Adult-onset Still's disease revealed by a pleuropericarditis


ABSTRACT: We report a case of adult-onset Still's disease (AOSD) revealed by pleuropericardial manifestations. A 40 yr old black woman was admitted for flu-like syndrome with pharyngitis, hectic fever, polymorphonuclear hyperleucocytosis and pleuropericarditis. The diagnosis of AOSD was supported by 3 major and 3 minor criteria after exclusion of infectious, haematological and connective tissue diseases. Pulmonary involvement is infrequent in AOSD, and consists of transient pulmonary infiltrates and chronic restrictive pattern. However, pleuritis, like pericarditis, is present in 25% of cases. Initial onset of pleuritis, associated with fever and hyperleucocytosis preceding articular manifestations could be responsible for a delay in diagnosis and a subsequent worsening in the prognosis of the disease. A rapid improvement is usually observed under nonsteroidal anti-inflammatory drug or corticosteroid treatment. Eur Respir J., 1990, 3, 1064-1066.

Adult-onset Still's disease (AOSD) is an uncommon connective tissue disease with symptoms similar to those described in children with Still's disease or systemic juvenile rheumatoid arthritis [1-3]. Three major symptoms are usually present: high-grade spiking fever, evanescent erythematous or salmon-coloured maculopapular rash involving the trunk and extremities and articular manifestations usually polyarthritis [3, 4]. However, a fever of unknown origin (FUO) can be the initial symptom and is sometimes associated with infrequent visceral involvement such as pleuropericarditis. This latter presentation suggests numerous diagnoses, namely infectious, neoplastic or connective tissue diseases. The difficulty of the diagnosis is illustrated by the present case report.

Case report

A 40 yr old Haitian woman was admitted on August 19, 1988, for a flu-like syndrome associated with a mediastinal chest pain. Her past medical history included an essential epilepsy treated with phenobarbital.

Since August 10, 1988, the patient suffered from headache, myalgias, sore throat and dry cough. She was treated with erythromycin (2 g qd). Eight days later, she developed a high grade fever (39°C) and a mediastinal chest pain. On admission, she was asthenic and had a recent 2 kg weight loss. The temperature chart (fig. 1) showed a 40°C spiky fever occurring in the late evening. Pulse rate was 90 per min, and arterial pressure 110/60 mmHg. The patient a pharyngitis involving several cervical lymph nodes. Cardiovascular and pulmonary examination was within normal limits. Arterial oxygen tension (\(P_{\text{aO}}\)) was 8.66 kPa and arterial carbon dioxide tension (\(P_{\text{aCO}}\)) 4.6 kPa (room air). Chest X-rays showed a small bilateral pleural effusion and a mild cardiomegaly. An echocardiogram revealed a moderate pericardial effusion. Thoracic computed tomographic (CT) scan confirmed pleural effusion without interstitial feature. Purified protein derivative (PPD) skin test was negative. Haemoglobin was 9.1 g·dl⁻¹, white blood cells (WBCs) 14,000 per µL, 87% polymorphonuclear cells (PMNs),
erythrocyte sedimentation rate (ESR) 110 mm-first hr\(^1\), hyper \(\alpha\), and hyper \(\tau\) globulinemia, serum creatinine level 70 \(\mu\)mol\(^{-1}\), \(\tau\) glutamyltransferase were 164 U\(^{-1}\) (N<30), serum glutamic oxalo-acetic transaminase (SGOT) 162 U\(^{-1}\) (N<60) and serum glutamic pyruvic transaminase (SGPT) 190 U\(^{-1}\) (N<80). Urinalysis was normal. Pleural fluid analysis revealed a clear yellow fluid with protein level 37 g\(^{-1}\), 12,000 cells-\(\mu\)l \pm with 95% nonimpaired PMNs and 5% lymphocytes. Fiberoptic bronchoscopy, bronchial biopsies, and bronchoalveolar lavage (10x10\(^3\)cells\(-1\)m\(^3\), 95% macrophages) were normal. Lymph node and bone marrow biopsies disclosed nonspecific process.

Pleuropericarditis associated with hectic fever, hyperleucocytosis, pharyngitis and cervical lymph nodes suggested infectious or immunological diseases. Thus, microbiological studies, including acid-fast bacillus (AFB) were performed on blood, pleural and spinal fluids, urines, faeces, intrauterine device and on joint fluids, urines, faeces, a negative result. Viral serologies were negative, in particular for human immunodeficiency virus (HIV\(_1\)) and HIV\(_2\). Immunochemical tests including rheumatoid factor, PEG immune complexes determination, antinuclear and antitissue antibodies were negative. C3 and C4 complement complexes determination, antinuclear and antitissue antibodies, and antinuclear antibodies were negative. C3 and C4 complement complexes were within normal limits.

During these investigations, several antibiotic courses were given and were ineffective on the fever. Simultaneously, pleuropericarditis disappeared. On August 28, the patient developed a marked left knee arthritis. Articular X-rays were normal. Synovial fluid was cloudy with 11,000 cells-\(\mu\)l \pm, 87% PMNs; Gram stain, culture and acid-fast bacilli were negative. A few days later, a polyarthritis set up and the diagnosis of adult Still's disease was performed. Prednisone (1 mg-kg\(^{-1}\) qd) was started. The patient became afebrile within 48 h and all symptoms disappeared in 2 wks. However, after an 8 mth follow-up, each attempt to taper prednisone dosage below 30 mg daily was associated with recurrence of a right wrist arthritis and increased ESR. Antimalarial agents were then started in order to obtain a corticosteroid sparing effect.

### Table 1. - Adult-onset Still's disease: diagnostic criteria

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
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<tbody>
<tr>
<td>Hectic fever &gt;2 wks</td>
<td>Arthragias</td>
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<tr>
<td>Cutaneous rash</td>
<td>Myalgias</td>
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<tr>
<td>Arthritis</td>
<td>Pericarditis</td>
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<tr>
<td>Hyperleucocytosis &gt;12,000-per (\mu)l (N\times2)</td>
<td>Increased GOT, GPT serum levels</td>
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<tr>
<td>Past history of childhood Still's disease</td>
<td>Pharyngitis</td>
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</tbody>
</table>

**Exclusion criteria**

- Microbiological identification
- Antibiotic therapy efficacy
- Other connective tissue disease or malignancy

The diagnosis is assessed by 4 major criteria or 3 major and 3 minor criteria and absence of exclusion criteria [3]. GOT: glutamic oxalo-acetic transaminase; GPT: glutamic pyruvic transaminase.

### Discussion

Since the first description of AOSD in 1971 by Bywaters [1] and Buiax et al. [2], about 250 cases have been reported [3–5]. The diagnosis of AOSD can be readily done when the three main symptoms are present in association with hyperleucocytosis (60–70%). Other clinical manifestations include peripheral lymph node enlargement which appears in approximately 50% of cases, sorethroat (40%), splenomegaly (42%), hepatomegaly (27%) with normal or abnormal liver enzymes (30%), pericarditis (30%) or even cardiac (3%) [3, 4, 6].

Pleurisy is revealed by chest pain or by systemic chest roentgenogram. In most of the patients, pleural effusion is bilateral and frequently associated with pericarditis. As observed in our patient, pericardial and pleural fluid analysis (6 cases) demonstrate a clear to cloudy, yellow exudate with a mild cellularity, mostly neutrophils; glucose level is usually within normal limits and contrasts with the low level observed in rheumatoid arthritis pleural effusion. In two cases, pleural histology has shown a nonspecific acute inflammation [2, 7]. A complete recovery is usually achieved with anti-inflammatory agents but clearing can occur spontaneously. Pleuritis does not appear to be a worse prognostic criteria. Parenchymatous lung involvement has only been reported in 11 cases [2, 4, 7–11]. Clinical manifestations are rare and nonspecific; an acute respiratory failure is reported in two cases [7]. Usually, pulmonary manifestations consist of radiological findings, namely pulmonary infiltrates involving the lower lobes. These infiltrates are eventually sensitive to salicylates or corticosteroids but radiological recurrence is possible. A chronic progression appears to be uncommon. Corbitt et al. [10] reported a patient with a chronic cough and exertional dyspnoea revealing a left lower lobe infiltrate. Symptoms were associated with a severe corticosteroid restrictive defect. Such a restrictive pattern is mentioned in 7 out of the 8 AOSD patients studied by Troum et al. [11]. Three pathological reports showed nonspecific findings: an acute alveolitis [11], a nonspecific chronic inflammatory...
infiltrate with patchy interstitial fibrosis [10] and some epithelioid granulomas in one case [7]. Bronchoalveolar lavage showed a mixed alveolitis (lymphocytes 15%; neutrophils 16%; eosinophils 6%) in one case [7] and was normal in our patient.

These pleuropulmonary manifestations can be related to AOSD when other criteria are present (table 1). Infections and malignancy as well as connective tissue diseases, i.e. vasculitis, systemic lupus erythematosus, rheumatoid arthritis or sarcoidosis, have to be excluded.

Treatment of the respiratory manifestations is based upon anti-inflammatory agents. In 20% of cases, salicylates or nonsteroidal anti-inflammatory drugs give improvement, but most of the patients require corticosteroids at dosage of 1-2 mg·kg⁻¹ body weight qd. In those patients requiring prolonged high-dose corticosteroid treatment to control the disease, slow-acting or sparing-agent can be required. Antimalarial agents, gold salts, penicillamine or immunosuppressive agents such as cyclophosphamide, azathioprine, or methotrexate [3] have been used.

Respirologists should be aware of this condition of AOSD which associates pleurisy, fever and hyperleucocytosis, all symptoms leading us to rule out infectious and other causes of chronic FUO. Therefore, diagnosis criteria of AOSD could enable clinicians to avoid recourse to invasive procedures.

References


RÉSUMÉ: Une femme de race noire, âgée de 40 ans, a été hospitalisée pour un tableau clinique associant un syndrome grippal avec pharyngite, une fièvre hémique avec hyperleucocytose et une pleuro-péricardite. Le diagnostic de maladie de Still a été porté sur la présence de 3 critères majeurs et de 3 critères mineurs, après avoir exclu une infection systémique, une maladie hématologique ou une connectivité définie. Les manifestations pulmonaires sont rares au cours de la maladie de Still et comportent des infiltrats pulmonaires transitoires et une atteinte restrictive. Cependant, pleurésies et péridicardites sont observées dans 25% des cas. Une pleurésie révélatrice, accompagnée d'un syndrome fébrile et d'une hyperleucocytose avant l'apparition de manifestations articulaires, peut être responsable d'un retard diagnostique à l'origine de complications. Les anti-inflammatoires non stéroïdiens et surtout la corticothérapie générale ont habituellement un effet rapidement favorable.