

Adult Onset Still's Disease with Autoimmune Haemolytic anaemia: Two rarities in combination

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Abstract

Adult Onset Still's Disease with Autoimmune Haemolytic anaemia is a rare combination, difficult to diagnose but easy to manage. Literature to date reports only two cases. Hereby, we describe first of such a case from Pakistan. A 35 year old male, known case of Autoimmune Haemolytic Anaemia, presented with the complaints of high grade fever, fatigue, myalgia, skin rash and joint pain. After thorough investigation he was diagnosed as Adult Onset Still's Disease, according to the Yamaguchi criteria, and methylprednisolone (40 mg/day) was initiated. While his fever was relieved, dramatic

improvement was seen with patient joint complaints and his anaemia was also under control. Prognosis is good with regular medication, and it is necessary to educate both patient and family, to enable them to have a complete understanding of the disease and its effects on their life.

Keywords: Adult Onset Still's disease, Autoimmune Haemolytic anaemia, AOSD, Yamaguchi criteria, Methylprednisolone, Pakistan.

Introduction

First described in children by George Still in 1896, Adult-onset Still's disease (AOSD) is a rare systemic

inflammatory disorder. Prevalence of AOSD is estimated to be 0.16 cases per 100,000 people. It presents with a variety of clinical symptoms, including quotidian (daily) fevers, arthritis, an evanescent rash, lymphadenopathy, and splenomegaly.¹ Despite the constellation of characteristic clinical manifestations, the diagnosis of AOSD is difficult in some instances, due to absence of specific serological and pathological findings.

Autoimmune Haemolytic Anaemia (AIHA), an acquired extra corpuscular blood disorder, is one of the earliest described immune disorders with an annual incidence of 1 per 80,000 cases to 2.6 per 100,000. Autoimmune Haemolytic anaemia may result from warm or cold autoantibody types; although rarely mixed types can occur. As a matter of course, the antibody is of the IgG isotype and causes the destruction of patient and the donor red cells at body temperature. The real cause of AIHA remains obscure and approximately 50% of all cases of autoimmune Haemolytic anaemia are idiopathic.²

Combination of both ASOD and AIHA is very rare, difficult to diagnose but is relatively easy to manage. Literature to date reports only two cases, one by Guzzini et al³ in Italy and the other by Narigasawa et al⁴ in Japan. Hereby we describe a patient of ASOD with AIHA who underwent several investigations and treatments throughout the city before finally being diagnosed. To the best of our knowledge; this is the first reported case of AOSD in combination with warm auto-immune haemolytic anaemia in Pakistan.

Case Report

A 35 years old male, known case of autoimmune haemolytic anaemia on low dose Azathioprine and Prednisolone for 5 years; now presented with the complaints of high grade fever, fatigue, myalgia, skin rash, shoulder pain, and pain as well as swelling in small joints of both hands. These symptoms had been present for 2 months, started shortly after the patient had sore throat and dry cough for 5 days. Fever predominantly spiked during the night and was concomitant with macular rash on the trunk and arms. He was diagnosed as a case of pharyngitis by many physicians and was treated with several courses of broad-spectrum antibiotics, without any relief in symptoms. Five years prior, the patient was admitted to our hospital with complaints of intermittent weakness and dizziness for one week. He was diagnosed and treated as a case of AIHA on the basis of following investigations: haemoglobin level of 4.2g/dL, reticulocyte count of 13.88%. Bone marrow and peripheral blood smear findings were consistent, showing marked polychromasia with spherocytosis and tear drop

nucleated red blood cells. The serum lactate dehydrogenase level was 590 IU/L (150-450 IU/L), total bilirubin 5.0 mg/dL (0.4-1.3 mg/dL), direct bilirubin 2.2 mg/dL, alkaline phosphatase 212 U/L (upto 279), SGPT(ALT) 80 U/L (M:upto 40), Gamma G.T, 20U/L (M:11-50), haptoglobin 38 mg/dL (70-380 mg/dL), and vitamin B12 750 pg/mL (225-1,100 pg/mL). The patient's blood group was A, and Rh positive. The direct coomb's test was positive. Anti-nuclear antibody and anti-double stranded DNA antibody tests were negative.

On physical examination the patient was afebrile, and his heart rate was 78 bpm. He had painless cervical and axillary lymphadenopathy, and his spleen was palpable three centimeters below the left costal margin. His pharynx was mildly erythematous. Musculoskeletal examination showed that his shoulders were painful when moved and the motion of his wrists was also restricted due to pain. The rest of the examination was unremarkable. Routine laboratory investigation disclosed the following results: erythrocyte sedimentation rate, 105 mm/hr; C-reactive protein 347 mg/L; haemoglobin 9.9 g/dl; platelets 179,000/ μ l; total WBC count 19,700/ μ L with a differential count of 72% neutrophils; ferritin level 1975ng/ml. Cultures were negative for microorganisms, whilst antinuclear antibody and rheumatoid factor were negative as well. An enzyme-linked immunosorbent assay test revealed negative IgM and positive IgG antibodies against the viral capsid antigen of the Epstein-Barr virus. An abdominopelvic ultrasonograph showed mild hepatomegaly and splenomegaly. Radiograph of the patient's hands displayed a typical presentation of bilateral carpal ankylosis the other radiography, including shoulders, feet, and sacroiliac joints, were normal. He was diagnosed as AOSD, according to Yamaguchi criteria,⁷ and methylprednisolone (40 mg/day) was initiated. As his fever was relieved, dramatic improvement was seen with patient's joint complaints and AIHA being reversed.

Discussion

Prevalence of AOSD is very rare and uncommon, but occurs worldwide and has been previously published in many case series. Although AOSD is considered a disease of young adults it can also be seen in the geriatric age group.⁵ The disease affects a slightly larger number of women as compared to men.⁶ Fever is a dominant symptom, while infectious etiologies must be ruled out, as AOSD patients usually require immunosuppressive treatment. This is particularly important because active autoimmune diseases are usually treated with immunosuppressant medications. The patient in our case had already taken several antibiotics without any benefit, this in itself rules out

Table: Diagnostic criteria for AOSD.

Yamaguchi, et al.⁷

Presence of 5 or more criteria, of which at least 2 are Major yields 96% sensitivity; 92% specificity

Major Criteria

- ◆ Fever > 39 degrees > 1 week
- ◆ Arthralgia/arthritis > 2 weeks
- ◆ Typical rash
- ◆ WBC > 10 K with 80% PMN's

Minor Criteria

- ◆ Sore throat
- ◆ Lymphadenopathy
- ◆ Increased LFT's
- ◆ RF and ANA negative

an infectious agent.

There is no specific test or combination of tests that can be used to establish the diagnosis of ASD. As a result, many sets of diagnostic criteria have been proposed. Yamaguchi's criteria⁷ is the most widely cited criteria and were shown to be the most sensitive one (Table). Patient in this case, fulfilled this criteria with fever, arthritis, rash, sore throat, lymphadenopathy and negative ANA and RF. A very high serum ferritin level (1,975 mg/ml) also supports our diagnosis.

Autoimmune haemolytic anaemia typically produces an anaemia of rapid onset that may be life-threatening. There was no identifiable etiology in this case and so was regarded as idiopathic. Immune haemolysis may also follow a number of viral infections or certain medicines. Majority of patients respond well to steroids, the other treatment modalities include immunosuppressant and splenectomy. A newer agent is Rituximab, which is a monoclonal antibody and is of use in refractory cases.² Corticosteroid and immunosuppressants were treatments of choice in our case. The Coombs antiglobulin test forms the basis for diagnosis in this case. The direct Coombs test is positive in autoimmune haemolytic anaemia, and the indirect Coombs

test may or may not be positive.

The combination of the two, AIHA and AOSD like in this case, is a rare entity and was only reported by Guzzini et al³ in Italy and Narigasawa et al⁴ in Japan. Both of them reported this rare combination in female patients, we report first male patient. The female patient in Italy with AOSD, at the onset of her illness developed autoimmune haemolytic anaemia due to cold agglutinin. Whereas in Japan a 37-year-old woman with autoimmune haemolytic anaemia (AIHA) was diagnosed as having adult-onset Still's disease (AOSD). In both cases fever ameliorated and physical symptoms disappeared immediately after a moderate dose of Prednisolone. But hemolysis recurred when attempts were made to reduce or withdraw the steroid.

While our patient was already on low dose steroid and immunosuppressant for AIHA, increasing the dose provided prompt relief. Prognosis is good with regular medication, and necessary patients and family education, to enable them to have a complete understanding of the disease and its effects on their life.

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