Case Report

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Case Report of a Female Patient with Adult-onset Still's Disease and Review of the Literature

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ABSTRACT

Background: Adult-onset Still's disease (AOSD), which presents many non-specific symptoms, such as rash leukocytosis, spiking fever, and sore throat, is a rare auto inflammatory disease. Other clinical features that are frequently observed include lymphadenopathy, arthralgia, serositis, splenomegaly, and hepatomegaly. Laboratory tests show high levels of C-reactive protein, ferritin, and erythrocyte sedimentation rate reflecting the systemic inflammatory process in AOSD patients.

Case Presentation: The patient was a middle-aged woman with a high fever (39.8 C), sore throat, rashes on limbs with pruritus, mainly at the joints (elbow, knee, and ankle), muscle aches, dizziness, infirmity, weakness, and poor appetite without arthralgia. The ferritin level was above 1500 (normal value: 14-233) ng/L. Antineutrophil, antinuclear antibodies, and rheumatoid factor were negative. Combining the symptoms such as fever, rash, stress-induced acute inflammation, arthritis, and ferritin levels, the patient was eventually diagnosed with adult Still's disease. She received methylprednisolone 40mg intravenously every 12 hours for one week. On the second week, the dose was reduced to 40mg in the morning and 20mg in the evening, and finally, the dose was reduced to 40mg oral intake in the morning and 8mg in the evening. After half a month of treatment, the patient's high fever and skin rashes subsided, and the other symptoms also gradually relieved.

Conclusion: A case of a middle-aged woman diagnosed with adult Still's disease is reported, and the possible pathogenesis and treatment of the disease are discussed. This case highlights the importance of early diagnosis and timely treatment of adult Still's disease to prevent potentially fatal complications.

Keywords: Adult-onset still's disease, case report, inflammatory disorder

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INTRODUCTION

Adult-onset Still's disease (AOSD) is a system autoinflammatory disorder of unknown etiology usually affecting young adults. Spiking fever, evanescent rash, pharyngalgia, and arthritis are commonly observed during the disease (1). In addition, a few AOSD patients may experience different life-threatening complications with acute respiratory failure, congestive heart failure, and abnormal central nervous system (2, 3). Furthermore, laboratory tests show that the levels of C-reactiveprotein, erythrocytesedimentationrate ,and ferritin are especially higher than those observed in other inflammatory diseases reflecting the systemic inflammatory process in AOSD patients (4). The author recorded the diagnosis and treatment of this instance of adult-onset Still's illness in order to give a reference for future diagnoses and treatments of comparable situations.

CASE PRESENTATION

Initial Presentation and Diagnosis

A 45-year-old middle-aged woman with high fever(39.8°C),sore throat, limb rash with itching (Figure 1) , mainly at the joints (elbow, knee, ankle), muscle aches, dizziness, infirmity, fatigue, poor appetite who complained of itching around the eyes and face, appeared without obvious cause 2 weeks ago, however, it went unnoticed. A rash scattered on the limbs developed from the proximal end to the distal end with itching. On July 7, 2020, she sought treatment in a hospital, where the doctor gave "Mizolastine Sustained-release Tablets and Eloxone Cream" for the treatment of "eczema". However, her body temperature rose to 39.2°C that night, accompanied by a sore throat and blood CRP concentration of 58.77 mg/L. Following this, she was then diagnosed with "fever and infectious rash" and given "cefuroxime and vitamin C" intravenous drip. But the symptoms were still not getting any better. After being admitted to our hospital on July 12, 2020, meropenem combined with moxifloxacin was given by intravenous drip for anti-infection treatment, but it was also ineffective. The heat and rash did not subside completely. A chest radiograph (day 4) showed increased texture and infiltration of both lungs (Figure 2). Viral serological tests and blood cultures were negative. Physical examination on admission showed no swelling of superficial lymph nodes in the whole body. Papules could be seen in the knees, ankles, and palms of both hands. The breath sounds of both lungs were clear and dry and wet rales were not heard. Serum creatinine, liver enzyme indicators, CPK, and

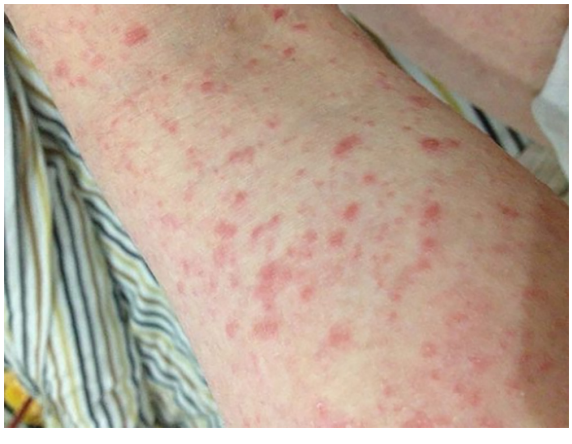

Figure 1. Rash of limbs on left leg in our patient with adult-onset Still's disease

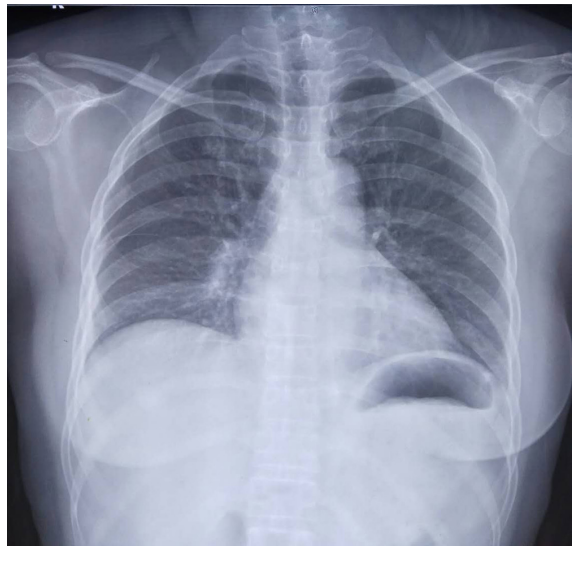

Figure 2. Lung X-ray in the patient with adult-onset Still's disease

platelet indicators were normal. The level of interleukin-6 (IL-6) was 736.90pg/ml (normal value ranged from 0.0 to 7.0 pg/ml) and tumor necrosis factor-α (TNF-α) was 27.8pg/ml on the sixth day (normal value ranged from 0.0 to 8.1pg/ml). The erythrocyte sedimentation rate (ESR) was 86mm/h on the seventh day (normal value ranged from 0.0 to 20mm/h). The ferritin level was above 1500ng/L (the normal value between 14 and 233ng/L). Antineutrophil, antinuclear antibodies, and rheumatoid factors were negative. These negative results preclude the diagnosis of autoimmune disease. Combining the symptoms such as intermittent hyperthermia, rash, stress-induced acute inflammation, arthritis, and high ferritin level, the patient was eventually diagnosed with adult Still's disease. Some laboratory parameters of the patient are shown in Table 1.

Medical Treatment

Methylprednisolone 40mg intravenous bolus was administered each12hrs. for 1 week, then, it was reduced to 40mg in the morning and 20mg in the evening on the second week, and finally, the dose was reduced to 40mg of oral intake in the morning and 8mg in the evening. Furthermore, the patient was given stomach protection as well as calcium and potassium supplements. The patient also received a CT scan of the lung, a follow-up blood routine, liver and kidney function, electrolyte, blood glucose test, and ferritin review. The patient's high temperature and skin rashes reduced after half a month of medication, and the other symptoms eventually improved.

DISCUSSION

AOSD is a rare systemic autoinflammatory disease with significant symptoms of high fever (>39°C), sore throat, and rash. The disease would be called "allergic subsepsis", but after 1987 it was renamed and was called AOSD. According to the report, the incidence is 0.22/100 thousand for males, and 0.34/100 thousand for females in Japan (5). In France, the AOSD incidence is 0.16/100 thousand, whereas, in the Norwegian population, it is 0.4/100 thousand (1, 6). The distribution of the disease has no racial and regional differences. Our country currently has no relevant epidemiology research. Women have a similar or slightly higher prevalence of AOSD than men. It is important to mention, nevertheless, that pregnant and postpartum women are at a greater risk.

The disease's origin is uncertain. The occurrence of the disease is related to infection, heredity, and immune suppression. The infection factors include streptococcus, staphylococcus, influenza virus, rubella virus, EB virus, mycoplasma pneumonia, and so on. Clinical features include fever, joint pain and/or arthritis, skin rash, neutrophil increase, and serious patients that can be infected with the system damage (7-9). Because there are no specific diagnostic methods and criteria, diagnosis and differential diagnosis are

Table 1. Partial laboratory indicators during the patient's hospital stay

Selected parameter and unit	Day-4	Day-1	Day+2	Day+5	Day+7
Temperature °C	39.2	39.8	39.1	38.8	38.0
Leukocytes $\times 10^9$/L	9.27	18.3	21.1	28.9	43.8
Neutrophils %	72.8	77.7	90.6	89.4	92.1
C-reactive peptide mg/L	8.0	58.77	132.16	160.05	105.43
Procalcitonin ng/ml	/	/	0.434	0.407	0.149
Creatinine μmol/L	/	/	55.0	40.0	/
Hemoglobin g/L	/	/	137.0	117.0	121.0
Erythrocyte$\times 10^{12}$/L	/	/	4.56	3.92	4.07
Platelet count $\times 10^9$/L	/	/	213	364	418

difficult. A large amount of the data indicates that the early stages of some diseases, such as tumors, infectious diseases, rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), skin Myositis/polymyositis, Sjogren's syndrome (SS) and other rheumatic diseases, look like AOSD's features (10, 11). Therefore, it is necessary to exclude tumors, infection, and other connective tissue diseases to consider the diagnosis. At present, three different clinical types of AOSD have been identified by analyzing the disease courses: I. Characterized by monocyclic episode; II. Performance for multiple models; III. Chronic type related to an associated active disease (12-14).

Inflammatory cytokines factors, such as IL-6 and the TNF-alpha which both factors were above normal value in this case. IL-6 is composed of T cells, B cells and macrophages of lymphatic factor, the factor can adjust the immune function in human body, and participate in the inflammatory response and stress response. Adult-onset still's disease, the happening of the disease can cause immune damage in the process, IL-6 plays an important role in the process. In adult-onset still's disease occurrence, development process, IL-6 could prompt T cells to differentiation, the release of inflammatory cytokines, and the level of rapid rise, aggravate the inflammatory response. TNF alpha is a synthesized from mononuclear macrophages release of protein, which is also an important endogenous inflammatory cytokines in human body, plays an important role in immune function regulation. At the same time, the factor of mononuclear macrophage activation, make its destruction ability enhancement, improving antigen-presenting ability. In the human body, if the TNF alpha at normal levels, it can protect; such as higher level, it will produce large amounts of cytokines, aggravate inflammation and tissue damage. For adult-onset still's disease, its condition explain the body's inflammatory response and the more severe tissue damage, so the level of TNF alpha will be in a state of high level. From what has been discussed above, in terms of clinical diagnosis, we can take a test with levels of IL-6, TNF alpha as an aid to assess their illness severity, and choose reasonable treatment plan.

Age is the main risk factor of adult Still's disease. The disease has two peak ages: 15-25 and 36-46. In terms of the gene, there are rarely multiple adult patients of the phenomenon in a family as a result, we do not believe there is a need to focus on the disease of hereditary risk (15, 16). The temperature of the patients usually rises abruptly with or without chills in the evening, up to 39°C above, but without the antifebrile process, the temperature of the patients can drop to normal in the morning the next day (17). Fever usually strikes once a day, but it can strike twice a day. It often lasts a week or an even longer time and is often accompanied by skin rash, pharynx, and joint pain, later it will relieve once the fever fades. A sore throat often appeared in the early disease, and may be accompanied by swelling and tenderness to the cervical lymph nodes, tonsil is swollen, pharyngeal swab cultivate is negative, but the antimicrobial treatment of the sore throat is invalid. The typical rash is orange maculae or macula papule, which is mainly distributed in the trunk, limbs, face, and the neck (18-20).

There is no specific diagnostic method for AOSD. International experts have developed several diagnostic or classification standards, but no acknowledged norm exists. The current standard includes Cush standards in the United States and Yamaguch standards in Japan. The main conditions include the following symptoms: I. Fever 39°C or higher, and continuous for more than a week; II. Joint pain persists for more than two weeks; III. Typical rash; IV. The index of white blood cells is 15×10^9/L or higher (21). Patients mentioned in this article are diagnosed with adult Still's disease based on intermittent hyperthermia, rash, stress-induced acute inflammation, arthritis, and high ferritin level.

However, the treatment of AOSD remains

largely empirical, lacking controlled clinical trials. There is no cure for this disease, but early detection and therapy can control attacks and avoid recurrences. Non-steroidal anti-inflammatory drugs (NSAIDs) may first be used alone to treat acute febrile inflammation; glucocorticoid hormones are often used, usually prednisone 0.5-1mg/kg/d, when the systemic symptoms predominate. If there is still no relief, the first choice is methotrexate. Some patients with refractory or warbler syndrome can be treated with glucocorticoids. When it is necessary, biological agents have been successfully used in refractory cases in recent years. At the moment, the AOSD therapeutic strategy focuses on preventing organ damage and life-threatening complications, minimizing treatment side effects, and treating pro-inflammatory symptoms and indications.

CONCLUSION

The symptoms and duration of AOSD patients vary, with a small minority of people having only one episode and no recurrence. It has a tendency to restrict itself. And most patients are prone to recurrence following remission. This case study emphasizes the necessity of early detection and treatment of AOSD to avoid the development of potentially fatal consequences. There are various types of chronic continuous activity that eventually appear as chronic arthritis, causing cartilage and bone damage. Even if AOSD is diagnosed, drugs should be modified during treatment and follow-up to enhance prognosis. At the same time, the doctor should pay attention to complications such as tumors, infections, and other concomitant disorders during long-term follow-up surveillance.

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AUTHORS' CONTRIBUTION

YG has been involved in drafting the article and has given final approval of the version to be published. WG J and QF have been involved in drafting the article. QS H has been involved in the management of the patient. AL M has made contributions to the acquisition of data. All authors have read and approved the final manuscript.

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AVAILABILITY OF DATA AND MATERIALS

All data analyzed during this study are included in the manuscript. The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

CONSENT FOR PUBLICATION

Written consent to publish this information was obtained from the study participants. Proof of consent to publish from study participants can be requested at any time.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Jiading District Hospital of Traditional

Chinese Medicine's Institutional Review Board approved this research. Each author declares that all investigations were done following the ethical norms.

Conflict of Interest: None declared.

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