Journal of Clinical and Nursing Research, 2024, Volume 8, Issue 6
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Adult-Onset Still's Disease Misdiagnosed as Acute Fibrinous and Organizing Pneumonia: A Case Report and Literature Review

Chunhua Huang, Chunting Lai*

Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Guangzhou 510000, Guangdong Province, China

***Corresponding author:** Chunting Lai, 2521843262@qq.com

Abstract: Adult-onset Still's disease (AOSD) is a rare condition that lies between autoinflammatory syndrome and autoimmune disease. The main clinical manifestations include fever, chills, rash, joint swelling and pain, peripheral blood leukocytosis, splenomegaly, etc. It is a systemic disease affecting between 1 and 34 people per million. The average age of onset is 35 years old, with a slightly higher prevalence rate in women. Since AOSD lacks early specific symptoms and signs, non-specialist doctors have limited understanding of the disease, and patients are prone to clinical misdiagnosis, mistreatment, and delayed disease progression. This paper reports a patient whose AOSD was misdiagnosed as acute fibrinous and organizing pneumonia.

Keywords: Adult-onset Still's disease; Acute fibrinous and organizing pneumonia; Lung disease

Online publication: July 22, 2024

1. Patient information

The patient, a male, 25 years old, was admitted to the hospital due to a periodic fever that lasted for one month. The patient developed a fever without obvious triggers one month ago (July 1, 2022), with a maximum body temperature (Tmax) of 41.0°C, accompanied by chills, chest tightness, shortness of breath, dry cough, sore throat, and general myalgia. Four days later, the patient developed symptoms such as chest pain, shortness of breath, shoulder pain, and weakness in both upper limbs. Physical examination yielded the following: The patient's mental state was good, had fluent speech, and a skin lesion of about 2.0 cm × 1.0 cm was seen on the nose with no bleeding or fluid oozing. Dot-like white lesions were seen on the mucosa of the posterior oral pharyngeal wall. Breathing was slightly short, the breath sounds in both lungs were weakened, and scattered moist rales could be heard in the left lower lung. The heart rate was 80 beats/min, regular, and no pathological murmur was heard in the auscultation area of each valve. The entire abdomen was soft, with no tenderness or rebound tenderness, no percussion pain in the liver and kidney areas, and no edema in both lower limbs. Complete blood test: white blood cells 13.90 × 10^9/L, neutrophils 11.55 × 10^9/L, C-reactive protein > 200 mg/L, procalcitonin 4.45 μg/L, cardiac troponin I 495 ng/L, N-terminal pro-brain natriuretic peptide 2540 ng/L, fasting

blood glucose 8.93 g/L, D-dimer 4.93 μg/ml.

According to the electrocardiogram: ST elevation was present in leads I, aVL, V2–V5. Urgent coronary angiography showed no abnormalities. After the operation, no obvious abnormalities were found in the etiological examination, which included influenza antigen test, dengue fever antigen, *Mycoplasma pneumoniae* antibody, urine bacterial culture, blood bacteria + fungi + anaerobic bacteria culture, serum tuberculosis antibody, sputum, DNA quantification of *Mycobacterium tuberculosis*, acid-fast bacilli in sputum, rheumatic immune-related, sexually transmitted diseases, tumor markers, and bone marrow cytology. The results of the contrast-enhanced computed tomography of the chest and abdomen were as follows: (1) There were scattered exudates in both lungs, and inflammation was considered on both sides. (2) There was a small amount of pleural effusion and interlobar fissure effusion, accompanied by incomplete expansion of the lower lobes of both lungs. (3) There was enlargement of the heart and a small amount of pericardial effusion. (4) Fatty liver. (5) Edema and a little infiltration around both kidneys. (6) Multiple small lymph nodes in the porta hepatis, abdominal aorta, and ileocecal area. Upon admission, the cause of the fever was investigated and the possibility of infectious diseases was considered. Anti-infectives (oseltamivir, cefuroxime sodium, piperacillin-tazobactam sodium, doxycycline, vancomycin, meropenem, and Baifule) are administered successively. The patient still had fever, chest tightness, shortness of breath, and other discomforts, the fever mostly occurred during the afternoon and night, and the body temperature fluctuated between 37.5℃ and 39.0℃. After multidisciplinary consultation, the diagnosis of acute fibrinous and organizing pneumonia (AFOP) was considered. After administration of intravenous methylprednisolone 40 mg every 12 hours (from July 21 to July 26) and oral methylprednisolone tablets 36 mg once a day (from July 26 to August 2), the patient's body temperature returned to normal. On August 2, the dosage of methylprednisolone tablets was reduced to 16 mg once a day. The patient developed a fever again with Tmax of 38.3°C, accompanied by chest tightness, sore throat, and dry cough. The electrocardiogram showed abnormal multi-lead T waves, and the cardiac color Doppler ultrasound showed left ventricular wall thickening; IgG-lambda type M protein was detected in the patient's serum (IgG monoclonal), blood and urine β2-microglobulin was elevated, and bone marrow cytology was improved; bone marrow biopsy and hematological tumor-related phenotypic analysis, as well as Congo red staining of bone marrow tissue, were performed to rule out lymphoma, multiple myeloma, and plasma cell disease. The patient had a periodic fever, significantly elevated white blood cells and neutrophils, obvious sore throat, swollen lymph nodes, and negative anti-nuclear antibody spectrum and rheumatoid factor. Infections, tumors, and rheumatic immune diseases were excluded, and adult-onset Still's disease (AOSD) was considered. High-dose intravenous methylprednisolone 0.5 g once a day was prescribed for three days, supplemented by intravenous gamma globulin 20 g once a day. Additionally, intravenous cyclophosphamide 0.6 g once a day was prescribed for two days, and cyclophosphamide was used every two weeks for five courses of treatment. After four weeks of outpatient follow-up, the patient had no fever, rash, or joint pain. The dose of methylprednisolone was gradually reduced to discontinuation, and the condition did not recur. The patient was informed of regular follow-up visits, and no abnormal symptoms were found during the 2-year follow-up.

2. Discussion and conclusion

AOSD is a systemic disease affecting between 1 and 34 people per million. The average age of onset is 35 years old, and the prevalence rate is slightly higher in women [1-3]. AFOP is a rare non-infectious lung disease with unknown causes, which may be related to a variety of factors, including autoimmune diseases [4], drug toxicity, environmental causes, infection, hematological tumors [5], organ transplantation, etc. Clinical and imaging examinations lack specificity. If the imaging findings are suspected of pneumonia and the anti-infective treatment is

ineffective, the possibility of AFOP should be considered. According to the case report mentioned above, AFOP is considered after the anti-infective treatment is ineffective. A lung tissue biopsy is not performed to confirm the diagnosis. Empirical treatment with prednisolone worsens when the hormone is reduced.

There are currently no specific diagnostic criteria for AOSD [6,7]. Clinical diagnosis is usually based on symptoms such as fever, rash, and joint pain on the basis of excluding other diseases. Since most clinicians lack a systematic understanding of AOSD, and as it involves liver and kidney damage, the condition is complex and changeable, making it prone to missed diagnosis or misdiagnosis. Among several diagnostic criteria that have been proposed, the Yamaguchi criteria [8] are the most commonly used, with a sensitivity of 96.3% and a specificity of 98.2%. These diagnostic criteria must exclude infectious diseases, tumor diseases, and rheumatic immune diseases. The main criteria include (1) Fever ≥ 39°C, intermittent for ≥ 1 week; (2) Joint pain > 2 weeks; (3) Typical rash; (4) White blood cells ≥ 10×10^9/L (Neutrophils > 80%). Minor criteria are (1) Sore throat; (2) Lymph node and/or splenomegaly; (3) Abnormal liver function; (4) Negative rheumatoid factor and anti-nuclear antibody. A diagnosis can be made if five criteria (including at least two major criteria) are met. Reviewing the patient's medical history, the patient should have been diagnosed with AOSD but was treated successively as an infectious disease and AFOP, and the treatment effect was poor. This case was difficult to diagnose. On the one hand, the clinical manifestations are non-specific, there are factors that affect the differential diagnosis, and no further lung biopsy is performed. On the other hand, most clinicians lack a systematic understanding of AOSD, with relatively few academic reports on AOSD. Most of the existing case reports are single-center case reports, lacking clinical research and diagnosis and treatment analysis of a large number of people. This case also provides a revelation for the clinicians. When investigating the cause of fever, if the condition exceeds expectations and is inconsistent with the laboratory results and clinical characteristics of the disease's occurrence and development process, we must investigate the cause in depth and consider both infectious and non-infectious diseases as well as common and rare diseases.

The treatment principle of AOSD is an anti-inflammatory and supportive treatment to avoid serious complications, such as hemophagocytic syndrome. Glucocorticoids are the first choice of treatment. Patients who have contraindications to or are refractory to steroids can use immunosuppressants such as cyclophosphamide and methotrexate, intravenous human gamma globulin, and biological agents. In this case, AFOP was considered when anti-infective treatment was ineffective. After treatment with methylprednisolone, the fever did not return for a short period of time, and the treatment effect was significant. This is also a reason for the misdiagnosis of this case in the early stage of treatment. When the hormone was reduced, the patient developed fever again and the condition worsened, accompanied by a decrease in platelets and a significant increase in ferritin. Combined with the obvious increase in white blood cells and neutrophils, obvious sore throat, lymphadenopathy, negative anti-nuclear antibody spectrum and rheumatoid factor, infection, tumor, and rheumatic immune diseases were ruled out and AOSD was considered. With high-dose methylprednisolone and gamma globulin therapy combined with multiple cyclophosphamide treatments, the patient recovered. Studies have shown that the mortality rate of severe AOSD is as high as 10% [9,10]. Clinically, it is found that an increase in serum ferritin of more than five times indicates AOSD [11]. Serum ferritin remains high or continues to rise during treatment often indicating poor prognosis [12]. Studies have discussed that increased serum ferritin is related to adult AOSD, and it has even been suggested that it is related to the severity of the disease [13,14]. A large-sample prospective study concluded that patients with persistently low platelets and poor response to treatment have an increased risk of death [15]. Some cases relapse, but the prognosis is generally good. A minimal number of patients develop severe complications and die. We need to be alert to the development of late-onset malignant tumors in some patients [16] and require regular screening and long-term follow-up.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Gao Q, Yuan Y, Ma N, et al., 2016, Analysis of Clinical Characteristics of Patients with Adult-Onset Still's Disease Complicated with Hemophagocytic Syndrome: A Report of 3 Cases and Literature Review. J Jilin Univ: Med Edit, 42(6): 1197–1202.

[2] Narvaez J, 2018, Adult-Onset Still's Disease. Med Clin (Barc), 150(9): 348–353.

[3] Cozzi A, Papagrigoraki A, Biasi D, et al., Cutaneous Manifestations of Adult-Onset Still's Disease: A Case Report and Review of Literature. Clin Rheumatol, 35(5): 1377–1382.

[4] Taira M, Matsumura T, Sumita Y, et al., 2022, A Rare Case of Acute Fibrinous and Organizing Pneumonia Associated with Systemic Lupus Erythematosus and Autoimmune-Associated Hemophagocytic Syndrome: The Involvement of CD163-Positive Macrophages. Intern Med, 61(4): 559–565.

[5] Nanno S, Koh H, Okamura H, et al., 2021, Acute Fibrinous and Organizing Pneumonia Following Hemophagocytic Syndrome in Two Adult Patients with Hematological Malignancies. J Clin Exp Hematop, 61(2): 93–96.

[6] Chinese Rheumatology Association, 2010, Guidelines for the Diagnosis and Treatment of Adult-Onset Still's Disease. Chin J Rheumatol, 14(7): 487–489.

[7] Xu F, Hou J, Zhang Y, et al., 2016, Adult Still's Disease Complicated by Acute Severe Liver Injury and Phagocytosis: A Case Report of Blood Syndrome. Journal of Clinical Hepatobiliary Diseases, 32(8): 1590–1591.

[8] Yamaguchi M, 1992, Preliminary Criteria for Classification of Adult Still's Disease. J Rheumatol, 19(3): 424–430.

[9] Zeng T, Zou YQ, Wu MF, et al., 2009, Clinical Features and Prognosis of Adult-Onset Still's Disease: 61 Case from China. J Rheumatol, 36(5): 1026–1031.

[10] Woo JH, Sung YK, Lee JS, et al., 2009, Association of Fc-Gamma Receptor Polymorphisms with Adult-Onset Still's Disease in Korea. J Rheumatol, 36(2): 347–350.

[11] Giacomelli R, Ruscitti P, Shoenfeld Y, 2018, A Comprehensive Review on Adult-Onset Still's Disease. J Autoimmun, (93): 24–36.

[12] Zhang S, Zhou X, Bao W, et al., 2018, Clinical Analysis of 108 Cases of Adult Still's Disease. Medicine and Philosophy, 39(22): 47–50, 60.

[13] Lian F, Wang Y, Yang X, et al., 2012, Clinical Features and Hyperferritinemia Diagnostic Cutoff Points for AOSD Based on ROC Curve: A Chinese ExPerience. Rheumatol Int, 32(1): 189–192.

[14] Novak S, Anic F, Luke-Vrbaniéc TS, 2012, Extremely High Serum Ferritin Levels as a Main Diagnostic Tool of Adult-Onset Still's Disease. Rheumatol Int, 32(4): 1091–1094.

[15] Moreau D, Timsit JF, Vesin A, et al., 2007, Platelet Count Decline an Early Prognostic Marker in Critically Ill Patients with Prolonged ICU Stays. Chest, 31(6): 1735–1741.

[16] Damevska K, Franca K, Nikolovska S, et al., 2019, Adult-Onset Still's Disease as a Cutaneous Marker of Systemic Disease. Clin Dermatol, 37(6): 668–674.