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War wounds and warty tuberculosis: a case report of multifocal tuberculosis verrucosa cutis

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ABSTRACT:

— ***Background:*** Tuberculosis (TB) remains a significant health issue globally, particularly in developing countries. Cutaneous tuberculosis is uncommon and accounts for only 1-2% of extrapulmonary cases. Tuberculosis verrucosa cutis (TBVC) is the most common form of exogenous cutaneous TB, which occurs in previously sensitized individuals by direct inoculation of mycobacteria. Multifocal TBVC is extremely rare and is a diagnostic challenge itself. To the best of our knowledge, only four cases of multifocal TBVC involving anatomically distant sites have been reported in immunocompetent individuals.

— ***Case Report:*** We report a case of multifocal TBVC in a 29-year-old healthy male armed forces personnel. Initially misdiagnosed as *verruca vulgaris*, he presented to our center with recurrence in the form of multiple warty lesions on the left ankle, right ear, and back. Histopathological examination revealed granulomatous inflammation, consistent with TBVC. Despite negative Ziehl-Neelsen staining and PCR for *Mycobacterium tuberculosis*, a positive Interferon Gamma Release Assay (IGRA) supported the diagnosis.

— ***Conclusions:*** This case highlights the complexities of diagnosing multifocal TBVC, particularly in immunocompetent individuals. The lesions showed a significant response within three months of starting anti-tubercular therapy, underscoring the necessity for a high index of suspicion and the critical role of histopathology. Multifocal cutaneous TB is rare, and this article emphasizes the importance of awareness among clinicians to avoid misdiagnosis.

— ***Keywords:*** Cutaneous tuberculosis, Tuberculosis verrucosa cutis, Multifocal, Infectious diseases, *Mycobacterium tuberculosis*, Polymerase chain reaction.

INTRODUCTION

Tuberculosis is a major health problem in developing countries and is the ninth leading cause of death worldwide[1]. Cutaneous tuberculosis (TB) is uncommon and accounts for only 1-2% of the extrapulmonary tuberculosis[2]. The incidence of cutaneous tuberculosis in India has decreased from 2% to 0.15% and remains rare in developed countries[3]. Cutaneous TB is caused by skin infiltration of the pathogenic bacilli, *Mycobacterium tuberculosis*, either directly through external injury (exogenous cutaneous TB) or acquired from hematogenous or lymphatic dissemination of bacilli from an internal infectious focus like pulmonary TB (endogenous cutaneous TB). Depending on host immunity and the mode of pathogen inoculation, it can present with a wide spectrum of clinical manifestations. This encompasses tuberculosis verrucosa cutis and lupus vulgaris at one end of the clinical spectrum, with good host immunity and tuberculous chancre, scrofuloderma, orificial tuberculosis, tuberculous gumma, and miliary TB at the declining end of cell-mediated immunity[4]. Tuberculosis verrucosa cutis (TBVC) is the most common form of exogenous

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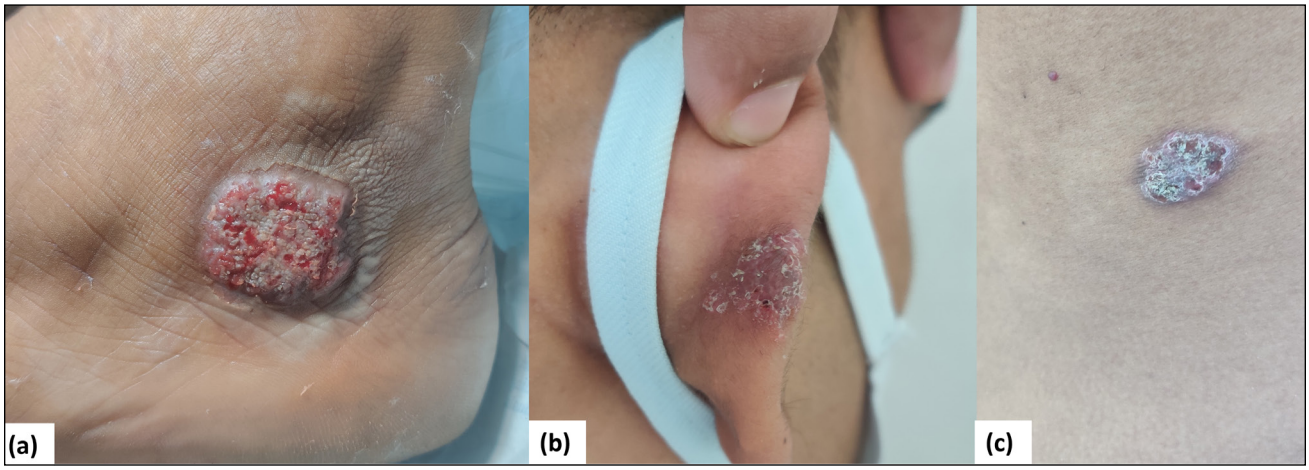

Figure 1. Well-defined verrucous plaques over the lateral aspect of the left ankle (**a**), the posterolateral aspect of the right ear helix (**b**), and the mid back (**c**).

tuberculosis, which occurs in previously sensitized individuals by direct inoculation of mycobacteria[4]. It typically presents as a solitary verrucous lesion in a single anatomical location. However, varied presentations like multifocal TBVC and the rarity of the disease make the clinical diagnosis challenging. Hereby, we present a case of multifocal TBVC in a young male patient with no other apparent infectious focus, who presented with multiple verrucous growths.

CASE PRESENTATION

A 29-year-old healthy male, an armed forces personnel, with no known comorbidities, presented to the dermatology outpatient department with complaints of dark-colored, raised, cauliflower-like growth over the outer aspect of the left ankle, which gradually increased in size over 1 year. He was initially diagnosed clinically, dermoscopically, and histopathologically as a case of *verruca vulgaris* in another dermatology center. He was treated with a single dose of 0.1 mL/cm^2 of intralesional bleomycin, 1 IU/mL. According to the patient, 50% of the lesions resolved post-injection. However, he developed similar lesions on the back and right ear after 4 months of initial presentation and was evaluated in detail for these at our center. There was no history of associated itching, discharge, or trauma before the onset of the lesion, weight loss, evening rise of temperature, cough, hemoptysis, or breathlessness. His general examination and systemic examination were unremarkable, with no lymphadenopathy. A Bacille Calmette-Guerin (BCG) scar was visible on the left deltoid, indicating the vaccination he received at birth. Dermatological examination revealed multiple discrete, well-defined verrucous plaques over the lateral aspect of the left ankle, the left side of the middle back and the posterolateral aspect of the right ear helix, ranging in size from 1 cm x 1 cm (right ear) to 3.5 cms x 4 cms (left ankle) (Figure 1). The base of the lesions was not fixed to the underlying structures. Dermoscopy of the verrucous lesion revealed multiple thrombosed vessels with a few dotted vessels and yellowish-white scales (Figure 2).

Biopsy of the lesion from the mid back revealed orthokeratosis, acanthosis, and papillomatosis in the epidermis. The mid-dermis showed multiple, discrete, well-formed granulomas comprising epitheloid cells and multinucleated giant cells, with a peripheral cuff of lymphocytes. The superficial dermis showed intense mixed inflammatory infiltrate comprising lymphocytes, plasma cells, and occasional eosinophils, along with focal suprapapillary thinning. No features were suggestive of malignancy (Figure 3). No acid-fast bacilli or fungal elements were seen on the Ziehl-Neelson (ZN) stain and Periodic acid Schiff (PAS) stain, respectively. Cultures for mycobacteria and fungi showed no growth after six weeks. Interferon Gamma Release Assay [IGRA, QuantiFER-

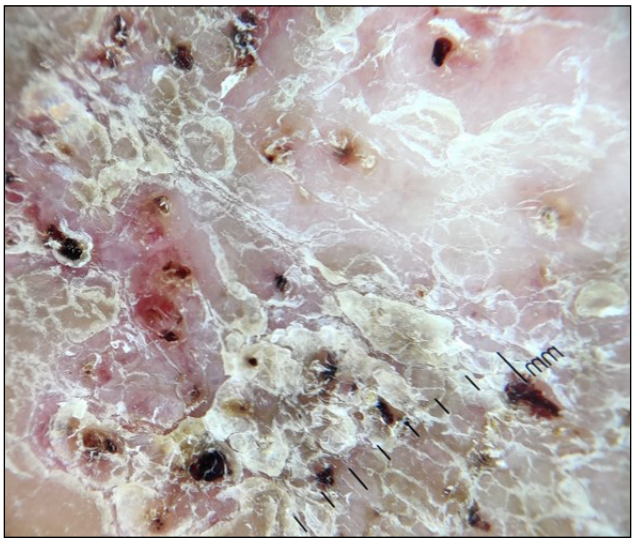

Figure 2. Dermoscopy of a verrucous lesion showing multiple thrombosed vessels with a few dotted vessels and yellowish-white scales.

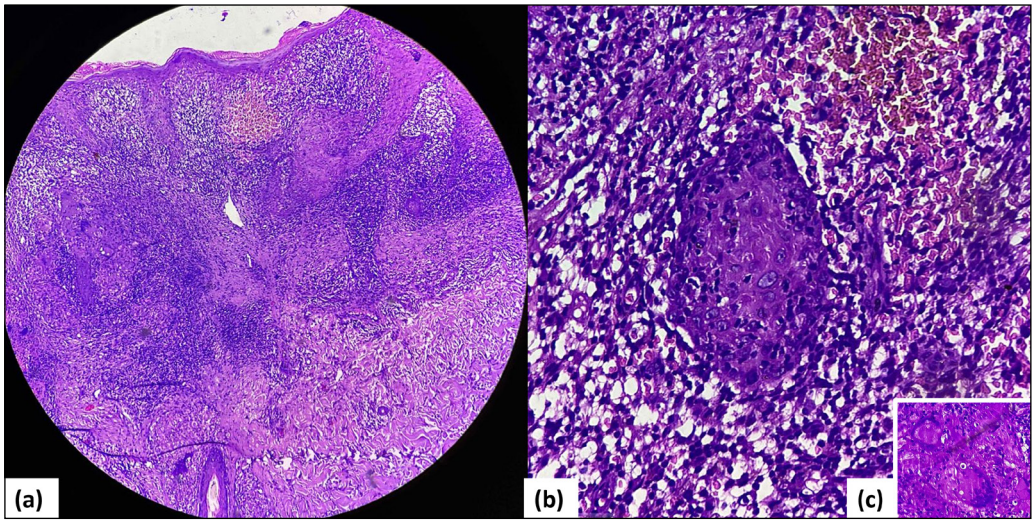

Figure 3. a, H&E (40X): Histopathology of the lesion revealed orthokeratosis, acanthosis and papillomatosis in the epidermis, and granulomatous infiltration in mid dermis, (**b**), H&E (100X): well-formed granuloma in dermis consisting of epitheloid cells and multinucleated giant cells with intense mixed inflammatory infiltrate comprising of lymphocytes, plasma cells, and occasional eosinophils, (**c**), H&E (400X): insert showing multinucleated giant cell.

ON® (QIAGEN Group) -TB Gold Plus Hilden, North Rhine-Westphalia, Germany] performed at the previous dermatology center was positive; however, the details were not available. In view of the above, the Mantoux test with an intradermal injection of 0.1 mL of purified protein derivative was performed, and it revealed induration of 10 mm. Hematological and radiological investigations were within normal limits. *Mycobacterium TB* polymerase chain reaction (PCR) of the lesional biopsy was negative.

He was clinically, immunologically, and histopathologically diagnosed as a case of multifiocal tuberculosis verrucosa cutis and was started on oral anti-tubercular drugs consisting of an intensive phase of 2 months of daily isoniazid (300 mg), rifampicin (600 mg), pyrazinamide (1,500 mg), and ethambutol (1,200 mg) followed by a continuous phase of 4 months of daily isoniazid (300 mg), rifampicin (600 mg) and ethambutol (1,200 mg). He tolerated therapy well, and his lesions began to resolve within 3 months of treatment (Figure 4).

DISCUSSION

Cutaneous tuberculosis is a major problem worldwide, with an increasing trend due to the emergence of HIV and increasing use of immunosuppressive agents. Tuberculosis verrucosa cutis is caused by the exogenous inoculation of *Mycobacterium* in a previously sensitized host. It is known by various names such as warty tuberculosis, anatomist's warts, prosector's wart, anatomic tubercle, *verruca necrogenica*, *lupus verrucosus*, etc[5]. It commonly presents as a slowly growing, painless, warty lesion and is seen among high-risk professionals, such as healthcare and laboratory workers. The common sites involved are trauma-prone sites such as the extremities and buttocks. In endemic countries, it is found in barefoot walkers and the buttocks of children post-exposure to soil contaminated with the microbe[5].

The diagnosis of TBVC is challenging owing to the wide range of clinical presentation as well as the rarity of the disease. An Indian study con-

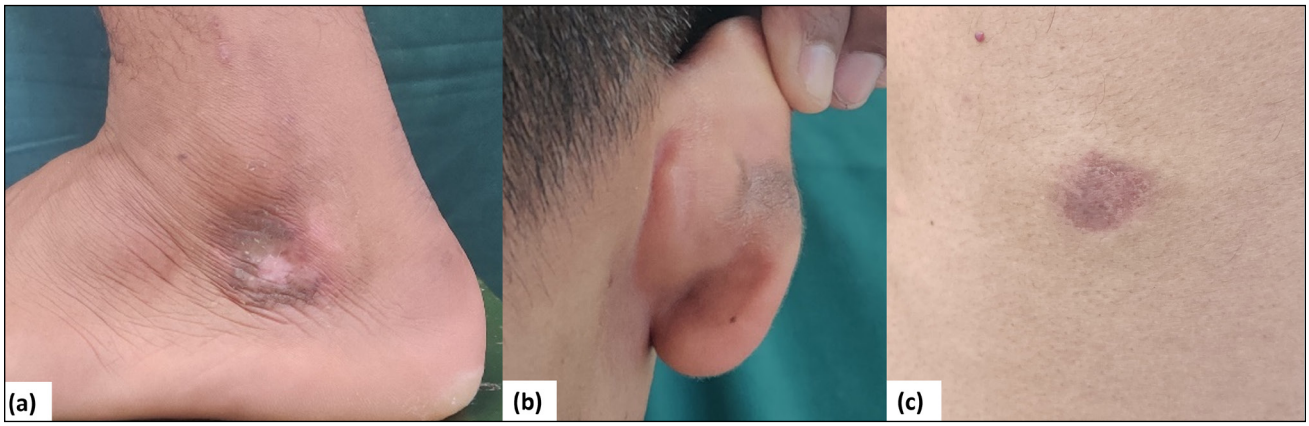

Figure 4. Resolving lesion over left ankle (**a**), right ear helix (**b**), and mid back (**c**) three months post anti-tubercular therapy.

ducted by Puri[6] showed that TBVC constitutes 5% of the cutaneous TB. Various atypical presentations of TBVC, such as exudative forms, deeply destructive papillomatous and sclerotic forms, exuberant granulomatous forms, and even multifocal TBVC, have been reported in the literature[7]. The histology of the lesion is characteristic of pseudoepitheliomatous hyperplasia, hyperkeratosis, and acanthosis of the epidermis, along with a mixed lymphohistiocytic infiltrate with occasional neutrophils. The mid-dermis or upper dermis shows tuberculoid granulomas with caseous necrosis[8]. A wide range of differential diagnoses should be considered for such a clinical presentation, including deep fungal infections like chromomycosis, fixed sporotrichosis and blastomycosis, atypical mycobacterial infection, and verrucous carcinoma[6,8]. Most of these conditions can be ruled out with appropriate microbiological tests such as culture, microscopy, and histological examination[9]. The use of PCR in the diagnosis of cutaneous tuberculosis should account for the differential sensitivities associated with different clinical types. Tan et al[10] found that the PCR positivity rate for paucibacillary cutaneous TB, like TBVC, was 55%, whereas it was 100% sensitive and specific in immunocompromised patients with multibacillary infections. As in our case, ZN stain, culture, and PCR are usually negative in TBVC, given the paucibacillary status and good host immunity. The initial diagnosis of *verruca vulgaris* for the solitary lesion was probably made based on the above, and the response to bleomycin injection can be explained by tissue necrosis caused by this agent. However, the recurrence suggested that the pathology caused by the *Mycobacterium* was not addressed.

The biopsy of the new lesion was undertaken in our center, and the histopathology showed the classical picture, and the previous positive IGRA correlated with the possibility of mycobacterial infection. The lesions resolved with anti-tubercular therapy, which itself supported the diagnosis[11]. Response to anti-tubercular treatment is usually seen within three to six months[8].

CONCLUSIONS

Multifocal cutaneous tuberculosis without any additional tubercular foci is extremely rare. To the best of our knowledge, only four cases of multifocal TBVC involving anatomically distant sites have been reported in immunocompetent individuals. Interestingly, our patient is an armed forces personnel without any apparent inoculation site. However, he was undergoing rigorous physical training, which can be considered responsible for the cutaneous inoculation of the pathogen at various sites of his body, such as the ear and trunk, through multiple unnoticed microtraumas, unlike the extremities, which are commonly involved in TBVC. Hence, this case is unique in being multifocal and emphasizes the importance of a high index of clinical suspicion, histopathology, and anti-tubercular therapy as an adjunct diagnostic tool for the timely management of this rare entity, which can be easily missed even in endemic countries.

Informed Consent:
Written informed consent was provided by the patient for permission to receive therapy and to publish this case report.

Ethics Approval:
Not applicable due to the design of the study.

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Authors' Contributions:
Dr. Padmapriya Srinivasan conceptualized the case report, Dr. Veena Kharayat analyzed it, and Dr. Jeeva John designed and drafted the manuscript. All listed authors contributed substantially to the data collection, result interpretation, manuscript editing, and approval of the final manuscript.

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Conflict of Interest:
The authors declare no conflict of interest.

Data Availability:
The patient records and related data are available from the corresponding author upon reasonable request.

AI Disclosure:
The authors utilized ChatGPT during the preparation of this work to improve grammatical accuracy. Following the use of this tool/service, the authors reviewed and edited the content as necessary and assumed full responsibility for the final publication.

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