A 22-YEAR-OLD MAN WITH LYMPH NODE TUBERCULOSIS AND ADULT ONSET STILL'S DISEASE: A RARE CASE REPORT

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Abstract

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory sickness with an unknown cause that is marked by a spiking fever that frequently exceeds 39o Celsius, evanescent skin symptoms, arthralgia or arthritis, and multiorgan involvement. Many diseases, such as infections, neoplasia, or immune diseases, can mimic AOSD. We found a rare condition lymph node tuberculosis (TB) with AOSD reported from Indonesia. A 22-year-old man had a prolonged fever, joint pain, reddish rash on extremities, and yellow eye membranes one week after taking a fixed combination anti-tuberculosis drug. The patient had a history of TB cervical lymphadenitis. Clinical examination disclosed salmon-colored rash, arthritis on wrists and shoulder, icterus, and hepatosplenomegaly. Laboratory results also revealed elevated leukocyte, bilirubin, c-reactive protein (CRP), and ferritin levels. Abdominal ultrasound found no cholestasis or obstruction. Immunological examinations showed negative antinuclear antibody (ANA), antibody streptolysin O (ASTO), rheumatoid factor, and hepatitis infection. According to Yamaguchi criteria, this patient fits the diagnosis of AOSD. Oral colchicine was also given with corticosteroids and cyclosporine. The treatment improved the patient's conditions, with normalization of leukocyte, ferritin, and CRP count. The dose of prednisolone was successfully tapered, and remission was achieved in 2 months after oral administration of colchicine. This case highlights the importance of consideration of AOSD as a potential diagnosis in the presence of abnormal liver function tests and that one should not be misled into a diagnosis of drug-induced liver injury (DILI). Colchicine treatment silenced the disease activity of AOSD.

Keywords: Lymph Node Tuberculosis, Adult-onset Still's Disease, DILI, Colchicine.

Introduction

A pandemic of significant proportions, tuberculosis (TB) continues to be one of the leading causes of human suffering and mortality. However, since the World Health Organization (WHO) public health initiatives were implemented and scaled up, significant success has been made in the fight against TB (1). Adult-onset Still's disease (AOSD) is defined by the characteristic trifecta of a typical salmon-colored rash, daily spiking fever, and arthritis. AOSD is an uncommon systemic inflammatory condition with an incidence ranging from 0.16 to 0.4 per 100,000 adults. It exhibits a dual age peak, occurring most frequently between 15-25 years and 36-45 years, and is thought to result from immune system dysfunction (1-3). It has a lengthy mean time to diagnosis and is one of the major reasons for hospital admissions for fever of unknown etiology (2, 3). The great variety of disease symptoms and courses point to the disease entity's heterogeneity. The etiology of AOSD involves the activation of macrophages and the subsequent overproduction of cytokines (3).

Because of the overlap of symptoms and the possibility of misdiagnosis, the convergence of AOSD and tuberculosis might pose diagnostic and treatment issues. AOSD symptoms include fever, joint pain, rash, and organ involvement, whereas TB symptoms include a persistent cough, chest pain, weight loss, and night sweats. Both illnesses can cause systemic inflammation as well as laboratory abnormalities such as higher levels of acute-phase reactants like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (1, 2). In this case report we found a rare condition lymph node TB with AOSD. To our knowledge, this is the first case report of AOSD with lymph node TB reported in Indonesia.

Case report

A 22-year-old man was referred from Ketileng Hospital to Dr. Kariadi Hospital with a chief complaint of prolonged fever. Three months before admission, the patient had a fever in the night, which was relieved with antipyretic

and no aggravating factors. One month before admission, the patient had a fever which got worse and made the patient unable to walk, and finally unable to sit because of joint pain. Two days before admission, the patient had a high fever to chills that were felt continuously throughout the day which improved with antipyretic drugs and was accompanied by joint pain, especially in the shoulder, making it difficult for the patient to move. Complaints were not accompanied by hair loss, headache, nosebleeds, cough, sore throat, bleeding gums, mouth sores, tightness, nausea, vomiting, decreased appetite, reddish rash on the hands and feet, calf pain, pain during urinating, and changes in defecation. There was however a history of weight loss of about 5 kilograms in 5 months, and yellowing eye membranes. The patient had a history of tuberculous cervical lymphadenitis. The patient also had a history of taking anti-tuberculosis drugs within 1 week since 8th October with fixed drug combination (FDC) anti-tuberculosis drugs, once a day. A history of hypertension, diabetes, liver disease, alcohol consumption, drug usage, or trauma was not present. A familial history of similar diseases was also not present. However, when the patient was 5 years old, his cousin had tuberculosis and they lived together in their grandparents' house.

On physical examination, the patient looked pale, with blood pressure of 110/80 mmHg and heart rate was 110 beats per minute. His respiratory rate was 20 breaths per minute, his body temperature was 38.2°C (axillary), oxygen saturation was 98%. His weight was 52 kg with a height of 170 centimeters and a body-mass index of 17.9 kg/m^2 (underweight). Physical examination of the patient showed malar rash, in arms and leg (Figure 1). His eyes were icteric and pale. The patient had no neck stiffness and no distention in jugular venous pressure. Heart examination was within normal references. Lung auscultation showed a vesicular breath sound. The patient's abdomen was soft, with no distention, tenderness, no mass, a liver span of 14 cm, dullness on Traube area percussion, no shifting dullness was found, no mass nor tenderness on palpation, spleen palpable on Schuffner 2. There were rashes in the arms and legs. There was lymphadenopathy in the right cervical areas.

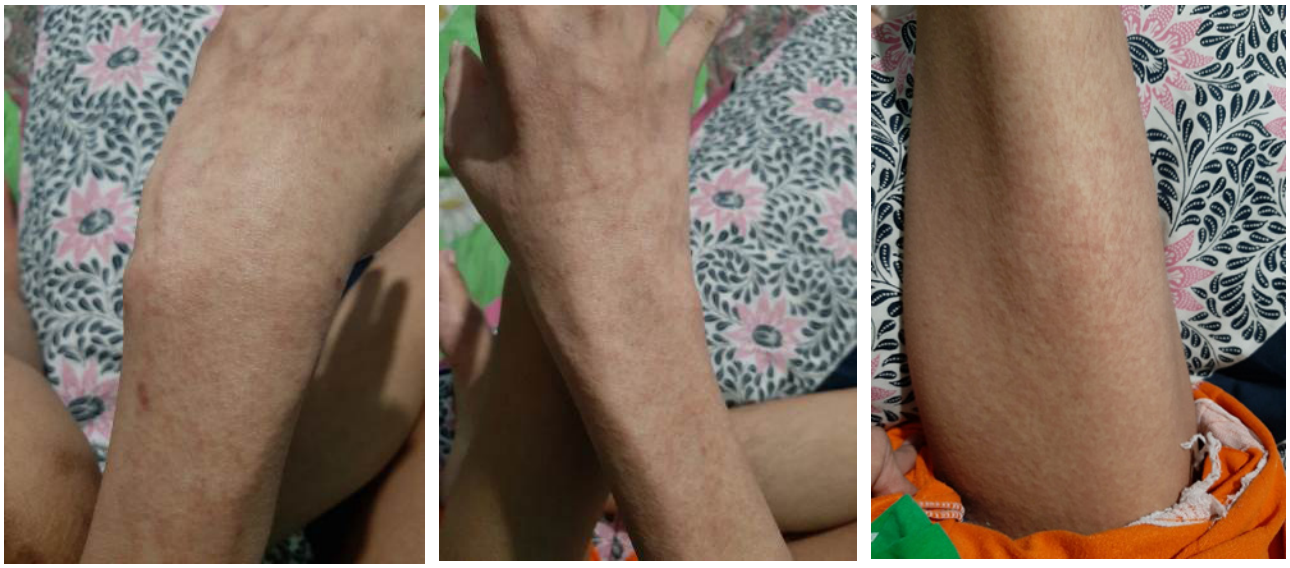

Figure 1: Clinical presentation of the patient, rash in arms and legs

Laboratory tests revealed microcytic hypochromic anemia (hemoglobin: 11 g/dL, mean cell volume 72.8 fL), with a total leukocyte of 30.4 x 109/L and platelets of 450 x 109/L. Liver function test (LFT) showed abnormality (aspartate aminotransferase/AST: 60 IU/L [15—34 IU/L], alanine aminotransferase/ALT: 27 IU/L [15—60 L], alkaline phosphatase: 227 IU/L [50—136 IU/L], gamma glutamyl-transferase: 152 IU/L [5—85 IU/L]). His total bilirubin was elevated (7.13 mg/dL [0.0—1.0 mg/dL) with direct bilirubin of 4.28 mg/dL [0.00—3.00 mg/dL] and indirect bilirubin of 2.85 mg/dL [0.1—0.5 mg/dL]. Serum creatinine (0.57 mg/dL), urea (23 mg/dL), albumin (3.1 g/dL), and electrolytes (sodium: 130 mmol/L [136—145], potassium: 3.5 mmol/L [3.5—51], chloride: 84 mmol/L [98—107]) was normal. Laboratory results also revealed elevated leukocyte, bilirubin, c-reactive protein (CRP), and ferritin levels.

Histopathology findings in cervical lymphadenopathy found a bilateral proliferation of large and small lymphoid cells with a prominent germinativum center and soft tubercle structures with an area of caseous necrosis in the central part surrounded by epithelioid cells of histiocytes, multinucleated Datia Langhans cells and lymphocyte inflammatory cells in cervical tissues, and no signs of malignancy. It was concluded that histopathological examinations showed bilateral tuberculous cervical lymphadenitis. Bone marrow punction showed mild hypercellularity bone marrow, bilineage

displacement, hyperplastic erythrocyte with myeloblast 2% and lymphoblast 1%, which suggested unspecified Myeloproliferative Neoplasia (MPN) (Figure 2). Chest X-ray showed a normal heart with no pulmonary infiltrates and nodes. An electrocardiogram showed sinus tachycardia with 111 beats per minute.

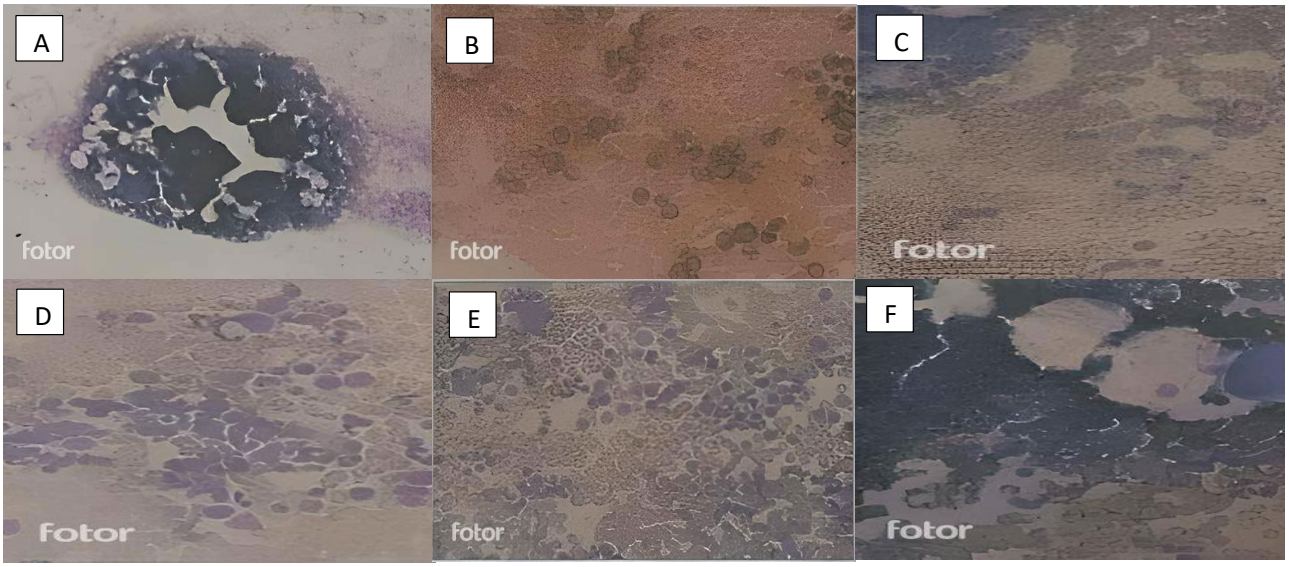

Figure 2: (A) Bone marrow aspiration shows hyperplastic erythrocytes; (B) and (C) show mild hypercellularity; (D) and (E) show myeloblasts at 2%; (F) shows lymphoblasts at 1%.

Based on the data above, the problems of this patient at admission were prolonged fever with polyarthritis, hepatosplenomegaly with abnormal liver function test, and microcytic hypochromic anemia. To rule out the differential diagnosis, the patient was planned to have abdominal ultrasound, right and left hands X-ray, antinuclear antibody (ANA) test, antibody streptolysin O (ASTO), Rheumatoid Factor, and another blood examination. Abdominal ultrasound found no cholestasis or obstruction. According to Yamaguchi criteria, this patient fits the diagnosis of AOSD. Immunological examinations showed negative ANA, ASTO, rheumatoid factor, and hepatitis infection in this patient.

The patient was treated with ringer lactate infusion of 30 drops per minute and a diet of 1700 kcal/day, oral ethambutol 1000 mg, moxifloxacin 400 mg, Vitamin B6 50 mcg once a day, and other antituberculosis drugs were stopped. The patient was also given lansoprazole 30 mg intravenously twice daily, methylprednisolone 62.5 mg intravenously twice daily in three days, and paracetamol 500 mg three times daily. Oral colchicine was also given with corticosteroids and cyclosporine. The patient's condition was improving and was allowed to be discharged. The dose of prednisolone was successfully tapered, and remission was achieved in 2 months after oral administration of colchicine.

Discussion

The infectious disease TB is a significant cause of death from a single infectious agent ranked above human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), one of the top 10 causes of death worldwide, and a major contributor to poor health. Mycobacterium tuberculosis, the bacillus that causes TB, spreads when TB patients discharge bacteria into the air, such as when they cough (1, 2). The disease TB is prevalent throughout the world. Despite the fact that extrapulmonary TB can affect many different places, the lymph nodes are the most commonly affected, followed by the pleura, bones and joints, genitourinary tract, disseminated miliary TB, meninges, and gastrointestinal (4). Symptoms and signs can be relatively vague and sometimes occur in normal chest radiographs and smear-negative. The diagnosis of extrapulmonary TB mostly depends on histological evidence (5).

There is no confirmed viral cause of AOSD, and there is conflicting evidence to support the idea that hereditary factors may play a role. A number of infectious triggers have also been proposed as potential causes (2, 6). According to Yamaguchi criteria, this patient was diagnosed as having an illness of AOSD. Only by identifying the remarkable constellations of clinical and laboratory anomalies is the diagnosis of AOSD achievable. Additionally, keep in mind that AOSD is an exclusionary diagnosis. In as many as 70% of patients, AOSD has been linked to noticeably increased blood ferritin levels (7, 8). Initially as an adult, an uncommon multisystemic inflammatory condition known as AOSD, hepatosplenomegaly, lymphadenopathy, recurrent polyarthralgia, and ephemeral neutrophilic eruption are its hallmarks (9). A unique skin manifestation of AOSD known as atypical persistent skin eruptions (APSEs)

has been discovered. Necrotic keratinocytes in the upper third layer of the epidermis and keratin whorls in the stratum corneum were the two most important diagnostic indicators seen in biopsy samples from such lesions (10).

Cyclosporine, a key immunosuppressive drug, takes center stage in the treatment of AOSD. It exerts its influence by regulating the hyperactive immune response, thus reducing the inflammatory onslaught associated with AOSD. Cyclosporine precisely limits the activation of T cells, which are key players in the immunological cascade, eventually controlling autoimmune reactivity. This measured action helps to alleviate the fever, arthralgia, and rash that frequently envelop people suffering from AOSD. Cyclosporine's immunomodulatory abilities are orchestrated in a delicate dance, an exquisite balance between reducing the abnormal immune response and guarding against potential negative effects (9, 10-13). Methylprednisolone enters the picture as a strong glucocorticoid in the quest for alleviation and remission. It quickly and firmly reduces inflammation by slowing the immunological response and alleviating the symptoms that affect those suffering from AOSD. Methylprednisolone enters the mix, focusing on cytokine storms and relieving the fever, joint pain, and systemic symptoms that are common in AOSD. Its quick action provides relief and allows people to resume some sort of normalcy, if temporarily (10, 11, 14).

Colchicine is a low-cost, commonly available medication. It can be used to treat a variety of autoinflammatory illnesses, including gouty arthritis and, more traditionally, familial Mediterranean fever (14, 15). Colchicine may reduce neutrophil recruitment by lowering L-selection expression in neutrophils and altering E-selection expression on the surface of endothelial cells. This results in the downregulation of numerous inflammatory pathways as well as neutrophil activity. It can inhibit the NOD-like receptor family, pyrin domain-containing 3 (NLRP3) inflammasome and caspase-1 activation, preventing the conversion of pro-interleukin (IL)-1 to active IL-1 and lowering the production of IL-1 and a variety of other interleukins, including IL-6 and tumor necrosis factor (TNF). Given this mechanism, it could be an excellent option for AOSD treatment, particularly for patients with APSEs (15).

In addition, the case report emphasizes the importance of coordination among rheumatologists, infectious disease specialists, and other relevant disciplines to ensure accurate diagnosis and proper care. More research is needed to determine the probable processes linking AOSD and TB, as well as to suggest effective treatment techniques in instances with shared clinical characteristics.

Conclusion

The case of adult-onset Still's disease with lymph node TB underscores the complex diagnostic challenges that clinicians may encounter. Awareness of the potential for TB to mimic AOSD is crucial, especially in regions with a high prevalence of TB. This case emphasizes the importance of a multidisciplinary approach to diagnosis and treatment, aiming to achieve optimal patient outcomes.

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Competing interests

The authors declare that they have no competing interests.

Informed consent

The authors attest that the patient has gotten the necessary patient consent form. The patient has provided her agreement in the form for her photos and other clinical information to be published in the journal. The patient understands that her name and initials will not be published and that all reasonable attempts will be made to conceal her identity; however, anonymity cannot be guaranteed.

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