Tuberculosis masquerading as polymyalgia rheumatica

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Polymyalgia rheumatica (PMR) is a connective tissue disorder of unknown aetiology. It is hypothesized that, in a genetically predisposed person, its pathogenesis is triggered by an environmental factor, possibly a hitherto unknown infectious agent. We present the case of a 68-year-old woman who is being treated for PMR. She developed tubercular lymphadenitis and erythema nodosum and improved with antitubercular treatment. We hypothesize that the trigger for pathogenesis of PMR in this lady was antigen of *Mycobacterium tuberculosis*.

Keywords:
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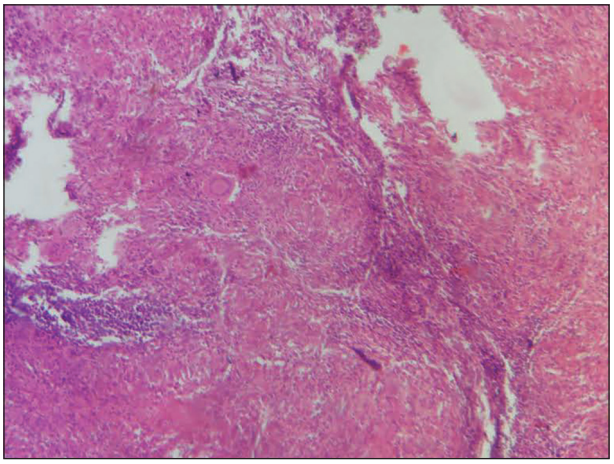
Introduction

Polymyalgia rheumatica (PMR) forms one end of the spectrum of a disorder; the other end of which is formed by temporal arteritis. The aetiology of this disease remains unknown. One hypothesis is that, in a genetically predisposed person, an environmental factor, possibly an infectious agent, causes monocyte activation to produce pathological features of this disease [1]. The following case report about a patient of PMR, who later developed tubercular lymphadenitis, strengthens this postulation.

Case report

A 68-year-old woman presented in March 2012 with complaint of pain and ache in the limbs, chiefly the limb girdle regions, for the past 6 weeks. She reported that the pain was more during night. She had no history of fever or any other systemic symptom. She was hypertensive and was taking a 5 mg tablet of amlodepine daily. Her physical examination was remarkable only for mild tenderness over the neck and shoulder girdles. Her laboratory investigations, including complete blood count, serum levels of urea, creatinine, transaminases, alkaline phosphatase, thyroid stimulating hormone and 25(OH) vitamin D were within the reference range. Her erythrocyte sedimentation rate (ESR) ranged between 60 and 72 mm. Her serum tested negative for antinuclear antibody, rheumatoid factor and anticyclic citrullinated peptide antibody. Serum protein electrophoresis did not reveal any myeloma band. With the diagnosis of PMR, oral deflazacort was administered at a dose of 15 mg daily. She reported remarkable improvement within days. She was advised to take deflazacort for subsequent 6 weeks and then taper it off. She presented in March 2013 with relapse of similar symptoms and reported that she would take deflazacort off and on, whenever she felt more pain. She had no new symptom or sign. Her ESR stood at 62 mm. Another course of daily deflazacort was administered and she improved. With relapse of pain and ache, she presented the third time in December 2013. During this visit, associated symptoms such as red, tender, nodular swelling over her right shin and Raynaud's phenomenon 'during this winter only' were reported. She reported sudden onset deviation of face to right side with slurring of speech that lasted for several hours, 1 day before presentation. Physical examination revealed a temperature of 37.8°C, cervical lymphadenopathy and erythema nodosum over her right shin. Her systemic examination was unremarkable. Her complete blood count, serum levels of glucose, urea, creatinine, transaminases, alkaline phosphatase, thyroid stimulating hormone, angiotensin converting enzyme and calcium were within the reference range. Her ESR was accelerated at 44 and 62 mm. Her serum C-reactive protein was 30 mg per litre (normal range: 0–6 mg/l). Her urine examination was normal. She tested negative for antinuclear antibody and antineutrophil cytoplasmic antibody. Chest radiography, ultrasonography of the abdomen and MRI of the brain were normal. Carotid Doppler showed normal flow pattern with no significant stenosis. Echocardiography revealed grade I diastolic dysfunction. Optic fundi showed grade II hypertensive changes in both eyes. Cervical lymph nodes were excised and biopsied. Histopathology revealed multiple epitheloid cell granulomas with Langhans type of giant cells and caseating necrosis (Fig. 1), consistent with tubercular lymphadenopathy. We administered standard antitubercular therapy with no steroids. She refused temporal artery biopsy. Over a period of weeks her body pains and aches improved along with resolution

Figure 1



Multiple epithelioid cell granulomas with a Langhans type of giant cell. Caseation necrosis is also seen.

of erythema nodosum. She was recently seen, during a routine follow-up, doing well, free of stiffness, ache and pain, and with no new cerebrovascular symptom. Patient has given her consent for publication.

Discussion

PMR is a clinical diagnosis made by the presence of typical symptoms of stiffness, aching and pain in the muscles of the hip and shoulder girdles, an increased ESR and a prompt therapeutic response to low-dose steroid [2]. The exact cause of PMR is unknown. One hypothesis is that, in a genetically predisposed person, an environmental factor, possibly an infectious agent, causes monocyte activation, which helps determine the production of cytokines that induce manifestations characteristic of PMR. Systemic macrophage and T-cell activation are characteristic of PMR. Patients often have an elevated interleukin-6 level, which is likely responsible for systemic inflammatory response in PMR. Most studies in PMR show that a decrease in the level of circulating interleukin-6 correlates with the remission of clinical symptoms. Some evidence suggests the presence of cell mediated injury to elastic lamina in blood vessels in the affected muscle groups in patients of PMR [1,3–7].

Tuberculosis (TB), a multisystem disease with myriad presentations and manifestations, is the most common cause of infectious disease-related mortality worldwide. Clinical patterns of musculoskeletal TB include spondylitis, osteomyelitis, septic arthritis and Poncet's disease. Poncet's disease is an aseptic form of insidious fever, weakness and arthritis, which occurs mostly in young adults suffering from extrapulmonary TB [8,9].

TB and PMR coexisted in our patient. We can infer following one of the three possible scenarios as reasons of this coexistence. First, two diseases involved same disease by chance. Second, patient had PMR and latent TB, which degenerated into overt TB by the use of steroids for treatment of PMR [10]. Third, the patient was having TB only and PMR arose as a part of immunological activation by tubercular antigens. As alluded to above, *Mycobacterium tuberculosis* antigen may have triggered monocyte/macrophage and T-cell activation and cytokine release in our patient to produce characteristic of PMR. This hypothesis of immunoactivation is further supported by the observation that attenuated BCG is used intradermally as an adjuvant in cancer therapy to stimulate T-cell mediated immunity [9].

As is commonly observed, PMR has a low prevalence and TB is a highly prevalent disease in our country, India. Therefore, question arises as to why the prevalence of PMR dose not parallel the prevalence of TB. This discrepancy in the magnitudes of prevalence of the two disorders questions the hypothesis of immune activation by TB antigen to produce PMR. The answer to this question is threefold. First, the symptoms of PMR could be getting masked by specific and constitutional symptoms of primary disease (i.e. TB). Second, the PMR may be getting triggered in only a small subset of patients of TB depending upon the immune status and genetic factors. Third, the diagnosis of PMR needs a high degree of suspicion and as its symptomatology mimics that of fibromyalgia and somatization, it may be underdiagnosed.

Our patient had experienced Reynaud's phenomenon for the first time in life. Although collagen vascular disease has been well described in the literature as being associated with Reynaud's phenomenon, to best of our knowledge, PMR or TB has not been. Although the transient ischaemic attack, which our patient suffered, could be ascribed to the risk factors such as chronic hypertension and old age of patient, coexistent giant cell arteritis, as a cause of transient ischaemic attack, cannot be ruled out.

This case report stimulates the need for research on whether patients with PMR should be screened for latent TB before steroid therapy and on the role of TB in the pathogenesis of PMR.

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The authors declare that manuscript has been read and approved by all the authors, that the requirements for

authorship have been met, and that each of us believe that the manuscript represents honest work.

Conflicts of interest
None declared.

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