WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 7, Issue 12, 935-940 Case Report ISSN 2278 – 4357

REFRACTORY SHOCK WITH MULTIPLE ORGAN DYSFUNCTION: A FATAL CASE REPORT ON ADULT ONSET STILLS DISEASE

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Article Received on
14 Oct. 2018,

Revised on 04 Nov. 2018,
Accepted on 23 Nov. 2018

DOI: 10.20959/wjpps201812-12810

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ABSTRACT

Adult onset Still's disease (AOSD) is a chronic multi-system inflammatory disorder characterized by high spiking fever, polyarthralgia and skin rash. Lymphadenopathy is another prominent feature of adult onset Still's disease. This report describes a 47 years old male presented with fever, multiple joint pains, cough and pus discharge from nails. Examination revealed fever, typical skin rash, generalized lymphadenopathy and polyarthritis. On investigation there were neutrophilic leukocytosis, high ESR, high ferritin level, raised liver enzymes, but RA test and ANA test were negative. All of his history, clinical examinations and laboratory findings fulfill the diagnostic Yamaguchi criteria for AOSD after the exclusion of other potential diagnoses. We report on a case of AOSD presenting with multiple organ failure which leads to death.

KEYWORDS: Fever, skin rash, polyarthritis, Adult onset still's disease, ANA, ESR.

INTRODUCTION

Adult-onset Still's disease (AOSD) is a rare inflammatory disease of unknown etiology, which commonly affects young adults. It is usually characterized by high spiking fevers, arthritis, and an evanescent, nonpruritic, macular and salmon coloured rash, appearing on the trunk and the extremities. Organomegaly, lymphadenopathy, serositis, and aseptic meningitis can also occur. Important laboratory findings include leukocytosis, with predominance of

neutrophils, negative testing for rheumatoid factor (RF), and antinuclear antibodies (ANA) as well as high serum ferritin levels and low serum glycosylated ferritin levels.[1-3]

Severe disease complications include pericarditis, endocarditis, hemolytic anaemia, and macrophage activation syndrome (MAS). The latter is characterized by thrombocytopenia, markedly elevated ferritin levels, hypofibrinogenemia, and elevated aspartate amino-transferase (AST).[1-3] AOSD is typically considered as a diagnosis of exclusion and a definitive diagnosis should be made based on the Yamaguchi or Fautrel criteria only after excluding infectious, malignant, and other connective tissue diseases. Timely diagnosis and treatment of the disease with corticosteroids followed by maintenance therapy with disease modifying antirheumatic drugs (DMARDs) or biologic drugs such as tumor necrosis factor -(TNF-) alpha agents or interleukin (IL-1) antagonists can prevent complications and lead to a favorable prognosis.[4]

CASE REPORT

Mr. 49-year-old male was presented with a history of fever, multiple joint pains, cough and pus discharge from nail end. On examination he was conscious, oriented, tachycardiac. Chest examination showed left infrascapular, infra axillary crepts, joints were swollen and tender. Chest x-ray revealed left side lower zone opacity suggestive of pneumonia.

He was evaluated outside hospital for complaints of generalized lymphadenopathy, pneumonia, anemia, pyoderma, hepatospleenomegaly, Biopsy of lymph node was reactive. In 2017, he was on treatment with steroids, iron supplement and later he developed Herpes oral ulcer and HSV1 was found positive. Colonoscopy showed inflamed right colon and biopsy showed positive result for CMV for which he was on T.Valgan (Valganciclovir). ANA was found to be negative. PET was done which showed loculated pleural effusion, circumferative mural thickening and enlarged multiple lymph nodes.

Hematological investigations showed leucocytosis of 34.5 × 10^{9}/L (93.8% neutrophils), elevated liver enzymes (alanine transaminase: 157 U/L; aspartate transaminase: 92 U/L). Haemoglobin and serum albumin level was partially decreased (4.50 and 1.7). Both the acute phase reactants were high with C-reactive protein (118mg/L) and erythrocyte sedimentation rate (ESR: 128 mm/hr). There were markedly elevated levels of serum ferritin (1551.6 ug/L). Anti-cyclic citrullinated peptide, antinuclear antibody (ANA) and rheumatoid factor (RF) were all negative. Serum creatinine and BUN levels were elevated. Coagulation profiles were

normal. Blood and urine cultures revealed no evidence of bacterial, fungal or viral infection. Sputum gram stain showed few inflammatory cells, gram positive cocci in short chain, gram positive cocci in budding yeast cells with pseudohyphae and gram negative bacilli seen.

Based on his clinical features and review of the laboratory evaluations, he was diagnosed to have differential diagnosis include Stills disease, pneumonia, Sjogren's syndrome, SLE, Adult onset still's disease. Possibility of adult onset still disease (on yamaguchi criteria) with left sided pneumonia was considered and was started on Inj. Ceftriaxone, he got clinically better and pulse steroids and Inj. Tocilizumab given. While in ward he developed worsened cough and haemoptysis, breathleness, increase in swelling joints and fever. He experienced one episode of **PLE** (protein losing enteropathy) mild to moderate in amount, bright red in color, painless and was started on two scoops of powder albumen with curd TID.

Pulmonology opinion was taken, CT chest was done was suggestive of necrotizing pneumonia. Antibiotics escalated to Inj. Meropenam and Inj. Clindamycin. In view of multiple abscess of skin, staphylococcal infection was considered and Inj.Vancomyicin added. He continued to detoriate in his general condition, developed hypotension and was shifted to MICU and was intubated put on ventilator support Inj.polymixin was also added. He continued to worsen, developed cardiac arrest, CPR initiated as per ASCLS protocol but could not be revived and death declared based on refractory shock with multiple organ dysfunction.

DISCUSSION

AOSD is a rare systemic inflammatory disease of unknown etiology. It was initially described by Eric Bywaters in 1971 as a distinct clinical entity in adults.[4] It has an estimated prevalence of 1.5 cases per 100,000–1000, 000 people. It has been described all over the world and has a bimodal age distribution with 2 peaks, the first peak affecting people within 15–25 years of age and the second peak affecting people within 36–46 years of age Although it usually affects the younger adult population, it can also affect elderly people. The disease affects predominantly females as compared to males.[4]

There is a correlation between several cytokines in the pathogenesis of AOSD, including Tumor necrosis factor alpha (TNF-α), interleukin (IL)-6 and IL-18. The levels of these cytokines are highly elevated in active AOSD.[5] Laboratory studies showed marked ESR elevation and leukocytosis with predominance of neutrophils. Disproportionately elevated

ferritin is characteristic of AOSD. Almost 70% of patients have hyperferritinemia, which was thought to be due to cytokine secretion induced by the reticuloendothelial system or hepatic damage.[5] In most cases however; the ferritin levels increased without obvious liver damage. Liver enzymes were elevated in almost three quarters of patients. Rheumatoid factor and antinuclear antibody were generally negative.[5]

In the early stages of the disease, diagnosis of AOSD is difficult. Before making a diagnosis of AOSD, other diagnoses including infections such as infectious mononucleosis, malignancies (especially lymphoma), and other rheumatic diseases such as systemic vasculitides should be ruled out. Investigations were done to rule out the possible causes before this patient's diagnosis was reached.[5]

High-sensitivity classification criteria have been proposed, since there is no single test to establish the diagnosis (Table 1).[6] In Brazil, disease onset is around 30 years. Fever, arthritis, and skin rash are the most common clinical signs, and elevated ESR, leukocytosis, absent antinuclear antibody, and absent rheumatoid factor are the most frequent laboratory findings.[7,8]

Table. 1. Classification criteria for adult-onset Still´s disease proposed by Yamaguchi et al.

Major criteria Minor criteria
Temperature of > 39oC for > 1 wk Sore throat
Leukocytosis > 10 000/mm3 Lymph node enlargement
Typical rash Splenomegaly
Arthralgias > 2 wk High transaminases Negative ANA, RF
(After excluding infections, malignancies, and other rheumatic diseases, adult Still´s should be considered if 5 criteria (2 of which being major ones) are met. ANA = antinuclear antibody; RF = rheumatoid factor)

Non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin are recommended as the initial treatment in AOSD, but low response rate has been reported.[9] Prednisolone should be started for patients not responding to NSAIDs or suffering from pericarditis, serositis, persistent anemia or markedly elevated liver enzymes.[10] Disease modifying anti-rheumatic drugs (DMARDs) such as methotrexate have been used to control the acute symptoms, and it is suggested that at least 6 months of therapy should be given to allow ample time for the assessment of the therapeutic effect.[11] Sulfasalazine appears to have severe adverse reactions in AOSD and should be avoided.[12]

For patients who do not respond to conventional medications such as corticosteroids and DMARDs, biologic agents should be considered. Since cytokines such as TNF-alpha, IL1 and IL6 involved are implicated in the pathogenesis of AOSD; biologic agents targeting these cytokines have proven to be effective in treating AOSD.[13]

CONCLUSION

AOSD still remains as a diagnostic dilemma for physicians as it presents with a combination of nonspecific symptoms that can be caused by a wide variety of diseases. However, the key point to remember is that, for patients who present with prolonged and unexplained fever combined with musculoskeletal symptoms and macular rash, the differential diagnoses should include AOSD.

Diagnosis is clinical and not based on serology. Extremely high serum ferritin levels is a peculiar characteristic of the disease (though the serum ferritin levels are elevated in many inflammatory, infections and malignant disorders but the levels in adult onset still's disease is much higher when compared to other above mentioned conditions). Hence, serum ferritin levels to be included as diagnostic criteria for Adult onset still's disease. Timely diagnosis and treatment of the disease can prevent complications and lead to a favorable prognosis with improved quality of life.

ACKNOWLEDGEMENTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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