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Adult-onset Still's Disease after COVID 19 Infection: Case Report

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Abstract

Adult-onset Still's disease (AOSD) is an inflammatory disorder that presents by quotidian fevers, arthritis, an evanescent rash and even life-threatening conditions like Macrophage activation syndrome. Still's disease in the adult was used to describe a series of adult patients who had features similar to the children with systemic juvenile idiopathic arthritis and did not fulfil criteria for classic rheumatoid arthritis. We reported a case of Adult-onset Still's Disease where the patient presented with frequent high grades of fever associated with sore throat, cough and intermittent sharp chest pains not responding to regular pain killers.

Keywords: Adult-onset Still's disease, Macrophage activation syndrome.

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1. Introduction

Adult-onset Still's disease (AOSD) is an uncommon inflammatory disorder of unknown aetiology. The major clinical features include quotidian fever, evanescent, salmon-coloured, macular rash that predominantly involves the trunk and extremities. Musculoskeletal manifestations include arthritis, myalgia and arthralgia. Other findings include pharyngitis, liver disease, cardiopulmonary disease, lymphadenopathy and splenomegaly. Haematological and gastrointestinal manifestations can also occur.

2. Case Report

A 27-year-old Jordanian male with history of COVID infection on 9th April 2021 and was placed in quarantine for 10 days with mild and manageable COVID symptoms. Two to three days after completing his 10-days home quarantine, he started to have high grades of fever associated with sore throat, cough and intermittent sharp chest pains, which were not responding to regular pain killers at home. He was then admitted on 23rd April 2021 at 4 p.m.

On arrival, his vitals were reported with temperature of 38.9℃, heart rate of 93 bpm, Respiratory Rate 22/min, SPO2 98% on room air. On Chest auscultation there was harsh vesicular breathing, congested throat, red rash on most of the body without itching sensation. On Cardiovascular examination there were normal first and second heart sounds, with tachycardia and without heart murmur. His abdomen was soft, lax and non-tender. His lower limbs were not swollen and showed no signs of deep vein thrombosis.

His laboratory results on 23rd April 2021 were as follows: White Blood Cell count of 18.90k/uL, Haemoglobin level of 14.0 g/dl, Haematocrit of 42.1%, platelet count of 218/ml, C-Reactive Protein 233.80 mg/L, Procalcitonin <0.5 ng/ml, D-Dimer 0.50 g/L, SGPT of 31U/L, SGOT of 23 U/L, Sodium level 142 mEq/L, Potassium level of 4.11 mmol/L, Bicarbonate level of 23.3 mEq/L, Calcium level of 8.71 mg/dl, Ferritin of 465 μg/ml, Lactate dehydrogenase level of 232 U/L, Creatinine level of 1.02 mg/dl.

Since admission to the hospital, the patient had frequent high grades of fever with intermittent sharp chest pain on deep breathing, on lying positions and minimal coughs. The patient also complained that he is not able to lie flat and that his pain is aggravated by deep breathing and improved by leaning forward. On the 24th of April due to complaints of chest pain, the patient was referred to the cardiology team. An Electrocardiogram was performed which showed sinus tachycardia with generalized ST-T elevation in I, AVL and inferolateral leads, ST-T depression in V1, AVR and lead III. Serial cardiac markers reported Creatinine Kinase level of 23 U/L and Creatine kinase-MB level of 0.516 along with borderline high level of Troponin 18.07ng/l.

The chest X-ray performed revealed significant bilateral effusion. The echocardiograph revealed mild concentric left ventricular remodelling, normal left ventricular systolic and diastolic function. The ejection fraction was 60%.

The patient was initially started on Ceftriaxone and Tazocin and later switched to Levofloxacin and Meropenem.

Computed Tomography pulmonary angiogram (CTPA) revealed an Interval increase in the amount of bilateral pleural effusion with maximum thickness measuring 3.5 cm and the left side, causing bilateral lower lobe collapsed consolidation. Faintly seen ground glass opacities and atelectasis. There was a rim of pericardial effusion noted as well.

He underwent high resolution chest computer tomography (HRCT) which revealed ground glass opacities, consolidations with air bronchogram, intralobular septal thickening and atelectasis involving both lower lobes that is more marked on the left lower lobe associated with bilateral mild pleural effusion that is increased on the left side.

The patient's general and hemodynamic condition was improving significantly. Mobilization out of bed along with chest physiotherapy were started. However, his fever was not settling despite being on antipyretics and broad-spectrum antibiotics like Linezolid, Meropenem with Tobramycin and Fluconazole. 6 grams of Beneprotein was given in view of Hypoalbuminemia and low total proteins.

On 5th May the patient continued to have persistent high-grade fever along with breathing difficulty. The patient was evaluated by a rheumatologist in line of possible Still disease. He was started on Intravenous Methylprednisolone the biological agent Tocilizumab, and he showed some improvement with less frequent fever.

On 10th May, the patient was showing drastic response to Tocilizumab and Intravenous Steroids. His fever has settled as well and he has also showed improvement in his chest and joint pains and his inflammatory markers were coming down. The patient was then discharged on 11th May 2021 in a stable condition without fever or cough. He continued taking tocilizumab for 3 months and during this period the patient had no complaints of joint pain or chest pain and was afebrile. However, the patient refused to continue taking Tocilizumab as he was afraid of the medication's adverse effects that he had read online.

On 25th September 2021, the patient presented to the emergency with complaints of recurrent central chest pain for 3 days. The pain was pressing in nature and radiating to the upper back and exacerbated when breathing and lying flat. Th Electrocardiogram showed no sinus tachycardia with flat T wave in lead III and Q wave in lead V2. The patient was admitted to the Cardiac ward and started on 300 milligrams of Aspirin orally 3 times daily. The laboratory investigations showed high white blood count of 12.79 and high CRP of 51.54.

The Echocardiography performed showed mild pericardial effusion.

The rheumatologist advised the patient to continue taking intravenous Tocilizumab 400 mg once monthly.

3. Conclusion

Adult Onset Still's Disease (AOSD) is a rare systemic inflammatory disorder. It was first described in children by George Still in 1896 (Still GF, 1897). It describes adults who presents with symptoms similar to the children with systemic juvenile idiopathic arthritis (JIA) and did not fulfil the criteria required for classic rheumatoid arthritis diagnosis (Bywaters, 1971).

A French study found that the annual incidence of AOSD to be around 0.16 cases per 100,000 people, with both genders equally affected (Magadur-Joly et al. 1995). Most people affected were between the ages of 15 and 25 and between the ages of 36 and 46 (Uson et al. 1993); (Steffe et al. 1983).

AOSD's aetiology is unknown although some genetic and infectious causes have been linked with it but with inadequate proof. Yersinia enterocolitica and Mycoplasma pneumoniae include one of the proposed pathogens (Ohta et al. 1990); (Colebunders et al. 1984). AOSD and Systemic JIA have both been associated with high levels of interleukin 6 (IL-6) and IL-18 (Nigrovic et al. 2018).

The clinical course of AOSD can be divided into three main patterns: monophasic, intermittent, and chronic (Pouchot et al. 1991); (Kontzias et al. 2008). The monophasic pattern typically lasts weeks to months and resolves within less than a year characterised by features like fever, rash, serositis, and hepatosplenomegaly. The intermittent pattern is characterised by one or more disease flares with complete remissions between episodes lasting from weeks up to one or two years. The chronic pattern manifests in patients with persistent active AOSD with articular symptoms (Fautrel, 2008).

The clinical picture of AOSD includes fever that is usually quotidian and occasionally double-quotidian that precedes other disease manifestations, the temperature swings can be dramatic, with changes of 4ºC (7.2ºF) occurring within four hours (Calabro et al. 1967). In 60 to 80% of AOSD cases, a macular or maculopapular evanescent salmon-pink skin rash appears together with the fever spikes. It is predominantly found on the proximal limbs and trunk (Crispin et al. 2005). A severe, nonsuppurative pharyngitis is common in AOSD, in a literature review of 341 cases, sore throat was noted in 69 percent (Nguyen et al. 1997). Arthralgias or arthritis are universal features of AOSD, the arthritis may be mild, transient, and oligoarticular, these manifestations evolve over a period of months in some patients into a more severe and potentially destructive polyarthritis (Elkon et al. 1982).

AOSD is accompanied by other systemic features like liver disease with hepatomegaly observed in different studies ranges from 12 to 45 percent, Splenomegaly and Gastrointestinal symptoms like abdominal pain was also observed in more than half of the patients reported (Gerfaud-Valentin et al. 2014), cardiopulmonary disease with pericarditis and pleural effusion with affected patients complaining of cough and pleuritic chest pain (Cheema et al. 1999). Macrophage activation syndrome (MAS) is a life threatening complication seen in AOSD as well as systemic onset juvenile idiopathic arthritis (sJIA). Its pathogenesis

is not clearly understood but involves cytokine induced hyperproliferation of activated CD8+ T-lymphocytes and macrophages in the reticuloendothelial system (Tristano, 2008).

Laboratory findings in fact show the AOSD profile which reflects the systemic inflammation and cytokine cascade present, the erythrocyte sedimentation rate (ESR) was raised in virtually all patients in three of the largest series described (Wouters et al. 1986). C reactive protein (CRP) may also be found to be raised (Akritidis et al. 1995). Elevated ferritin level is a nonspecific but common finding and a helpful feature for diagnosing AOSD (Meijvis et al. 2007).

Liver dysfunction is common in adult-onset Still disease (AOSD); indeed, liver dysfunction is one of the diagnostic criteria that was also described (Yamaguchi et al, 1992).

Treatment options include corticosteroids which remains as the first-line treatment for AOSD, regardless of the clinical presentation (Moulis et al. 2010). Up to 20 percent of patients achieve control of the signs and symptoms of mild AOSD with NSAIDs (Reginato et al. 1987). Methotrexate could be considered early for its steroid-sparing effect. Usually, methotrexate (7.5–20 mg/week) enables complete remission of the disease (70%) or at least a significant reduction of daily corticosteroid intake (Fautrel et al. 1999).

In the event of failure of corticosteroid treatment or steroid-dependence, disease-modifying anti-rheumatic drugs (DMARDS) can be considered (Kim et al. 2012).

Initiating treatment with the IL-1 antagonist anakinra as monotherapy may be effective in AOSD, especially early in disease, and avoid serious adverse effects that are often associated with the use of glucocorticoids. Anakinra is a recombinant human IL-1 receptor antagonist and represents our preferred first-line biologic therapy for AOSD because of its efficacy, short half-life (six hours), and easy titratability (Ter Haar et al. 2019). In patients with new-onset AOSD where incipient or active MAS remains a concern, we typically combine anakinra with glucocorticoid therapy (Eloseily et al. 2020).

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