Adult-Onset Still's Disease in an Elderly Patient Presenting as Aseptic Meningitis: A Case Report

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Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders
Volume 16: 1–4

DOI: 10.1177/11795441231195636

ABSTRACT: Adult-onset Still's disease (AOSD) is a rare auto-inflammatory disease of unknown origin characterized mainly by fever, arthritis, and a rash. Aseptic meningitis is a rare complication of AOSD and is seen most commonly in young adults. Here, we report a case of AOSD in a 78-year female with fever and altered sensorium with lymphocyte predominant pleocytosis in the cerebrospinal fluid who was initially managed as tubercular meningitis. Adult-onset Still's disease was diagnosed as there was no response to antitubercular drugs even after 3 months and based on persistent fever, inflammatory arthritis, rash, and highly raised inflammatory markers.

KEYWORDS: Adult-onset Still's disease, aseptic meningitis, elderly

RECEIVED: April 25, 2023. **ACCEPTED:** August 1, 2023.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS : The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Adult-onset Still's disease (AOSD) is a multi-system auto-inflammatory disease of unknown cause characterized by the classic triad of high-grade fever, inflammatory arthritis, and an evanescent rash. It is associated with profound systemic inflammation marked by highly raised inflammatory markers, leukocytosis, and high ferritin levels. There is a bimodal age distribution of disease with peaks at 15 to 25 years and a second peak at 36 to 46 years.[1] There is no confirmatory test for its diagnosis. It is made after ruling out other infectious, inflammatory, and neoplastic conditions. Neurological complications such as aseptic meningitis, seizures, cranial nerve palsies, and peripheral neuropathy have been described in AOSD.[2] Here, we describe a case of AOSD in an elderly female who presented with meningitis.

Case Description

A 78-year-old female from Kathmandu, Nepal, presented to us with one day of altered sensorium characterized by irrelevant talking, increased talkativeness, and inability to recognize family members. On further questioning, she had been having fever for two weeks that was high-grade occurring every day in the evening which was associated with malaise and body ache. Her family members had noticed loss of appetite for the same duration. She had no history of cough, abdominal pain, jaundice, loose stools, burning micturition, or rash. She had no history of travel outside of Kathmandu over the past few months. Her medical history included hypertension, bilateral knee osteoarthritis, and stable chronic obstructive pulmonary disease (COPD). Her medications included losartan 50 mg, furosemide–spironolactone (40 mg/25 mg) once daily and salbutamol inhaler on an as-needed basis. She was a social drinker and non-smoker but had a history of using firewood for cooking. She had no significant illness in her family.

On examination in the emergency department, her Glasgow coma scale (GCS) was 15/15, blood pressure 140/90 mm Hg, pulse rate 108/min, regular, SpO_2 92% on room air, and temperature 98°F. Neurological examination was unremarkable without any features of meningeal irritation. Examination of other systems was within normal limit. Initial investigations showed anemia with neutrophilic leukocytosis, raised C-reactive protein (CRP), and normal electrolytes (Table 1). Computed tomography (CT) scan of the head was normal. Her cerebrospinal fluid (CSF) analysis showed increased protein, normal sugar, and lymphocyte predominant leukocytosis. The patient was admitted with the working diagnosis of subacute meningitis and was started on intravenous ceftriaxone 2 g twice daily, vancomycin 1 g twice daily, acyclovir 500 mg thrice daily along with other supportive therapy. Meanwhile, polymerase chain reaction (PCR) for Japanese encephalitis, herpes simplex, and mycobacterium tuberculosis was negative. Her magnetic resonance imaging (MRI) of the brain showed chronic infarct involving left caudate and lentiform nuclei. During her stay in the ward, her sensorium was normal, but she was still having fever with worsening laboratory parameters. At this time, tubercular meningitis was suspected because of subacute onset of symptoms and CSF picture of lymphocyte predominant leukocytosis with high protein. Visceral malignancy was an important differential given her age, but there was no evidence for either.

As she was not responding to the above treatment, antitubercular therapy (ATT) that included rifampicin 600 mg, isoniazid 300 mg, ethambutol 1100 mg, pyrazinamide 1600 mg along with dexamethasone 6 mg four times a day was started on

Table 1. Laboratory investigations.

	DAY 1	DAY 2	DAY 3 (AFTER STARTING STEROID AND ATT)	25 DAYS AFTER DISCHARGE	AT SECOND ADMISSION	AT FOLLOW-UP (AFTER 1 MONTH OF TREATMENT)
Hemoglobin (g/dL)	10.1	10	9.6	9.6	8.8	9.2
White cell count (/mm^3)	21 960	22 630	11 100	23 330	19 320	7510
Differentials	N83L08E01M08	N82L08	N67L23M10	N93L03	N77L11E04M08	N66L18E07M09
Platelets (/mm^3)	294 000	228 000	212 000	482 000	177 000	422 000
Erythrocyte sedimentation rate (ESR) (mm/h)					65	54
C-reactive protein (mg/L)	70.925	76			46.883	2.158
Random blood sugar (RBS) (mg/dL)	112					107.2
Serum creatinine (mg/dL)	0.8	0.72	0.6	0.4	1.13	0.6
Serum urea (mg/dL)	33	27	39	30.5	48.6	20
Serum sodium (mmol/L)	145	134	132			142
Serum potassium (mmol/L)	3.9	4.3	3.2			4.1
Serum ferritin (ng/mL) (4.63-204)					21 773.5	80.9
Serum total bilirubin (mg/dL)					2.15	0.42
Serum direct bilirubin (mg/dL)					1.54	0.20
Alanine transaminase (ALT) (IU/L)	83.3	389	158	61	70.6	15.1
Aspartate transaminase (AST) (IU/L)	28.6	306	302	68	161.4	11.4
CSF analysis						
Protein (mg/dL) Sugar(mg/dL) Total count (mg/dL) Differential count Adenosine deaminase (ADA) (U/L)	220 56 540 N08L92 7.69					
Urine RE/ME Albumin 2+ RBC: 1-2/HPF WBC: 2-4/HPF Epithelial cells: 2-3/HPF						

Abbreviations: ATT, antitubercular therapy; CSF, cerebrospinal fluid; RBC, red blood cell; RE, routine examination; ME, microscopic examination; WBC, white blood cell; HPF, high power field.

an empirical basis. She was afebrile on the next day with no further episodes of altered sensorium. Her total white count and CRP improved gradually (Table 1). Her blood and urine cultures along with work-up for other infectious causes were negative. Her thyroid function test was normal. She was then discharged after 12 days of stay in the hospital with the final diagnosis of tubercular meningitis on ATT and prednisolone 60 mg for another 2 weeks to be tapered off within 1 month.

She presented again after 25 days of discharge with 1 day of fever that was documented to be 104°F and erythematous rash involving bilateral upper and lower limbs and trunk. At this time, she was on ATT and prednisolone 30 mg. Examination showed macular erythematous rashes involving bilateral upper and lower limbs and trunk. Blood investigations at that time showed anemia with neutrophilic leukocytosis and thrombocytosis with raised liver enzymes (Table 1). However, she was managed symptomatically and sent home. She did not come for follow-up for the next 35 days but was admitted again with irrelevant talking and fever after 3 months of taking ATT. Antitubercular therapy was held in view of rising liver enzymes

(Table 1). The patient was thoroughly evaluated during this admission. This time, she gave history of multiple joint pain involving bilateral knees, hands, wrists, elbows, ankles, and shoulders which had been there for 3 months. On examination she had multiple tender and swollen large and small joints bilaterally. Blood investigations again showed anemia with neutrophilic leukocytosis and raised CRP. Contrast enhanced CT of the chest and abdomen was normal. At this time in view of persistent fever, bilateral symmetrical polyarthritis, persistent neutrophilic leukocytosis, and raised inflammatory markers, AOSD was considered as a possibility. Serum ferritin was sent, which was more than 21 000 ng/mL (Table 1). She was immediately started on prednisolone 60 mg once daily and methotrexate 10 mg/week. Within the next day, she had no symptoms of joint pain, fever, or altered sensorium. She was then discharged with the final diagnosis of AOSD. On follow-up after 1 month, she had no further episodes of fever, joint pain, rash, or altered sensorium. Her white cell count, CRP, and serum ferritin were within normal limits.

Discussion

Adult-onset Still's disease is a rare auto-inflammatory disease, which is typically characterized by high-spiking fever, arthralgia (with or without synovitis), an evanescent skin rash, neutrophilic leukocytosis, and hyperferritenemia.[3] The cause of this disease is currently unknown, but interplay of various genetic and environmental factors has been implicated in causing the disease.[4] The predominant clinical features in AOSD include fever (93%-100%), arthritis (85%-100%), skin rash (58%-87%), and other manifestations like myalgia, sore throat, pleuro-pericarditis, hepatosplenomegaly, and lymphadenopathy.[3] Neurological involvement in AOSD is a rare phenomenon that most commonly presents as aseptic meningitis. In one study, neurological involvement was seen in 7.5% patients, among which 64.3% had aseptic meningitis.[3] Till now, only ten cases of aseptic meningitis have been described in the literature.[5-11] Most of the reported cases are relatively young and have neutrophilic leukocytosis in the CSF. Our patient was unique in two aspects, i.e., her age at presentation and her CSF picture. There are only a few case reports in the literature with such a late onset of the disease.[12] Our patient had lymphocytic pleocytosis in CSF, in contrast to other cases of AOSD where there is neutrophilic pleocytosis. Our patient's history of 2 weeks of symptoms with CSF showing high protein lymphocyte predominant leukocytosis was suggestive of subacute meningitis which is most commonly caused by tuberculosis (TB) in this part of the world as Nepal is considered a high-prevalence country for TB with a prevalence of 416 per 100 000 population.[13] Therefore, it is common practice to give ATT on an empirical basis to patients with such a clinical picture. The improvement in her symptoms immediately after starting ATT was most likely because of the adjuvant high-dose steroid that was given. The reoccurrence of fever after 25 days of ATT is explained by the rapid tapering of prednisolone to 30 mg. The raised liver enzymes that were assigned to ATT were again part of the clinical spectrum of the disease that got better after starting proper treatment. Our patient was extensively evaluated for other causes of fever such as infection and malignancy. Infection was less likely as there was no response to multiple antibiotics and ATT and no identifiable source of infection could be found. Contrast-enhanced computed tomography (CECT) of the chest and abdomen did not show any evidence of malignancy. She fulfilled four major and two minor criteria for AOSD and had a dramatic response to steroid with improvement in both clinical and laboratory parameters.[13,14] After 1 month of steroid and methotrexate, all of her symptoms including fever, altered sensorium, and joint pain resolved. She had complete normalization of all the laboratory markers including serum ferritin. The above clinical and laboratory picture along with a dramatic improvement with immunosuppressives corroborates the diagnosis of AOSD. Diagnosis of the disease was delayed because of age, atypical presentation, and early presumptive diagnosis of TB meningitis.

Conclusions

Adult-onset Still's disease should be suspected in all cases of meningitis that do not respond to multiple antibiotics and have a negative work-up for infection and malignancy.

Declarations

Ethical Approval and Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions

Ujjwol Risal: Conceptualization; Data curation; Resources; Supervision; Validation; Writing – original draft; Writing – review & editing.

Krishna Dhungana: Resources; Supervision; Writing – review & editing.

Mrikchhya Ghimire: Resources; Writing – review & editing.

Acknowledgements

None.

Availability of Data and Materials

Not applicable.

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