CASE REPORT

Post BCG vaccination Lupus vulgaris: A case report

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ABSTRACT
Cutaneous tuberculosis is a rare skin disorder caused by Mycobacterium tuberculosis, Mycobacterium bovis, and the Bacille Calmette-Guérin vaccine. Cutaneous tuberculosis can be acquired exogenously or endogenously and presents with different clinical features. Diagnosis of these lesions can be difficult, as they resemble various other skin diseases. Lupus Vulgaris can occur at the site of BCG vaccine. We report a 6 years old female child with lupus vulgaris at the site of vaccination with BCG.

CASE REPORT
A 6 years old female patient presented with asymptomatic lesion on left shoulder at the site of BCG vaccination. The condition started as small nodule one month after BCG vaccination. The lesion enlarged very slowly over 6 years duration. The patient had no fever or fatigue. The patient reported the skin lesion had progressively increased over the past 4 months. She had been previously diagnosed as a case of eczema and was treated with multiple topical therapies, including emollients and potent topical corticosteroids without any relief. Cutaneous examination showed solitary scaly erythematous plaque lesion with irregular reddish brownish border (Fig. 1). No other skin lesions with same features were observed at any other site. Family history of the same condition was negative. No history of cough or bloody sputum. On physical examination, vital signs were within normal limits. The patient had no lymphadenopathy. Routine investigations including CBC, liver and renal profiles, thyroid profile were within normal limits. A skin biopsy from a representative lesion showed multiple nodular tuberculoid granulomas formed of lymphocytes, histiocytes and giant cells. These granulomas were situated in upper, mid dermis and extending to dermoepidermal junction. Also, there was mild band dermal granulomatous

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Fig. 2 Multiple nodular granulomas in upper and middle dermis extending to dermoepidermal junction.

Fig. 3 Tuberculoid granuloma formed of epithelioid histiocytes, giant cells and lymphocytes.

DISCUSSION

Cutaneous Tuberculosis (CTB) is a rare skin disorder all over the world, although it is still an important infective disorder in India and parts of Africa. The epidemic of HIV/AIDS in parts of Africa has been followed by an epidemic of tuberculosis in its wake. It has been estimated that nearly eight million new cases of tuberculosis occur in the world each year. Cutaneous tuberculosis is a relatively rare manifestation of tuberculosis accounting for only 0.14% of all reported cases. With the eradication of tuberculosis in cattle, human infections with *Mycobacterium bovis* are rarely seen these days. Accordingly, cutaneous tuberculosis can be categorized into two major etiological groups: infections caused by *Mycobacterium tuberculosis*, and those caused by non-tuberculous (atypical) mycobacteria. Infections by non-tuberculous mycobacteria will be considered separately. In some of the so-called ‘developed countries’, such infections are more numerous than those caused by *M. tuberculosis*.

Not all people exposed to *M. tuberculosis* become infected. There is a complex interaction between the organism, the environment, and the host. Corticosteroids may upset this balance leading to the reactivation of non-active disease. The increasing use of biological therapies for the treatment of inflammatory skin diseases, particularly psoriasis, has also led to an increase in tuberculosis. Genetic susceptibility to *Mycobacterium tuberculosis* (OMIM 607948) involves many genes. One such gene maps to chromosome 2q35, which includes the NRAMP1 gene (natural resistance-associated macrophage protein 1), and the
MTBS1 gene. Another TB susceptibility locus is found at chromosome 8q12-q13. X-linked susceptibility has also been proposed. Patients with hypomorphic mutations of the nuclear factor κB essential modulator gene may also have increased susceptibility to mycobacterial disease. A review on the genetically determined susceptibility to mycobacterial infection. The review discussed in detail the genetic abnormalities in the interleukin 12 (IL-12) dependent, high output interferon-γ (IFN-γ) pathway that results in increased susceptibility to infection. Early classification of CTB was based on lesion morphology. As knowledge of the disease increased, it became apparent that although lesions appeared clinically similar, their development, progression, and prognosis were different. Tappeiner and Wolff proposed the most widely accepted classification based on the route of infection. Exogenous inoculation occurs after the direct inoculation of Mycobacterium tuberculosis into the skin of a person who is susceptible to infection. This leads to TVC, tuberculosis chancre, and some cases of LV. Endogenous infection occurs in patients who were previously infected either by lymphatic spread, hematogenous spread, or contiguous extension. Lymphatic spread is seen occasionally in LV. Hematogenous spread is seen in acute miliary TB, metastatic TB abscess (gummatous TB), papulonecrotic tuberculid (PNT), and LV. Contiguous extension is seen in scrofuloderma and orificial tuberculosis. An additional classification system designed to enhance the Tappeiner and Wolff system included further distinction based on bacterial load. This system is extremely similar to Ridley and Jopling’s description of Mycobacterium leprae in Hansen’s disease. In the multibacillary forms, a plethora of mycobacteria can easily be identified on histological examination utilizing the Ziehl-Neelsen staining (AFB) method and culture. In the paucibacillary forms, sparse bacilli are seen on histological examination and culture isolation of mycobacteria is the exception rather than the rule. Lupus vulgaris is the most common form of reinfection tuberculosis, occurring predominantly in young adults. There is one report of its occurrence in siblings. It is caused almost exclusively by M. tuberculosis although rare reports implicating the M. avium-intracellulare complex, M. fortuitum, and M. bovis have been published. It has followed BCG vaccination, and also tattoo inoculation. Lupus vulgaris affects primarily the head and neck region, although in Southeast Asia it appears to be more common on the extremities and buttocks. Penile involvement can occur. Lesions involving the nose and face can be destructive. Alopecia often develops in lesions of the scalp. The usual picture is of multiple erythematous papules forming a plaque, which on diascopy shows small ‘apple jelly’ nodules. Our patient presented with lupus vulgaris at site of BCG vaccination and the lesion was positive with diascopy. Crusted ulcers, local cellulitis sporotrichoid lesions, ‘turkey-ear’ lesions, and dry verrucous plaques are sometimes seen. It may develop within a scar, or following tattooing. The disease runs a chronic course and may result in significant scarring. Late complications include the development of contractures, lymphedema, squamous carcinoma and, rarely, basal cell carcinoma, malignant melanoma, and cutaneous
lymphomas.\textsuperscript{13-16}

In lupus vulgaris there are tuberculoid granulomas with a variable mantle of lymphocytes in the upper and mid dermis. The granulomas have a tendency to confluence.\textsuperscript{17} Rarely they have a perifollicular arrangement. Caseation is sometimes present. If prominent caseation is present in a facial lesion, granulomatous rosacea also needs consideration. Multinucleate giant cells are not always numerous. Langerhans cells are present in moderate numbers in the granulomas. The overlying epidermis may be atrophic or hyperplastic, but only rarely is there pseudoepitheliomatous hyperplasia.\textsuperscript{18,19} Transepidermal elimination of granulomas through a hyperplastic epidermis is rarely seen. Bacilli are usually sparse and difficult to demonstrate in sections stained to show acid-fast organisms.\textsuperscript{20} They can now be demonstrated using PCR.

In one report, Michaelis-Gutmann bodies were present in macrophages in the infiltrate.\textsuperscript{21} Variable fibrosis accompanies the lesions. Effective antituberculous therapy leads to a substantial reduction of fibrosis. Sometimes the histological appearances resemble sarcoidosis, with only a relatively sparse lymphocytic mantle around the granulomas: a consequent delay in making the correct diagnosis is common in such cases. An atypical CD30+ lymphoid infiltrate has also been described. The infiltrate was eventually regarded as being of reactive type.

Diagnosis of CTB is complicated and requires a full work-up, including a detailed history and physical examination; careful consideration of clinical presentation; TST; serum QFT-G (and possibly other laboratory testing); skin biopsy with histological analysis and special staining methods for identification of AFB; and the use of other diagnostic tests, such as chest x-ray and sputum culture.\textsuperscript{22-26} The QFT-G is an in-vitro diagnostic aid that measures a component of cell-mediated immunity to \textit{Mycobacterium tuberculosis} and is based on the quantification of interferon-gamma released from sensitized lymphocyte. QFT-G was approved in 2005 by the US Food and Drug Administration for the diagnosis of both latent and active TB infections. The antigens used in QFT-G are not shared by BCG vaccine strain or by nontuberculous mycobacterium. According to the Centers for Disease Control and Prevention guidelines of 2005, QFT-G can be used in place of the TST as it has increased specificity, lack of cross-reactivity to BCG, and convenience for both patient and provider.\textsuperscript{27} Concordance rates between TST and QFT-G range from 60 to 90 percent. The cost effectiveness of QFT-G test still needs to be studied. Mycobacterial culture remains the most reliable method to determine the presence of mycobacteria and their sensitivities, but the yield is often low and often takes many weeks. Culture sensitivity is much lower than specificity, with sources ranging from 80 to 85 percent and 98.5 percent, respectively.\textsuperscript{28} Mycobacterial growth is better on an egg-based medium, but quicker on agar medium. Liquid systems allow for rapid growth (1-3 weeks), while growth on solid media can take from 3 to 8 weeks. Two cases of EIB have been confirmed using guinea pig inoculation.\textsuperscript{29} An AFB smear is useful if lesions have a high bacterial load as seen in LS, miliary TB, and TB gumma. With the advent of polymerase chain reaction (PCR), even the smallest tissue sample can be analyzed and amplified for mycobacterial DNA sequences, confirming its presence. In the future, it is believed...
that PCR will become more advanced to detect *Mycobacterium tuberculosis* in all lesions.\(^{30}\) Currently, PCR appears to be the most useful in multibacillary forms of CTB. In one report of AFB-negative specimens, the overall sensitivity of PCR was found to be 50 to 72 percent. Another source reported AFB-positive respiratory specimens to have a sensitivity and specificity of 95 and 98 percent, respectively. In a comparison study of PCR and standard culture technique in pulmonary TB, one group found the positive rate of PCR was 82 percent compared to 16 percent in standard culture. A study detected *Mycobacterium tuberculosis* DNA in 77 percent of cases of various types of CTB. Although PCR has shown to have high specificity and good positive predictive value, it seems to work best as a confirmatory test in patients with a high pre-test probability. In multibacillary CTB, PCR has the highest likelihood of yield. Nonetheless, a combination of diagnostic tests is needed when a case of CTB is suspected to confirm a diagnosis.\(^{31}\) In developing countries, PCR is not always readily available and therefore physicians must rely on a positive response to anti-TB drugs to confirm difficult cases. It is essential to search for extracutaneous foci of TB by urine, blood, and sputum samples; x-ray or CT scan of the chest; and bone scans.\(^{32}\) The treatment of cutaneous tuberculosis usually involves the concurrent use of four drugs - isoniazid, rifampicin, pyrazinamide, and either ethambutol or streptomycin for a period of 8 weeks. This quadruple therapy is followed by a 16-week course of isoniazid and rifampicin.\(^{33}\) Our patient was treated with quadruple protocol with good result and follow up for one year did not reveal recurrence.

Variations in schedules of treatment of TB have been used successfully. Pyridoxine may be added to this protocol to prevent the neurotoxicity of isoniazid. Drug-resistant strains are becoming more frequent. Drug-resistant tuberculosis is defined as disease resistant to the first-line drugs rifampicin and isoniazid ± resistance to other drugs. In India, organism resistance to isoniazid varies from 13 to 45%, and for streptomycin it is 3-12%. In such cases, the treatment can be changed to ethambutol, ofloxacin, and thioacetazone. Because there is sometimes difficulty in making and/or confirming the diagnosis of cutaneous tuberculosis, a therapeutic trial of antituberculous therapy is sometimes commenced. It is generally thought that 6 weeks of therapy with three or four antituberculous drugs is adequate to prove or disprove the diagnosis.\(^{33}\)

**REFERENCES**

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