Type 2 Lepra Reaction as a Cause of Pyrexia of Unknown Origin

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Abstract

Leprosy, a commonly encountered disease, can rarely present as a reactional state de novo with fever as the main presenting feature. Here we describe an uncommon presentation of leprosy [with type 2 lepra reaction] as pyrexia of unknown origin with prominent rheumatologic manifestations [acute polyarthritis], renal involvement and generalized lymphadenopathy with rare presentation of type 2 lepra reaction without the classic skin lesions of erythema nodosum leprosum, occurring in a treatment naïve patient without prior history of leprosy.

Introduction

Pyrexia of unknown origin [PUO] can be a vexing diagnostic problem. Although varied causes like connective tissue diseases and malignancies are implicated, infections continue to account for majority of cases of PUO, more so in our country. Leprosy is a chronic infectious disease which commonly presents with skin lesions and nerve involvement. Here we report a case of unusual presentation of leprosy as PUO.

Case Report

A 48 year old farmer from rural Tamil Nadu without prior comorbidities presented to the general medicine department of our hospital with complaints of fever for 1 month duration. He also complained of having had pain and swelling of knees, ankles and elbows of both sides for 20 days and similar involvement of left wrist for 10 days before the present admission. There was no history of chest pain, breathlessness, cough, expectoration, skin rash, photosensitivity, diminution of vision and reduced urine output. Patient did not report any history of sore throat, diarrhea or genital infection preceding above complaints. Patient was evaluated in a different hospital with cultures of blood and urine, chest radiograph, haemogram and routine biochemistry being non contributory.

Patient continued to have continuous fever [101 to 103°F] during the present admission. Examination revealed a thinly built middle aged man with mild conjunctival pallor and active skin rash. He had generalized lymphadenopathy with involvement of axillary, inguinal and epitrochlear nodes of both sides. On a closer look, he was found to have multiple, subtle hypopigmented skin lesions over his face (Figure 1), arms and back [numbering more than five] with retained sensations which were overlooked easily earlier probably because of his dark complexion. Right great auricular and both ulnar nerves were palpably thickened but non tender. There was mild impairment of fine touch sensation distally over both hands and feet but tendon jerks were preserved. Testes and eyes were normal. Other systemic examination was normal.

His haemogram revealed normocytic, normochromic anaemia [Hb:8.5g/dl], neutrophilic leukocytosis [TLC: 20,200/µl with 84% polymorphs], normal platelets [2.3 lakhs/ µl] and peripheral blood smear did not show any abnormal cells. ESR was elevated [56 mm after 1st hour]. His renal function was deranged [serum creatinine: 3.9mg/dl] although he was maintaining a normal urine output. Urine microscopy did not reveal active sediments and 24 hour urine protein excretion was 300mg. Chest radiograph was normal. Cultures of blood and urine were repeatedly sterile. Echocardiography did not reveal any evidence of active carditis or infective endocarditis. HIV ELISA, HBs Ag ELISA, anti HCV antibody ELISA and ANA were negative. Antistreptolysin O[ASO] antibody titre was elevated [320 IU/l] but throat swab did not reveal Streptococcus pyogenes infection. CRP was positive.

Slit skin smears from skin lesions were positive for acid fast bacilli and bacillary index varied between 2+ to 4+ at different sites. Histopathology of skin biopsy showed shrunken epithelium with superficial dermis showing collection of lymphocytes, epithelioid histiocytes, neutrophils forming ill defined granulomas with occasional multinucleate giant cells (Figure 2). Fite’s stain revealed numerous acid fast bacilli (Figure 2). Right epitrochlear lymph node biopsy revealed ill defined aggregates of histiocytes with foamy changes resembling epithelioid histiocytes and numerous AFB were seen on Ziehl Neelsen and Fite’s staining (Figure 3). A diagnosis of multibacillary leprosy [histopathology-borderline lepromatous type as per Ridley Jopling classification] with type 2 lepra reaction was made based on these findings.

Ultrasonography of the abdomen revealed slightly reduced renal size [both kidneys :7.8 cm] with increased cortical echogenicity. Patient refused renal biopsy. He was started on oral prednisolone at a dose of 1mg/kg/day. His fever and joint pains dramatically responded to steroids and he was put on WHO recommended multidrug therapy for multibacillary leprosy [dapsone-100mg daily, clofazimine 50mg daily and 300mg monthly, rifampicin 600mg monthly] after a week of starting steroids. Prednisolone was gradually tapered over 8 weeks and multidrug therapy was continued. After 2 weeks, patient’s serum creatinine had come down to 1.9 mg/dl which has stabilized at 1.5 mg/dl at 3 months of follow up.

Discussion

Leprosy is a chronic granulomatous infectious disease involving mainly the skin and peripheral nerves caused by Mycobacterium leprae. The current prevalence in our country is 0.88/ 10,000 population. Lepra reaction can uncommonly be the presenting manifestation of leprosy and can occur
before treatment initiation as in our patient. When fever is the predominant complaint with other systemic manifestations but without obvious skin lesions or past history of leprosy, the diagnosis can be quite challenging, especially for a general physician.

Type 2 lepra reaction, also known as erythema nodosum leprosum (ENL), is an immune complex mediated hypersensitivity reaction (Gell and Coombs type III hypersensitivity) which occurs in patients with polar lepromatous or borderline lepromatous leprosy and follows initiation of leprosy treatment in majority [90% of cases] but can rarely precede or even follow completion of treatment. Type 2 lepra reaction is commonly associated with the classical skin lesions of ENL [crops of erythematous, palpable, tender, papular, nodular or plaque lesions distributed bilaterally and symmetrically, seen most commonly on face and extensor aspect of extremities]. Skin biopsy of ENL papules reveals vasculitis or panniculitis, sometimes with many lymphocytes but characteristically with polymorphonuclear leucocytes as well. Elevated levels of circulating TNF-α have been demonstrated in ENL which plays a central role in the pathogenesis of this syndrome.

Type 2 lepra reaction can be associated with fever, systemic manifestations like polyarthritis, lymphadenopathy, immune complex glomerulonephritis, epididymoorchitis and iridocyclitis. Type 2 reaction is usually precipitated by multidrug therapy for leprosy but intercurrent infections, pregnancy, trauma, surgery, physical and mental stress can also precipitate this reaction. Some patients experience recurrent bouts of this reaction during leprosy treatment. Corticosteroids [prednisolone-0.5 to 1 mg/kg/day] are the first line drugs for treatment of type 2 reactions followed by clofazimine [300mg/day] and thalidomide [400mg/day], which are useful in severe reactions not responding to steroids. Thalidomide is contraindicated in pregnancy as it is teratogenic.

Type 2 reaction without the skin lesions of ENL, as seen in our case, has been rarely reported in literature. Our patient had acute polyarthritis, generalized lymphadenopathy, renal involvement and neutrophilic leucocytosis as described in literature.

Rheumatologic manifestations like acute polyarthritis [seen in lepra reactions], chronic symmetric polyarthritis resembling rheumatoid arthritis and neuropathic arthropathy [Charcot’s joints] have been described in leprosy. Generalised lymphadenopathy and presence of M. leprae in lymph node biopsy as seen in the index case has been described by other authors in the patients of leprosy. Renal involvement in leprosy and lepra reactions has also been reported. Eighty percent of patients with type 2 lepra reaction showed renal involvement in a study and leprosy patients with reaction had a significantly higher incidence of renal involvement than those without reaction. Our patient had mild increase in 24 hour urinary protein excretion, reduced glomerular filtration rate, renal dysfunction and reduction in renal size on ultrasonography as described in literature.

The presentation with fever, acute polyarthritis, lymphadenopathy and renal involvement lead to initial diagnostic confusion and consideration of possibilities like connective tissue disease, acute leukaemia, infective endocarditis, acute rheumatic fever, reactive arthritis and systemic vasculitis before careful clinical examination revealed subtle skin lesions and thickened nerves which provided clues for further work up. There are rare case reports of leprosy presenting as pyrexia of unknown origin. This case underscores the need for general care physicians to be aware of leprosy and its varied manifestations.

To conclude leprosy can rarely present as pyrexia of unknown origin without obvious skin lesions and with prominent systemic manifestations like polyarthritis, lymphadenopathy and renal involvement, which the physicians need to be aware of.

References