

A Significant Response to Anakinra in Management of Adult Onset Still's Disease: A Case Report

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1. Abstract

Adult Onset Still's Disease (AOSD) is a rare rheumatological condition that is characterized by a clinical triad of (daily spiking Fever, arthritis and rash) and a biochemical triad (hyperleukocytosis with neutrophilia, hyperferritinemia and abnormal liver function test).

The diagnosis of ASOD in most of cases is lengthy and there is no specific diagnostic test for it. Therefore, there are many proposed diagnostic criteria but Yamuguchi criteria which was published in 1992 is the most frequent used.

Supportive therapy, NSAIDs, Steroids and DMARD is usually the initial management. In more severe cases and refractory cases other lines can be used which showed good response like IL-6 receptor antibody (tocilizumab), IL-1 inhibitors (anakinra and canakinumab) and anti-TNF agents (infliximab, adalimumab).

Herein we are presenting a 23 years old Omani male who presented with acute history of sore throat, fever, arthritis, polyserositis, raised liver enzymes and hyperferritinemia. He was diagnosed to have AOSD based on Yamuguchi criteria after the exclusion of other potential diagnosis like Lymphoma and Tuberculosis (TB). The patient did not show good response to prednisolone, IV Immunoglobulin (IVIG) and Tocilizumab infusion. And then He responded dramatically to Monotherapy, Anakinra (IL-1 inhibitor) and he returned back to normal activity and normalised ferritin.

2. Introduction

Adult Onset Still's Disease (AOSD) is a rare rheumatological <http://acmcasereports.com/>

condition that is characterized by a clinical triad of (daily spiking Fever, arthritis and rash) and a biological triad (hyperleukocytosis with neutrophilia, hyperferritinemia and abnormal liver function test) [1].

AOSD has equal gender distribution and majority of reported cases are between 16 and 35 years of age [2,3]. The diagnosis of ASOD in most of cases is lengthy and challenging due to the absence of serological biomarkers [4]. Therefore, there are many proposed diagnostic criteria but Yamuguchi criteria which was published in 1992 is the most frequent used one [3,5].

There are two distinct ASOD phenotype based on the clinical presentation; Acute systemic febrile illness, with polycyclic or monocyclic pattern which is highly symptomatic and need prompt treatment as it can be fatal if not timely diagnosed and treated. The other form is more slowly evolving illness with arthritis and less symptomatically [4].

The management of ASOD includes NSAIDs, Steroids, Disease-Modifying Anti-Rheumatic Drugs (DMARDs), like IL-6 receptor antibody (tocilizumab), IL-1 inhibitors (anakinra and canakinumab) and anti-TNF agents (infliximab, adalimumab) [4].

3. Case Presentation

A 23-year-old man with no significant past medical history presented with progressive worsening multiple symptoms including fever, back pain, shortness of breath, chest pain, headache and sore throat.

Physical examination revealed a young male with abnormal he-

modynamic of (Temperature of 38.5 °C, Pulse of 95 beats/minute, blood pressure of 99/58, respiratory rate of 22 breaths/minute, SpO₂ of 99% at room air). He had bilateral lower limb oedema; diffuse tenderness was elicited in both legs upon flexion, muscle with restriction of neck flexion. No lymphadenopathy, no cyanosis, not dehydrated, no clubbing. Rest of the examination was unremarkable.

Initial Laboratory Investigations showed leucocytosis of 13.1 (Absolute Neutrophil Count 10.4), C-Reactive Protein of 280 and Erythrocyte Sedimentation Rate of 90. Biochemistry showed high ferritin level of 18450 and Troponin of 357 which normalized later on. Infectious work up revealed a positive EBV, ASO titer. On the other hand, it showed negative sepsis screen, HIV, COVID19, monospot test, throat swab and all Respiratory viral panel was also negative.

Chest X-ray done and showed Bilateral per-hilar LN infiltrate. ECG done and showed changes suggestive of acute pericarditis so colchicine and ibuprofen started, ECHO was normal. As he also have neck stiffness, CT brain was done to exclude intracranial lesion and meningitis which reported normal. Whereas LP not done as INR was high. Despite CT findings, he was started on dexamethasone with IV ceftriaxone as prophylaxis.

Patient's condition improved little with these medications but his symptoms got worsened later on with very low BP and tachycardia. Also rash increased with generalized body pain and eventually he was shifted to ICU. Another set of investigations sent and revealed negative ANA, anti-ds DNA and sputum for TB. CT chest, pelvis and abdomen showed hepatosplenomegaly and pleural effusion. ECHO was repeated and showed mild pericardial effusion on anterior wall so initial treatment was continued.

As autoimmune disease in which pericarditis is a part of the disease was suspected, Injection of methylprednisolone was started and patient showed dramatic improve with it then tapered to prednisolone were he got relapsed with significant worsening of shortness of Breath so ECHO repeated again and showed massive posterior wall pericardial effusion and plural effusion. Tapping was done and revealed exudate with neutrophils, PCR done and showed positive CMV and EBV but TB culture came negative and was started on Vancyclovir. Therefore, still's disease was suspected after excluding other disease like infections and malignancy and applying Yamaguchi criteria were it came high.

Intravenous Immunoglobulin started with mild improvement then tocilizumab was started were he developed allergic reaction so Anakinra was started where it showed dramatically improvement of both clinical symptoms and laboratory investigation.

He was discharge home after 20 days of admission with regular follow up. Anakinra continued for 2 months and antiviral tapered down based on labs finding. Patient continue to improved and no flare up noticed.

5. Discussion

This case highlights the multiple manifestations and how is challenges in diagnosing Still's disease. A patient presenting with quotidian fevers, evanescent rash and various types of arthritis is the typical presentation of AOSD or systemic juvenile idiopathic arthritis [1,4].

The etiology is currently proposed as a mix of infectious triggers and predisposed genetic factors but the exact mechanism of the disease still unknown [7-10].

In our case, the patient presented with multiple symptoms as mentioned which match the typical manifestation of still's disease. The disease has many clinical presentation of various intensity including high spiking fever, polyarthralgia which found in 69% of cases and evanescent salmon colored rash. Furthermore, patient can have hepatomegaly (12–45%), abdominal pain (1–48%) and cardiopulmonary disease (30–40%) such as, pleural effusions, pericarditis and transient pulmonary infiltrates. Also Laboratory investigation reveals elevation of serum ferritin, CRP and ESR and abnormal liver function test [1,11, 12].

The diagnosis of AOSD remains challenging with no specific diagnostic test and in most of cases it is lengthy [4]. Therefore, the little delay in diagnosing our patient and doing extensive investigation not of exception and brings no surprises.

Because of the challenging diagnoses, several sets of different classification criteria have been proposed for AOSD over the time Including (Calabro, Glodman, Reginato, Kahn Cush, and Yamaguchi) [10]. In fact, the most frequent used criteria which showed superior accuracy as per Masson et al study in 1996 is the Yamaguchi criteria. This criteria consist of 4 major criteria (fever >39 °C, lasting 1 week or longer, typical rash, arthralgia or arthritis lasting 2 weeks or longer and leukocytosis >10 000/mm³ with >80% polymorphonuclear cells), 5 minor criteria (sore throat, recent development of significant lymphadenopathy, hepatomegaly or splenomegaly, negative tests for ANA and rheumatoid factor or abnormal liver function tests) and exclusion criteria (malignancies, Infections, and other rheumatic/ systemic vasculitides). To diagnose still's disease by following this criteria; at least five features should met with at least two of these being major diagnostic criteria. Therefore, we apply it for our patient and it showed high score [4,10]. To facilitate early diagnosis of AOSD, Serum ferritin can be used as a biomarker [13,14]

Many types of therapy have been tried for the treatment of Adult Onset Still's Disease. Beside supportive therapy, NSAIDs, Steroids and DMARD is usually the initial management. In more severe cases and refractory cases other lines can be used which showed good response like IL-6 receptor antibody (Tocilizumab), IL-1 inhibitors (Anakinra and Canakinumab), anti-TNF agents (Infliximab, Adalimumab). In presented case, NSAID and IV steroids were started were the patient showed good initial improvement but

after tapering steroids the patient got relapsed were the decision came to start anakinra which showed significant improvement in his symptoms and laboratory findings [4].

The prognosis of AOSD is generally good for those patient with 90% of the patients being able to continue their daily activities even when they are suffering from chronic type disease [1].

6. Conclusion

Fever, rash and polyarthralgia are not only for infections or inflammatory diseases. High suspicions of index of Adult Onset Still's Disease should be consider in patient have this triad of symptoms with the laboratory findings. Immediate identification and management of AOSD is very important to prevent complications and lead to a favorable prognosis. Supportive management and early starting of Anakinra showed significant improvement.

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