g/dL)          | 13.5–18       | 8.8            | 8.7             | 8.2            | 8.3           | 11.2          | 11.6          | 7.6           | 10.6          |
| Platelet count (10⁹/L)      | 155–435       | 481            | 353             | 498            | 765           | 534           | 406           | 147           | 830           |
| Serum creatinine (μmol/L)   | 64–104        | 88             | 110             | 79             | 65            | 46            | 56            | 36            | 45            |
| Blood urea (mmol/L)         | 3–7.5         | 5.5            | 6.5             | 6.6            | 7.9           | 4.0           | 4.6           | 3.9           | 3.7           |
| Total bilirubin (μmol/L)    | 3–20          | 14.4           | 11.2            | 9.7            | 5.6           | 4.9           | 4.6           | 19.0          | 7.9           |
| Alanine transaminase (U/L)  | 0–55          | 145            | 92              | 164            | 300           | 18            | 17            | 16            | 37            |
| Aspartate transaminase (U/L)| 0–55          | 38             | 69              | 51             | 63            | 11            | 13            | 26            | 25            |
| Alkaline phosphatase (U/L)  | 89–365        | 50             | 31              | 32             | 55            | 37            | 33            | 25            | 48            |

### Table 2 Yamaguchi diagnostic criteria for Adult-onset of Still's disease

| Major criteria                                                      | Minor criteria                                      |
|--------------------------------------------------------------------|-----------------------------------------------------|
| Fever >39°C for at least 1 week                                     | Sore throat or pharyngitis                          |
| Arthralgia or arthritis for >2 weeks                                | Lymphadenopathy                                     |
| Non-pruritic salmon-pink coloured rash (usually over trunk or extremities while febrile) | Hepatomegaly or Splenomegaly                       |
| Leucocytosis >10 000/mm³                                           | Abnormal liver function tests/aminotransferases     |
| Neutrophils >80%                                                   | Negative tests for antinuclear antibodies or rheumatoid factors |
| Exclusion criteria                                                 | At least 5 criteria, including 2 major and no exclusion criteria |
| Absence of infection                                               |                                                     |
| Absence of malignant disease                                       |                                                     |
| Absence of inflammatory disease                                    |                                                     |
and mild myxoid degeneration with no evidence of inflammation or vegetation (Figure 3).

On follow-up, he was stable with mild exertional dyspnoea. His international normalized ratio was in therapeutic range, and he was following the rheumatology clinic as well and he is kept on low dose steroids. His follow-up echocardiography showed normally functioning mitral prosthesis with left ventricular ejection fraction of 55%.

Discussion

Adult-onset Still’s a disease is a systemic disorder with no clear aetiology. It is rare, with a prevalence of 1.5 cases per 100 000–1 000 000 people. The disease is more prevalent in females than in males. Although it has been reported with bimodal age distribution, the disease commonly affects the younger population, with three-quarters of patients reported are between age 16 and 35 years.5,6 Exact aetiology is unknown but genetic, altered cytokines production and microbial aetiologies have been suggested in the literature.7,8 The most common clinical manifestations include the triad of a typical salmon-pink rash, high-spiking fever, and arthralgias or arthritis. Fever and joint involvement are present in most of the cases and skin rash can be found in up to 72% of cases.1,8–10 Adult-onset Still’s disease is also known for its systemic involvement which includes myalgias, hepato-splenomegaly, pleural effusion, renal and haematological complications.8,10,11

The diagnosis of AOSD is exclusively dependent on clinical manifestation due to the absence of diagnostic tests and serological markers. The Yamaguchi criteria are most widely recognized for the diagnosis of AOSD with a statistical endorsement with a sensitivity of 96.2% and a specificity of 92.1%.2 (Table 2). The diagnosis of AOSD is made if at least five features are positive, and two of them should be major diagnostic criteria. It is crucial to exclude infections, inflammation, and malignancy before applying them to make this diagnosis. Our patient fulfilled three major and two minor criteria which are fever, arthritis, leucocytosis, liver dysfunction, and negative RF and ANA factors. The other laboratory tests in AOSD show the picture of the inflammatory process and most commonly include elevated ESR, thrombocytopenia of >400 000, and elevated ferritin levels. Although elevated ferritin levels are the non-specific but five-fold rise of serum ferritin levels highly suggests AOSD.12 The patient described in this report showed high ESR, thrombocytopenia, and elevated ferritin levels, which further strengthen the diagnosis of AOSD.

Cardiac involvement is not a unique feature of AOSD, and it ranges from pericarditis to myocarditis. Clinical presentation is variable from pericardial effusion to cardiac tamponade. Myocarditis can present as arrhythmias, heart failure, and even cardiogenic shock.1,3,13 It can rarely affect endocardium resulting in non-infective endocarditis and valvular regurgitations. Initial treatment of choice is non-steroidal anti-inflammatory drugs, and whenever required corticosteroids and immunosuppressive therapy can be utilized with good outcomes. Adult-onset Still’s disease carries an excellent prognosis with low mortality rates with a recurrence rate of up to 10% per year.14

The case we are reporting here is a young male, who was initially diagnosed as infective endocarditis due to suspected vegetation on the mitral valve along with severe mitral regurgitation. He was febrile with persistent negative blood cultures. Intravenous antibiotics led to neutropenia without any response to fever and clinical status. On further workup, he was diagnosed to have AOSD, and he responded dramatically to oral steroid therapy. Later his mitral valve was surgically replaced as it was flail anterior mitral leaflet, which is not suitable for repair.

In summary, AOSD is a systemic illness with diagnosis is based on clinical features and exclusion of other illnesses. Adult-onset Still’s disease should be considered as a differential diagnosis in culture-negative endocarditis, especially in those with systemic features and non-responders to antibiotics.

Lead author biography

Dr Shabir Hussain Shah is a qualified Cardiovascular and Thoracic Surgeon since 2005 with more than 13 years’ experience (post-M.Ch./post-doctorate) in operative cardiovascular and thoracic surgery with keen interest in the areas of Research and Development. After finishing clinical fellowship in advanced adult cardiac surgery at Mazankowski Alberta Heart Institute (MAHI), University of Alberta, Canada, he joined King Fahad Medical City, Riyadh, Saudi Arabia. He is a Consultant Cardiovascular Surgeon and head of cardiovascular intensive care unit. He is also serving as programme director of cardiac surgery residency programme at the same centre.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.
Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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