Atypical Presentation of Common disease : An Interesting Case Series and Review of literature

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Abstract: Tuberculosis is a very common disease which may present in an atypical and uncommon form. It needs careful analysis and examination , especially when there is atypical presentation like erythema nodosum. Erythema nodosum is an inflammatory disease of skin (Panniculitis)and subcutaneous tissues presenting as ill defined acute erythematous painful nodules usually on the extensor aspect of lower legs. Majority of patients are females. A careful thorough clinical and laboratory investigation in patients with erythema nodosum is required to detect a possible systemic underlying condition.

We report a case series of three patients who presented with erythema nodosum as the sole presentation of tuberculosis. Their diagnosis was confirmed on histopathological examination of skin biopsy which showed septal panniculitis and chronic dermal inflammation. All the three patients responded well to treatment with anti-tubercular drugs.

Key-words: Erythema Nodosum, Tubercular protein hypersensitivity panniculitis,nodules

Introduction:The atypical presentation of tuberculosis may be due to increased hypersensitivity reaction to tubercular protein in patients with or without active disease like phlyctenular conjunctivitis, erythema nodosum, increased dermal protein hypersensitivity, reactive polyarthritis(Poncet's disease). Occurence of more than one reaction in a single patient is very uncommon[1]. This led us to report these cases and review the concerned literature. Erythema Nodosum is a dermal inflammation and panniculitis characterised by pretibial erythematous tender nodules that occur in deep dermis and subcutaneous tissues. It is a hypersensitivity reaction and results from a variety of infections, inflammatory connective tissue disorders and certain drugs like sulphonamides, estroprogestins, amoxicillin etc and some systemic illnesses.It usually presents as tender red nodules on extensor part of shins knees or ankle. Rare causes include viral infections(HIV, EBV, Hepatitis B and C) parasitic infections like amoebiasis and giardiasis and lymphoma and other malignancies[3]. Many of the underlying causes are treatable, hence emphasizing the need to fully investigate all possible causes.Erythema Nodosum is mainly a clinical diagnosis and does not need a tissue biopsy as thorough workup and careful history usually helps to reach a diagnosis. Tuberculosis is one of the infectious causes of Erythema Nodosum but Erythema Nodosum as a sole presentation of Tuberculosis is very rare. Coexistence between Erythema Nodosum and arthritis has been described due to *Yersinia enterocolitica* and Loeffler's syndrome[4]

Case report1: A twenty year old girl was referred to us from the Dermatology Department with a diagnosis of Erythema Nodosum. She complained of painful red nodules on feet with ankle swelling and pain for last month. There was a progressive increase in the severity of pain. There were no symptoms of cough, expectoration, evening rise of temperature or weight loss. There was no history of contact of tuberculosis in the family and no history of skin rash and joint swelling in the past. She was not taking any medication before fifteen days when she consulted Dermatology OPD. She was treated with 30 mg of prednisone and 500mg of clarithromycin twice daily for fifteen days but there was little relief of her symptoms . Her ankle swelling, erythematous nodules and fatigue returned after one month. General examination did not reveal any abnormality except for bilateral ankle swelling , painful

erythematous rash on the anterior aspect of left shin and an erythematous nodule on right shin. Lab investigations were negative for Hepatitis B and C, HIV. ASO titre was normal. Renal , liver and thyroid function tests were normal. Chest radiograph was normal. Tests for autoantibodies like ANA and anti dsDNA and Rheumatoid factor were also negative. Serum Angiotensin Converting Enzyme level was normal . The Mantoux test was significantly positive .After thorough investigation no other focus of active tuberculosis was found anywhere. In the light of positive Mantoux test and reactive arthritis with Erythema Nodosum, tuberculosis was the likely diagnosis . Patient was started on anti Tuberculosis treatment and was told to come for follow up in Pulmonology OPD. At the end of the first month of treatment her ankle swelling and skin nodules subsided significantly. This case is unique because EN is the sole manifestation of tuberculosis here .

Case 2: A 30 year old woman presented to dermatology OPD with painful red nodules and swelling over both ankles for past 20 days,it was not preceded by any cough fever medication intake ,chest pain fatigue or weight loss.Examination showed tender red nodules near ankles and some excoriation of overlying skin. Her detailed workup revealed normal hematological parameters ,Mantoux test was positive (10x12mm)her chest Xray was normal and Ultrasonography abdomen was also found to be normal. She was prescribed 2 weeks course of prednisolone 1mg/kg wt with Doxycycline 100 mg twice daily with no relief in her symptoms she was referred to Pulmonology clinic for evaluation for Tuberculosis as antecedent cause of her symptoms.Patient was treated with antitubercular drugs and reviewed at 2 weeks interval her tender skin nodules subsided significantly and there was marked improvement in her malaise and fatigue ,treatment was continued for six months with full resolution of her symptoms apart from some hyperpigmentation patches on ankles.

Case 3: Our 3 patient was a 45 year old patient who came to us for complaint of tenderness over left ankle for 1 month she was taking amlodipine 10 mg per day for hypertension for last 2 years ,her detailed history and examination was within normal limit except for Mantoux test (10x11 mm),ANA level,CRP in serum as well Chest X Ray and sonogram abdomen was normal. Dermatology department started her on Antitubercular medication after thorough evaluation as latent tuberculosis was likely diagnosis in the light of her clinical presentation and laboratory investigations.Patient reported gradual subsiding of tender ankle swelling in two weeks time with improvement in her appetite as well and a feeling of general well being.

Discussion

Erythema nodosum is a skin manifestation of some systemic involvement[5]. It is a type 4 hypersensitivity reaction in response to a variety of antigens which manifests as diffuse panniculitis ,immune complex deposition in subcutaneous tissues granuloma formation which result in occurrence of tender nodules which have predilection for anterior aspect of lower extremities. . It is a hypersensitivity reaction which is commonly seen in conditions like sarcoidosis, chronic diseases like irritable bowel syndrome or it may be idiopathic.[5] It is common in young adults aged 18 to 34 years though it may occur in children and elderly as well. It usually presents as bluish red tender and nodular lesion which is poorly demarcated. Arthralgia is also commonly associated with eruption of these nodules. EN commonly shows predisposition to ankle , knee and wrist joints. There are no underlying destructive changes in the joint as seen by negative RA factor and ANA titer. It is important to rule out any history of drug intake and oral contraceptive use by female patients. Sarcoidosis and tuberculosis need to be ruled out as the possible etiology by blood investigations, computed tomography, mantoux and chest radiograph. Sometimes it may be difficult to detect the underlying disease which may result in late diagnosis as approximately 95% of individuals exposed to Mycobacterium Tuberculosis are clinically asymptomatic, while primary tuberculosis which is localised to lungs occurs in 5% of the patients. EN is a delayed hypersensitivity reaction which occurs in response to infections, autoimmune diseases or drugs , nearly 70 percent of cases are idiopathic. Tuberculosis is a common cause of EN in endemic region.[6] Thus EN is a strong predictor of tuberculosis or it may be an early symptom of primary or extrapulmonary tuberculosis in high burden countries like India. It needs careful history and examination to reach the diagnosis of the disease. It may occur even before the development of positive skin test reaction to tuberculin[7] and sometimes it may be the only manifestation of the disease in patients with strongly

positive skin tuberculin test as reported in our case series. To conclude, there is also debate whether demonstration of Mycobacterium tuberculosis infection and EN should be treated as active tuberculosis by standard anti TB regimen or it should be taken as latent tuberculosis and treated with prophylactic treatment. Our patients come from tuberculosis endemic country and had positive Mantoux test, reactive arthritis and EN and rapid resolution of symptoms with anti tuberculosis treatment.This case series also highlights the importance of careful history taking and clinical evaluation of affected individuals so as to avoid wrong diagnosis and treatment for other similar condition like cellulitis by treating physicians.

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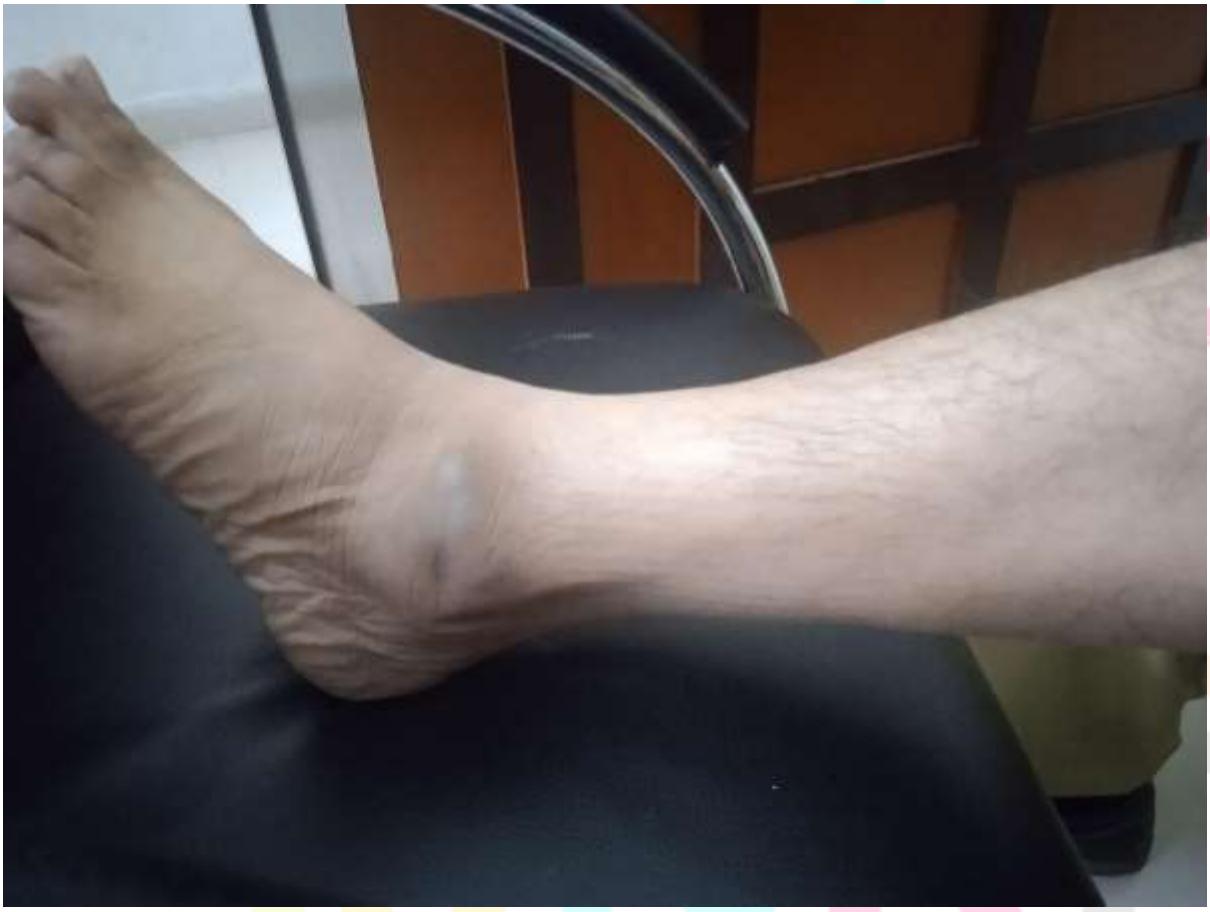

Ankle swelling and nodule in a 45 yr old female patient .