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Case Report

Parenchymal lung involvement in a patient with adult-onset Stills disease: a rare case report

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Introduction

Adult-onset Stills disease (AOSD) is an autoimmune inflammatory disorder of unknown aetiology, characterized by quotidian fever (fever occurring daily), arthritis and an evanescent rash [1]. The clinical course of AOSD can be categorized into two main patterns: systemic pattern and chronic articular pattern. In patients with the systemic pattern, the disease course typically lasts only weeks to months and systemic features including fever, rash, serositis and hepatosplenomegaly are predominant. Patients with the chronic articular pattern have persistently active disease in which articular symptoms predominate, and this usually leads to destructive arthritis [2,3,4].

The major clinical features of AOSD are fever, arthritis and skin rash, which occur in about 75-90 percent of patients. Minor clinical features of AOSD include hepatomegaly, pleuritis, myocarditis and pericarditis [5]. Parenchymal lung involvement in AOSD is rare and encompasses a wide spectrum of disease including idiopathic interstitial pneumonia, nonspecific interstitial pneumonia, pleuritis, pleural effusion, atelectasis, transient pulmonary infiltrates and acute respiratory distress syndrome (ARDS) [6]. Macrophage activation syndrome (MAS) is a rare, potentially life-threatening complication of AOSD [5].

Laboratory findings in AOSD are nonspecific. A rise in acute phase reactants such as ESR, CRP, and serum ferritin are observed along with a neutrophil predominant leukocytosis with some immature cells. An elevated serum ferritin can be a striking feature and is commonly seen at levels above those typical of an acute phase response to other disorders [5].

There are several diagnostic criteria being proposed for AOSD, all of them requiring exclusion of other disorders which mimic AOSD such as infection, other rheumatological conditions and malignancy, especially lymphoma. Among them, Yamaguchi criteria are often used since they are more specific and sensitive for the diagnosis of diagnose AOSD [5].

Treatment of adult-onset disease is determined by severity of disease condition, grouped into mild, moderate and severe disease. Mild disease can be treated with nonsteroidal anti-inflammatory drugs [7]. Moderate and severe forms of the disease should be treated with glucocorticoids and methotrexate as first line disease modifying drugs. In case of refractory AOSD of the systemic and the chronic articular form, treatment involves blockade of the interleukin 1 (IL1) and interleukin 6 (IL6) pathways respectively [6].

Case Presentation

A 43-year-old, married woman with no significant past medical illness from Puttalam was transferred to Teaching Hospital, Jaffna for further evaluation and management of prolonged pyrexial illness. She initially presented to a private hospital with a history of fever and inflammatory polyarthritis involving the large joints with morning stiffness lasting less than 15 minutes. She also reported other symptoms such as sore throat, dry cough and exertional shortness of breath (mMRC-GradeⅢ/Ⅳ) of 3 weeks duration. She denied any history of dysuria, haematuria and lower abdominal pain. She did not have nausea and vomiting. Her bowel habits and urine output were normal. There was no contact history of TB. She strongly denied a history of high-risk sexual behavior. She did not have focal symptoms of malignancies or symptoms of autoimmune connective tissue diseases.

On examination, she was neither pale nor icteric. Her pulse rate was 96 beats per minute with a blood pressure reading of 120/70. Auscultation of the chest revealed bilateral basal fine end- inspiratory crackles. There were no enlarged lymph nodes in the axillary, cervical, inguinal and retro trochlear region. Other system examinations were largely normal. She was commenced on empirical broad-spectrum antibiotic treatment with meropenem 1 g IV tds and clarithromycin 500 mg per oral bd.

Full blood count revealed leukocytosis (28.21/μL) with predominant neutrophils (94.6%) and thrombocytosis (553/μL). Other cell lines were within normal limits. Erythrocyte sedimentation rate, C-reactive protein, lactate dehydrogenase and serum ferritin were 98 mm/1st hour, 347.6 mg/L, 525 U/L and 13967 ng/ml respectively. Her chest Xray showed bilateral nodular shadows with a predilection for the lower zones and complete liver and renal function tests, urine analysis and coagulation profile were normal. Melioidosis antibody, anti-nuclear antibody, rheumatoid factor and anti-streptolysin 'O' titre were negative. C-anti-neutrophil cytoplasmic antibody was positive at a low titre. Blood culture and urine culture revealed no growth. Blood picture did not reveal any overt evidence of hematological malignancies. Transthoracic echocardiogram was normal. Ultrasound scan of

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the abdomen revealed only mild splenomegaly. High resolution computed tomography showed ill-defined airspace nodules of ground glass density in random distribution. She was initiated on anti-TB drugs as for a "clinically diagnosed pulmonary tuberculosis" since delaying the treatment of milliary TB would potentially lead to devastating consequences. Bronchoscopy study was normal. Tuberculin skin test was negative. Bronchoalveolar lavage for TB, fungal and bacterial culture exhibited no growth and BAL GeneXpert MTB/RIF was also negative. Anti-TB treatment was terminated later as the diagnosis of miliary TB was considered less likely based on consensus opinion. An alternative diagnosis adult-onset Still's disease was made and she was started on methyl prednisolone pulse 500 mg IV daily for 3 consecutive days followed by high dose prednisolone 60 mg oral daily. Her symptoms and signs dramatically improved following initiation of steroid therapy and she was discharged from the ward and is being followed up at the rheumatology and respiratory clinics.

Discussion

AOSD is a sophisticated inflammatory disease. Pathogenesis and aetiology are still not known. There are no specific serological markers to establish the diagnosis of AOSD. The confirmation of AOSD relies on the exclusion of other likely diagnoses. Yamaguchi criteria are often used for diagnosis of AOSD because of their high sensitivity and specificity. These criteria require the presence of 5 criteria, at least 2 of which should be major criteria, and exclusion of other likely diagnoses such as infection, malignancy and other rheumatic conditions [7,8,9].

Despite AOSD being considered as a seronegative disorder, according to Yamaguchi criteria, it should be taken into diagnostic consideration in patients with compatible clinical and laboratory findings even if they are seropositive [10].

Our patient had three major (fever, arthritis, leukocytosis) and minor (sore throat, splenomegaly, negative ANA and RF) Yamaguchi criteria. Though this patient was seropositive for c-ANCA, she did not have many clinical features to support the diagnosis of ANCA associated vasculitis. She was diagnosed to have AOSD since she had many compatible clinical and laboratory findings.

Parenchymal lung involvement (PLI) may be associated with AOSD and occurs in 5 % of cases. This association can be categorized into two groups; one with ARDS and another with other parenchymal lung involvement. ARDS is the more severe form and is the leading cause of death in AOSD related PLI. The non- ARDS- PLI may occur during systemic AOSD but is rare in the chronic pattern. The clinical features are nonspecific and include exertional dyspnea and bilateral fine crackles. Imaging may reveal bilateral lower lobe interstitial and alveolar infiltrates as occurs in connective tissue disease [6].

Severe disease is defined by the presence of life-threatening organ involvement and/or conditions such as severe hepatic involvement, cardiac tamponade and/or disseminated intravascular coagulation. Such patients require high-dose or pulse glucocorticoid therapy and should receive early intervention with a biologic agent such as an interleukin (IL) 1 or IL-6 inhibitors [7].

Our patient had parenchymal lung involvement which was evident in the clinical findings and on imaging. (Table 1) She was started on pulse methylprednisolone 500 mg IV daily for 3 consecutive days followed by prednisolone 60 mg per oral daily. She was discharged home when she was afebrile and clinically well. She reported marked improvement of arthritis and other constitutional symptoms when she was reviewed in the rheumatology clinic as an outpatient.

Conclusion

Despite AOSD being a seronegative disorder, it should be considered in patients with compatible clinical and laboratory findings even if they are seropositive. AOSD related parenchymal lung involvement is rare and if left untreated can cause devastating consequences.

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