Original Research Paper

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General Medicine

A CASE REPORT OF ADULT ONSET OF STILL'S DISEASE.

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ABSTRACT Adult Onset stills disease is an autoinflammatory disorder characterized by a myriad of features like fever, arthralgias, leukocytosis, salmon colored rash and other less specific features like lymphadenopathy, sore throat and raised acute phase reactants (1). The current case report describes a 27-year-old female who presented with fever, arthralgia, sore throat, leucocytosis, lymphadenopathy. The clinical picture presented an overlap between various disorders but after exclusion of other possible diagnoses, she was diagnosed with AOSD.

KEYWORDS :

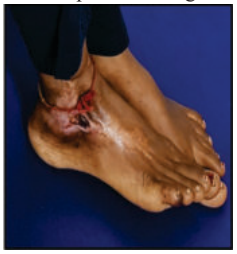
INTRODUCTION

AOSD is an autoinflammatory disorder of unknown etiology, with both genetic and environmental factors playing a possible role in its pathogenesis. The annual incidence of the disease is around 0.16 cases per 1,00,000 people making it an extremely rare autoimmune disorder (2). The disease presents with a spectrum of symptoms which mimic various other disorders like infections, malignancies, drug hypersensitivity and other rheumatologic conditions making its diagnosis difficult

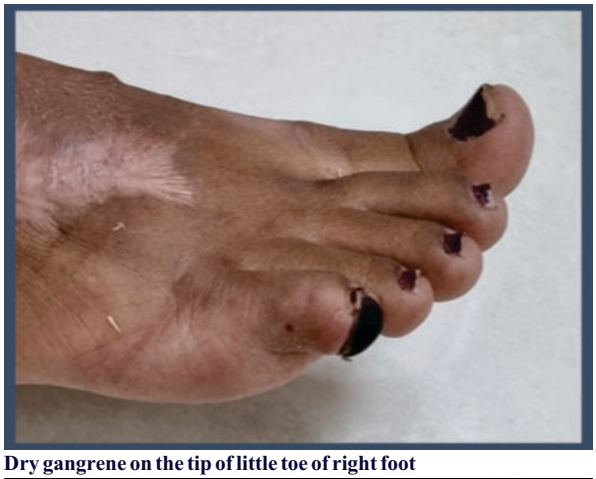
CASE STUDY

A 27-year-old unmarried female, who was a known case of hypertension for the last 3 years on irregular treatment presented to the OPD with chief complaints of fever for 10 days, which was high grade, continuous, associated with chills and rigors, sore throat, pinkish erythematous rash on left foot and pain in bilateral knees causing difficulty in walking for the last 2-3 days. Patient had similar complaints of episodes of pain in joints over the last 5 years involving bilateral knees, elbows, wrists and proximal interphalangeal joints associated with fever which resolved on taking local medication the records of which were not available. Normal mensural history

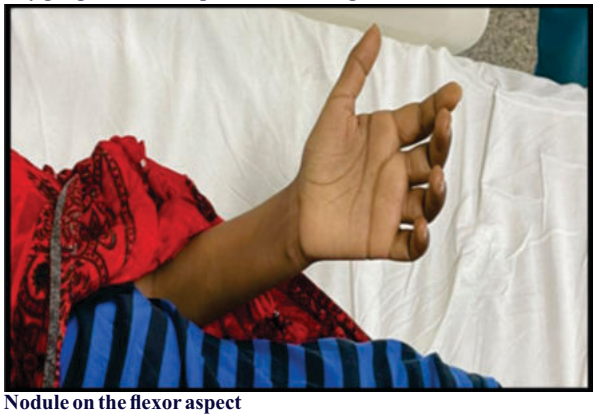
On general physical examination, the patient appeared ill, with marked pallor, right submandibular, cervical and inguinal lymphadenopathy, ulcer on lateral aspect of right foot of size 5 cm x 3cm, gangrene at the tip of little toe of the right foot and clawing of left hand. Oropharyngeal examination revealed an ulcer proliferative growth in the oropharynx.



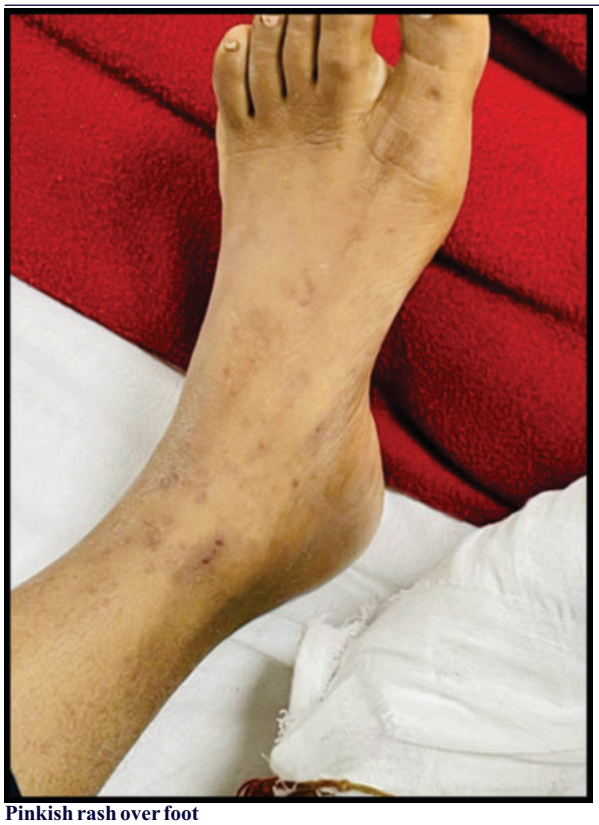
Non healing ulcer on the lateral aspect of right foot



Dry gangrene on the tip of little toe of right foot



Nodule on the flexor aspect



Pinkish rash over foot

On systemic examination, the power in the flexors, extensors, abductors and adductors of left hand was grade 3 whereas it was grade 5 in the right hand and loss of sensations in the whole of left palm could be appreciated. On musculoskeletal examination, there was tenderness of the right knee joint with minimal swelling. The rest of the systemic examination was within normal limits.

The patient was admitted and all relevant investigations were sent. Hemogram of the patient showed hemoglobin- 6.7g/dl(11-15g/dL), TLC – 20,320/c.mm with 86% neutrophils(4000-11000/uL), platelet count-6.42 lacs/c.mm. PBF showed anisocytosis with presence of microcytes exhibiting mild hypochromia, leukocytosis with mild neutrophilia and eosinophilia with abundant platelets. ESR and CRP were 63mm/hour(0-29mm/hr.) and 107 mg/L (<10 mg/L) respectively. Her liver function tests showed Bilirubin (Total) – 0.5 mg/dL (0.00-2.00), bilirubin(direct) – 0.19 mg/dL (0.00-0.20), AST – 103 IU/L(0-35 U/L), ALT – 51 U/L(0-45 U/L), ALP – 206 (153U/L) , Total protein-5.2 g/ dL(6.4-8.3 g/dL), Albumin – 2.2 g/dL(3.5-5.2 g/dL). Her Renal Function Tests showed urea – 57.4 mg/dL, Creatinine – 2.86 mg/dL(0.70-1.30 mg/dL) and serum electrolytes showed serum sodium- 134 mEq/L, serum potassium – 4.99 mEq/L, serum chloride-103.8 mEq/L. Iron studies revealed serum ferritin – 1000 ng/mL(11-307 ng/mL), serum iron – 38.56 mcg/dL(60-170 mcg/dL), TIBC- 451 mcg/dL(240-450 mcg/dL), UIBC – 412.64 mcg/dL(111-343 mcg/dL) & % Transferrin Saturation – 8.55 %(20-50%) and LDH levels of 110 U/L(105-333 IU/L). RF – 12 IU/ml (0-20 IU/L) and ANA, Anti-CCP were negative, C-ANCA, P-ANCA were negative. Thyroid function tests were within normal limits, widal test – negative, viral markers – non reactive and tests for CMV/EBV were non-reactive. Her USG abdomen showed bilateral medical renal disease and marginal resistive index in left kidney and renal artery doppler of right limb showed no evidence of thrombus and normal flow. CECT neck was done which showed oropharyngeal ulcer proliferative growth on left side involving ipsilateral posterior 1/3rd of tongue, soft palate, uvula, vallecula, faucial pillar and tonsillar fossa along with cervical lymphadenopathy. A biopsy from the oropharyngeal lesion showed acute on chronic inflammatory pathology and a wedge biopsy taken from the foot ulcer showed features consistent with a non-healing ulcer. Her 2-D echo was a normal study which ruled out bacterial endocarditis and X – ray of the right ankle showed no abnormalities. Her blood culture and urine culture were returned back sterile. NCV done revealed axonal neuropathy of left median and ulnar nerves and Fundus examination done showed Disc edema (? HTN papillopathy).

Differential Diagnosis Infections

Viral Infections

The fever, rash, arthralgias, lymphadenopathy present in this patient mimic the clinical picture of acute viral infections. However, the longstanding history of recurrence of arthralgias and fever in the past along with negative viral serologies points against the diagnosis of viral infections like hepatitis, parvo virus, HIV.

Bacterial infections

Features like fever, leukocytosis, elevated ESR and CRP favor the diagnosis of an acute bacterial infection. However, the blood cultures and urine cultures failed to establish the presence of a focus of infection and lack of other potential diagnostic clues made the diagnosis less likely.

Vasculitis

Symptoms like Fever, rash, arthralgias and lymphadenopathy favor the diagnosis of vasculitis. However negative ANA and ANCA profiles suggest otherwise.

Malignancy

A malignancy with metastasis was a probable diagnosis in this patient owing to features like recurrent fever, cervical and inguinal lymphadenopathy, severe anemia along with presence of a non-healing ulcer on the foot and an ulcer proliferative growth in the oropharynx. The biopsy results and ultrasound findings however counter the presence of any such malignant foci and make the diagnosis less likely.

Rheumatologic

Rheumatologic diseases like SLE can have similar features of rash, arthralgias, leukocytosis but are much more commonly associated with a positive ANA test. Further, the atypical pattern of rash with negative RF levels makes Rheumatoid Arthritis a less probable diagnosis.

Drug Reaction

The current spectrum of manifestations like cutaneous eruptions, leukocytosis, persistent fever can also be present in several hypersensitivity reactions occurring due to exposure to drugs. Hypersensitivity reactions are more commonly associated with eosinophilia and lymphocytosis and not with neutrophilia as was the case in our patient.

Diagnosis

The diagnosis of ASOD can be made based on the clinical manifestations meeting the Yamaguchi Criteria which requires presence of any 5 criteria with at least two major criteria being present.

Yamaguchi Criteria

Major Criteria

Fever of at least 39 degrees Celsius, intermittent, lasting one week or longer
Arthralgias or arthritis, lasting two weeks or longer
Typical rash
Leukocytosis (≥10,000), with 80% or more granulocytes.

Minor Criteria

Sore throat
Recent development of significant lymphadenopathy
Hepatomegaly or splenomegaly
Abnormal Liver enzymes, particularly aminotransferases and lactate dehydrogenase
Negative tests of ANA and RF

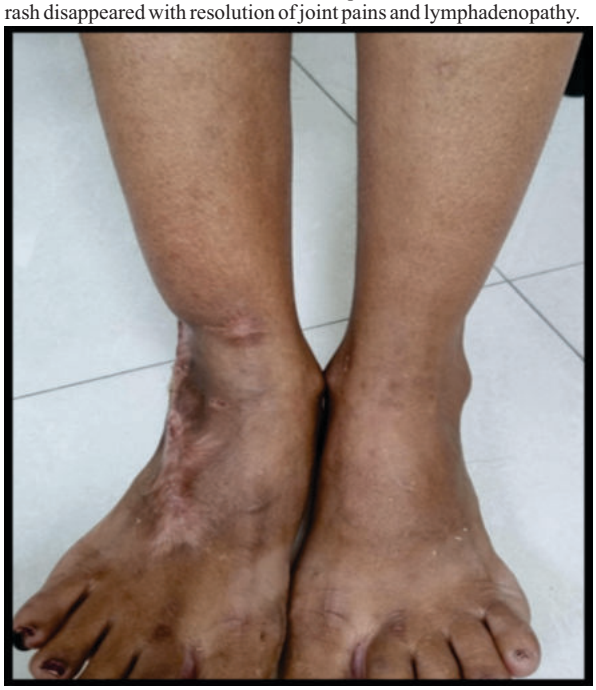
Exclusion Criteria

Infections
Malignancies
Other rheumatic diseases

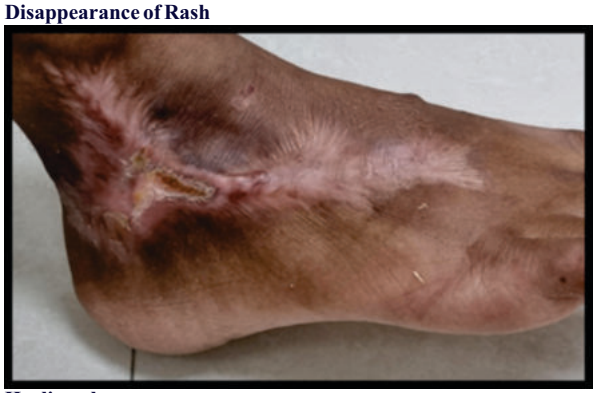
Our patient who presented with fever(> 1 week), arthralgias(>2 weeks), sore throat and lymphadenopathy was found to have leucocytosis (>10,000/cmm with 86 % granulocytes) and after exclusion of other possible diagnoses, a tentative diagnosis of Adult Onset Still's Disease was made with other co-morbidities of Hypertension with Chronic Kidney Disease with Anemia(Iron deficiency + Anemia of chronic disease). Early in the course of treatment , patient was given NSAIDs for the management of arthralgias but later after ruling out infections and malignancy, patient was started on methylprednisolone along with NSAIDs.

Follow up :

After a course of 2 months of steroids, patient's fever had subsided, rash disappeared with resolution of joint pains and lymphadenopathy.



Disappearance of Rash



Healing ulcer

Patient able to walk independently

Lipstick sign noted

DISCUSSION

ASOD is a rare autoimmune disorder that often escapes diagnosis owing to its low incidence and presentation that overlaps with a variety of other diseases.

The etiology of ASOD is largely unknown. Although, some environmental and genetic factors have been suggested to be involved, there has been no trial establishing a direct relationship between the causative factor and the disease. Factors like HLA type and some infections including Mycoplasma pneumoniae and Yersinia enterocolitica are some of the proposed agents(3,4)

The clinical features of AOSD include fever which is usually quotidian or even double quotidian and the prolonged and obscure nature of the fever can often lead to the diagnosis of PUO. Fever often precedes other symptoms like development of an evanescent salmon coloured rash that predominantly involves the trunk but can also be present on palms and soles. Arthralgias and arthritis are common during the course of evolution of symptoms and can range from mild, transient, oligoarticular joint pains to severe debilitating, polyarticular destruction of joints. Lymphadenopathy can also be present in patients of ASOD. Haematological features like leucocytosis with predominant granulocytosis and a normocytic normochromic anaemia can also be present. Other manifestations include pericarditis, pleural effusion, elevated liver enzymes and generalized abdominal pain. (4,5,6)

One of the life-threatening complications of AOSD include Reactive Hemophagocytic Lymph histiocytosis (RHL) which can occur either at the time of treatment or during the course of treatment. It is characterized by features like high fever, falling leucocyte counts, transaminitis, hypertriglyceridemia and hyperferritinemia. RHL can also be precipitated by drugs like IL -1 and IL – 6 inhibitors and is associated with high mortality. High dose steroids, cyclosporine A and cyclophosphamide are the various treatment regimens used for treatment of RHL.

Other less frequent complications of AOSD include haematological complications like DIC, cardiac complications like pericarditis, myocarditis, pulmonary complications like pleuritis, interstitial infiltrates, fulminant hepatitis and secondary amyloidosis.

The diagnosis of AOSD is mostly clinical with nonspecific biochemical and haematological abnormalities. Elevated acute phase reactants like ESR, CRP, Ferritin can be present. Haematological findings include leucocytosis ana a normocytic normochromic RBC picture.

Amongst the several diagnostic criteria proposed for ASOD, the Yamaguchi criteria has the highest sensitivity (4).

Based on the severity of the disease, different treatment options are employed. Patients presenting with a milder form of the disease with mild fever, rash, joint pains can be managed with NSAIDs (7,8). However, for more severe features like destructive arthritis, serositis, internal organ involvement, glucocorticoids can be used. In patients with signs of systemic toxicity of glucocorticoids or glucocorticoid dependence, DMARDs like Methotrexate can be added. Other glucocorticoid sparing agents that can be used for chronic management include Anti IL-1 agents like Anakinra and Anti TNF agents like Infliximab (9,10).

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