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Spiculated lung infiltrate mimicking actinomycosis in adult-onset Still's disease complicated by macrophage activation syndrome

ABSTRACT

This study reports a case of adult-onset Still's disease (AOSD) complicated by macrophage activation syndrome (MAS) in a 19-year-old patient with a spiculated infiltrate located in the right lung. The diagnosis of AOSD was made after the onset of MAS and excluded neoplastic and infectious causes despite the initial suggestion of actinomycosis. MAS was treated successfully with dexamethasone and intravenous immunoglobulins and the treatment with prednisone was continued in the outpatient department. Lung involvement in AOSD is rare and may elude initial diagnosis so awareness in clinicians is needed.

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KEY WORDS: adult-onset Still's disease; auto-inflammatory disease; macrophage activation syndrome; parenchymal lung involvement; lung infiltrate

INTRODUCTION

Adult-onset Still's disease (AOSD) is an uncommon clinical entity of unknown aetiology belonging to the group of auto-inflammatory syndromes. The most common symptoms are recurring fevers, evanescent salmon-pink rash, arthritis, sore throat and lymphadenopathy but it may involve virtually every organ and mimic various infectious, autoimmune and proliferative diseases, thus so far it remains a diagnosis of exclusion and usually requires broad diagnostic workup [1]. Up to 15% of cases of AOSD are complicated by potentially life-threatening hyperinflammatory hyperferritinemia syndrome termed hemophagocytic lymphohistiocytosis (HLH), in the case of AOSD referred to as macrophage activation syndrome (MAS) [2]. This study presents a case of a 19-year-old male hospitalized in the rheumatology department in a tertiary centre in Poland from December 2019 to January 2020 due to a fever of unknown origin and a constellation of symptoms highly suggestive of AOSD, with spiculated lung infiltration in chest high-resolution computed tomography (HRCT), eventually complicated by MAS. The infiltrate found in CT initially raised suspicion of actinomycosis as the source of symptoms and laboratory abnormalities. The spiculated lung lesion resembling neoplasm or actinomycotic infection was most likely a transient pulmonary infiltrate being a rare manifestation of AOSD. Parenchymal lung involvement (PLI) is present in less than 5% of AOSD patients and may pose a diagnostic challenge like in the hereby case [3].

CASE REPORT

A 19-year-old male was admitted to the rheumatology clinic in December 2019 with a history of recurring fever of unknown origin up to 39.4°C, sore throat and arthralgia affect-

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ing wrists and knees. Before this admission, the patient had been hospitalized in a local general hospital in April 2019 and October 2019 with the suspicion of myocarditis due to fever and sinus tachycardia accompanied by elevated troponin levels as well as neutrophilic leukocytosis, high C-reactive protein (CRP) and liver enzymes. Every time myocarditis has been excluded and the fever resolved after empiric antibiotic therapy although no infectious cause was identified. So far the patient was otherwise healthy, with unremarkable family history.

On admission, he had a low-grade fever, tachycardia 120 beats per minute, signs of pharyngitis, cervical lymphadenopathy and wrist joints tenderness on palpation with no oedema. Laboratory tests revealed leukocytosis (20 G/L) with neutrophilia (90%), high erythrocyte sedimentation rate (75 mm/h) and CRP (288 mg/L), only slightly elevated ferritin [472 μg/L (norm: 20–300 μg/L)], hypoalbuminemia, a transient spike in procalcitonin with spontaneous normalization, elevated lactate dehydrogenase, β2microglobulin and liver function tests. Complement components, troponin, N-terminal pro-B-type natriuretic peptide, calprotectin, immunoglobulin G subclasses (IgG1–4) and lymphocyte subpopulations were within normal range. Blood and urine cultures as well as interferon-gamma release tests were negative. *Legionella* and pneumococcal urinary antigens, serological and molecular tests for HBV, HCV, HIV, EBV and CMV infections were all negative. Anti-citrullinated peptide antibodies, rheumatoid factor, antinuclear antibodies and antineutrophil cytoplasmic antibodies were absent.

Chest HRCT scan showed a spiculated infiltrative mass, 24 × 19 mm in size, located in the 6th segment of the right lung. CT scan of the abdomen and pelvis revealed splenomegaly. Bronchoscopy revealed oedematous and hyperaemic bronchi mucosa while the cytological examination of the bronchial washings led to the identification of colonies of *Actinomycetota*-resembling bacteria. Bronchoalveolar lavage examination was unspecific. Repeated bronchoscopy, specific cultures and thorough microbiologic assessment did not allow to confirm *Actinomyces*, *Nocardia* or *Mycobacteria* infection. In the throat swab, *Serratia marcescens* was cultured which was considered part of the commensal flora, as well as the bacteria found in bronchial washings cytology. Nevertheless, empiric antibiotic therapy with benzylpenicillin was initiated. Despite that, at the beginning of January 2020 spiking fever up to 40°C recurred and control laboratory tests showed pancytopenia and hypofibrinogenemia with remarkable hyperferritinemia. Bone marrow aspiration was performed which allowed the detection of hemophagocytes, thus the diagnosis of HLH was made. The patient was treated with dexamethasone 10 mg/m^2 according to the HLH 2004 protocol and intravenous immunoglobulins at 1 g/kg. The treatment led to rapid clinical and laboratory improvement. Control chest CT scan showed complete regression of lung lesion. Eventually, the diagnosis of AOSD complicated by MAS was made (the patient also fulfilled AOSD classification criteria) and the lung lesion deemed an AOSD-related infiltrate. Dexamethasone was switched to prednisone in a gradually tapered dose and the treatment was continued in the outpatient clinic. After 2 years of follow-up, the patient remains in sustained remission.

DISCUSSION

Pulmonary manifestation of Still's disease in adults is very rare. Consequently, there are very few case reports of patients with PLI associated with AOSD in the literature. The main criterion differentiating PLI from AOSD is the presence of acute respiratory distress syndrome in the course of the disease. Because the diagnosis of AOSD is based mainly on the exclusion of other causes and the fact that parameters such as IL-18 or glycated ferritin are difficult to obtain and not completely reliable, diagnostics of this disease entity requires many laboratory and imaging tests. Yamaguchi and Fautrel classification criteria may be also helpful with the diagnostics of AOSD. In this case, both criteria were satisfied [4, 5]. Due to the rarity of lung lesions in AOSD, spiculated infiltrate in this patient was initially attributed to other causes than the auto-inflammatory disease. An additional difficulty in making the diagnosis was the detection of *Actinomyces* bacteria in the cytological examination of the bronchial lavage fluid. This resulted in the use of antibiotics and looking for the infectious cause. In other similar cases [6, 7] pulmonary involvement mimicking an infectious disease was treated firstly with antibiotics without suspicion of AOSD as in the present case. Ruscitti et al. [8] reported that pulmonary involvement was associated with decreased survival rate. Pleural effusion (12–53%) and transient

pulmonary infiltrations (6–27%) are the most common clinical manifestations of pulmonary involvement in AOSD [9], although forms of lung involvement of AOSD reported in the literature vary [10].

Another variation in the clinical picture was the HLH syndrome (in this case termed MAS) during hospitalization. HLH is caused by the uninhibited production of pro-inflammatory cytokines and uncontrolled activity of lymphocytes and macrophages. This syndrome is often associated with rheumatological diseases, including AOSD. The coexistence of AOSD and MAS was connected to a higher risk of lung disease [11].

In conclusion, AOSD with pulmonary involvement is difficult to diagnose because of different clinical manifestations, symptoms mimicking pneumonia and low incidence of AOSD cases.

Typical clinical and laboratory presentation of auto-inflammatory disease in the context of a lung infiltrate nearly always prompt diagnostics of infectious cause, however, in case of inconsistency in the clinical picture and lack of antibiotics efficacy, other causes should be considered.

CONFLICT OF INTEREST

None declared.

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