Case Report

# A Rare Case of Multidrug-Resistant Lupus Vulgaris with a Mixed Pattern of Resistance – A Long Journey to Diagnosis and Treatment

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## Abstract

An 18-year-old male presented with a single round to oval well-defined irregular erythematous plaque 10 cm × 6 cm, with a verrucous surface, central atrophy, and crusting at the periphery on the right knee of one-year duration. The patient had received ATT (anti-tubercular treatment) twice in the past without any improvement. MGIT (mycobacteria growth indicator tube) and CBNAAT (Cartridge-based nucleic acid amplification test) were performed, and drug sensitivity testing was done, which led to a diagnosis of multidrug resistance (MDR) with a mixed pattern. The management of cutaneous tuberculosis (TB) is becoming difficult due to an increase in resistance to category-I ATT. Patients harboring MDR and extensively drug-resistant (XDR) strains present a fearsome challenge for the clinician. A cure is possible with early identification of resistance and the use of an appropriate regimen.

**Keywords:** *Lupus vulgaris, mixed pattern, multidrug resistance*

## Introduction

Cutaneous tuberculosis constitutes about 1.5% of extra-pulmonary tuberculosis.[1] It can manifest as lupus vulgaris, tuberculosis verrucosa cutis (TBVC), scrofuloderma, tuberculous gumma, tuberculous chancre, miliary tuberculosis, papulonecrotic tuberculid, and lichen scrofulosorum. Scrofuloderma (SFD) is the most common cutaneous variant, followed by lupus vulgaris (LV) and tuberculosis verrucosa cutis (TBVC). The diagnosis of cutaneous tuberculosis relies mainly on histopathology, culture on Lowenstein Jensen (LJ) medium, or radiometric BACTEC (Becton Dickinson and company) 460 TB culture system and polymerase chain reaction (PCR). Drug-resistant tuberculosis (TB) is a very well-known scenario within the practice of pulmonary medicine; however, the same is not encountered in cases of cutaneous tuberculosis. This could be attributed to a lower prevalence of cutaneous TB and delayed diagnosis of drug resistance. Hence very few cases of drug-resistant cutaneous TB have been reported.

## Case Report

An 18-year-old male presented with a gradually progressing ulcerated lesion on the right knee of one-year duration with occasional itching and scanty foul-smelling yellowish discharge [Figure 1]. There was no history of fever, cough, weight loss, or contact with any known patient of tuberculosis. A biopsy was performed, and anti-tubercular treatment (ATT) was prescribed, which the patient stopped after four months as there was no improvement. Another physician prescribed rifampicin 450 mg for three months, which reduced the pus discharge but not the lesion size. Then, the patient presented to us with a single round to oval well-defined irregular erythematous plaque 10 × 6 cm, showing a verrucous surface with erosions and crusting at the periphery on the right knee without any regional lymphadenopathy or sinuses. We considered the differential diagnoses of lupus vulgaris and chromoblastomycosis. Routine hematological and biochemical investigations revealed no abnormality, but the Mantoux test was positive (24 × 20 mm), and the chest X-ray was suggestive of bronchiolitis. Biopsy showed irregular epidermal hyperplasia with lichenoid infiltrate (40x), and the dermis showed well-formed granuloma with plasma cells and a few giant cells (400x) [Figure 2a and b]. Periodic acid



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Schiff (PAS) stain, Grocott's methenamine silver (GMS) stain, and tissue culture for fungal, bacterial, and acid-fast bacillus (AFB) were all negative. The diagnosis of lupus vulgaris was considered based on histopathological findings. Category II ATT was prescribed, which the patient stopped after eight months as there was only a mild improvement.

As the patient had been taking ATT in the past with little improvement, we sent TB and atypical mycobacterial culture for mycobacteria growth indicator tube (MGIT) and Cartridge-based nucleic acid amplification test (CBNAAT). In the culture report for CBNAAT, MTB (Mycobacterium Tuberculosis) was negative, but in MGIT, MTB complex was identified. TB line probe assay (LPA) for 1st and 2nd line drugs, i.e., drug sensitivity testing (DST), was performed, which showed resistance to rifampicin, isoniazid, ofloxacin, pyrazinamide, moxifloxacin (lower concentration), and ethionamide with sensitivity to kanamycin, linezolid, ethambutol, moxifloxacin (higher concentration), clofazimine, PAS, amikacin, and capreomycin. Our patient had multidrug-resistant lupus vulgaris with a mixed pattern of resistance. All the routine investigations were within normal limits. According to DST, weight band - inj. kanamycin 750 mg I.M., tab. cycloserine 750 mg, tab. moxifloxacin 800 mg, tab. linezolid 600 mg, cap. clofazimine 100 mg, tab. PAS 16 gms, and tab. pyridoxine 100 mg were prescribed daily for eight months in the intensive phase, following which, inj. kanamycin was stopped, and all other drugs continued. The patient had almost complete resolution of the lesion at four months, leaving a depigmented atrophic scar [Figure 3]. Unfortunately, the patient did not follow up subsequently due to the lockdown.

## Discussion

Globally, drug-resistant tuberculosis (TB) is one of the most urgent and difficult challenges. Strains resistant to isoniazid and rifampicin cause multidrug-resistant (MDR) TB which is incurable by first-line treatment. Extensively drug-resistant (XDR) TB refers to MDR-TB strains that are also resistant to fluoroquinolones and second-line injectable drugs.

Ramesh *et al*.[2] reported six out of 303 cutaneous TB patients who showed multidrug resistance to ATT. Another case report by Regnier *et al*.[3] reported cutaneous miliary TB resistant to first-line ATT. Olson *et al*. reported a case of cutaneous extensively drug-resistant TB.[4]

Only a few other case reports of multidrug-resistant TB were found in the literature.[4,5]

On histopathology, cutaneous TB shows granulomatous inflammation with caseous necrosis, however, this cannot distinguish it from infections caused by non-TB mycobacteria, mycobacterium leprae, and from other granulomatous diseases unless AFB is detected in the specimen. Therefore, culture is needed for a definitive diagnosis. However, sensitivity is low due to the paucity of organisms in the skin, and it takes a few weeks to grow for identification.[6] This paucity of organisms also makes it tedious to assess drug resistance.

Nucleic acid amplification tests can detect nucleotide sequences unique to MTB directly in specimens and give results within a few hours, thus offering better accuracy than AFB smear microscopy and greater speed than culture.[7] Most cases of TB of the skin are related to TB of

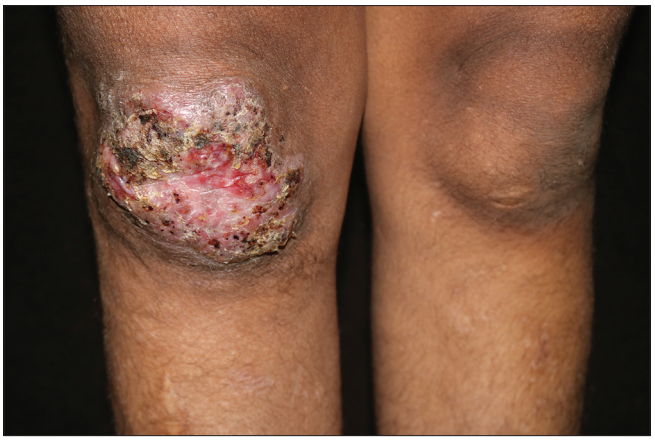

**Figure 1: Solitary round to oval well-defined irregular erythematous plaque with verrucous surface; erosion and crusting on the right knee**

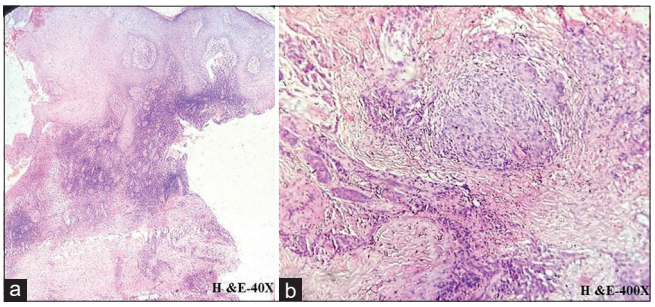


**Figure 2: (a) Irregular epidermal hyperplasia with lichenoid infiltrate (Hematoxylin and eosin stain (H and E)-40X). (b) Dermis shows well-formed granuloma with plasma cells and few giant cells (H and E-400X)**

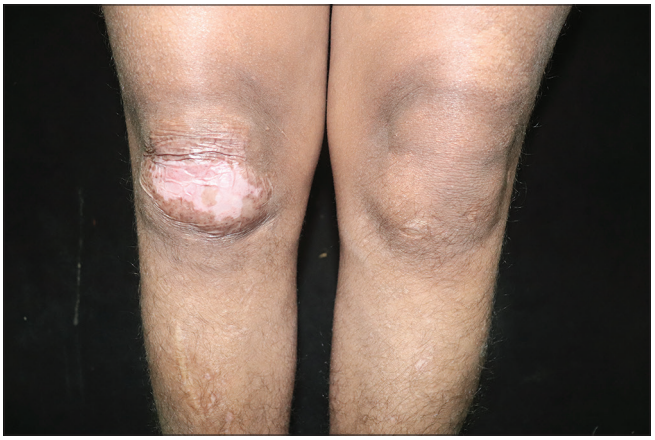

**Figure 3: Complete resolution of plaque leaving a depigmented atrophic scar**

other organs, unlike our case, in which we could not detect any systemic focus. The bacillary load in the skin is usually less than that in other areas, so treatment regimens, such as those used to treat pulmonary TB are usually sufficient for treating cutaneous TB.[8]

Patients may be prescribed anti-TB therapy for therapeutic trial when cutaneous TB is suspected since definitive diagnosis is difficult with present diagnostic methods. Patients who do not respond should have their diagnosis reviewed. However, a therapeutic trial loses its value in cases of MDR-TB. Even more alarming is the unscientific use of rifampicin monotherapy and administration of ATT for an inadequate duration. In our patient, we speculate that it may have contributed to the drug resistance.

## Conclusion

With the continuing spread of MDR-TB, more cases of cutaneous MDR-TB are likely to be encountered by physicians. When a patient is not responding to 1st line ATT, one should always suspect multidrug-resistant organisms. Culture, advanced testing like CBNATT and MGIT followed by drug sensitivity tests (DST) should be done prior to starting 2nd line anti-tubercular therapy. Rifampicin monotherapy should never be prescribed.

Our patient had no systemic focus on tuberculosis or local trauma. Our patient seemed to be having primary MDR TB, which would have been worsened by inadequate therapy and rifampicin monotherapy.

## *Declaration of patient consent*

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## *Conflicts of interest*

There are no conflicts of interest.

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