Letters to Editor

Cutaneous tuberculosis

Sir,

We read with interest the case ‘Erythema nodosum: Atypical presentation of a common disease’ by Whig et al.\(^1\) and have the following comments to offer:

The patient described had multiple erythematous, tender, papulonodular skin lesions of 8 - 10 mm size over both legs, more on the shins. The authors have labelled them as erythema nodosum. Histopathology showed multiple epithelioid cell granulomas with Langhans giant cell reaction in subcutaneous tissue without any evidence of caseous necrosis. However, we feel that the skin lesions were actually lesions of cutaneous tuberculosis (TB). How did the authors rule out cutaneous tuberculosis in the patient? The histopathology in cutaneous tuberculosis will be exactly similar, i.e. the presence of characteristic tubercular granulomas with epithelioid cells, Langhans’ giant cells and lymphocytes.\(^2\) On the other hand, erythema nodosum represents an inflammation of the septa in the subcutaneous fat tissue: A septal panniculitis. Histopathology will show a neutrophilic infiltrate around proliferating capillaries resulting in septal thickening in early lesions that may be associated with hemorrhage. Actinic (Miescher’s) radial granulomas—small, well-defined nodular aggregates of tiny histiocytes around a central stellate cleft—are a characteristic finding. Erythema nodosum is usually not associated with vasculitis, although small vessel inflammation and hemorrhage can occur rarely.\(^3\) Lupus vulgaris is the most common clinical type of cutaneous TB in adults, and the second most common type seen in children. Clinically it can present in five different patterns: Plaque form, ulcerative and mutilating form, vegetating form, tumor like form and papular and nodular form.\(^4\) It can develop from direct inoculation, haematogenous spread, direct extension from an underlying organ or by lymphatic spread. The common sites of involvement are head and neck followed by arms and legs. The lesion is usually single and starts as a tiny reddish-brown nodule, which later becomes raised and infiltrated.\(^4\)

We feel that the patient described in the case had cutaneous tuberculosis and responded to antituberculous therapy.
Letters to Editor

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New therapeutic approach for latent tuberculosis infection

Sir,

It is estimated that about 2 billion people living with latent tuberculosis infection (LTBI) represent a vast reservoir of potential cases of tuberculosis around the world. LTBI occurs when Mycobacterium tuberculosis is able to survive in granulomas with a central necrotic core and an outermost layer of foamy macrophages (FM) that represent an important immunosuppressive barrier.

LTBI itself progress to active disease in approximately 5 to 10% of infected persons. The rate of progression is much greater in immunocompromised individuals, e.g. person with HIV infection.

Current approach for the treatment of latent tuberculosis infection

The objective of treatment for LTBI is to prevent the development of overt tuberculosis (TB) disease in infected, but asymptomatic individuals. At present, a 9-month course of daily isoniazid (INH) is recommended as first line therapy for LTBI. Alternative regimens include a shorter 6-month course of INH, which is inferior to a 9-month course, or a 4-month course of daily rifampin (RIF) or a 2-month course of RIF plus pyrazinamide (PZA).

Unmet medical needs

Isoniazid use is limited by its hepatotoxicity, poor compliance because of long duration, and in India, by the presence of high primary resistance to the drug (10%). On the other hand, the incidence of liver injury is higher among people receiving short-course (two-month) rifampin and pyrazinamide therapy for LTBI than among those receiving isoniazid.

Alternative approach for the treatment of latent tuberculosis infection

A better chemotherapeutic treatment of LTBI patients can be achieved, by administering INH for a short period of time, i.e. 4 weeks, with only 1 or 2 doses of therapeutic vaccine. The rationale of this therapy is first to take advantage of the bactericidal properties of chemotherapy to kill active growing bacilli, eliminate the outermost layer of FM and reduce local inflammatory responses. After chemotherapy, therapeutic vaccine can be inoculated to reduce the probability of regrowth of the remaining latent bacilli.

One therapeutic vaccine, currently under phase II clinical development is RUTI® (a vaccine developed in Spain). RUTI® is a therapeutic vaccine made from virulent Mycobacterium tuberculosis bacteria, grown in stressful conditions, fragmented, detoxified, heat inactivated and liposomed. RUTI® not only provides a strong humoral and cellular immune response against antigens from active growing and latent bacilli, but also against structural antigens, as it has been proved in animal models of latent tuberculosis infection and in phase I clinical trial of healthy volunteers. The preclinical experiments of RUTI® showed the induction of a mixed Th1/Th2/Th3, polyantigenic response with no local or systemic toxicity.

The vaccine has been designed to be used against LTBI as a therapeutic vaccine after 1-month of chemotherapeutic treatment, instead of the current treatment based on 6-9 months of chemotherapy.

The therapeutic vaccine for LTBI can help in developing shorter and/or more intermittently administered regimens that are easier to supervise and that are active against multidrug-resistant latent TB infection (MDR-LTBI). Thus, it can help in counteracting the hepatotoxicity, poor compliance and high resistance associated with other longer regimens commonly used in India for treating LTBI. This might be very helpful in Indian context as the prevalence rates of LTBI in India ranges from 9-80% in various populations.

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