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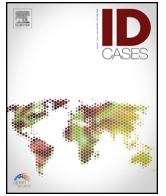
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Case report

Recurrent cutaneous tuberculosis in an immunocompetent 7-year-old male

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ABSTRACT

Cutaneous tuberculosis (TB) makes up a small proportion of the 10.4 million cases around the world. Although it is more commonly found in the developing world, cutaneous TB is rarely reported in the developed countries. It is fairly challenging to diagnose without histological examination. In this report, we present an immunocompetent 7-year-old male with a complex medical history diagnosed with cutaneous *Mycobacterium tuberculosis* after multiple ventriculoperitoneal shunt (VPS) revisions. This case of cutaneous TB in an immunocompetent patient is remarkable in its uncharacteristic presentation with no obvious source of TB infected contacts or travel history.

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Introduction

In 2015, an estimated 10.4 million people were living with tuberculosis (TB) across the globe [1]. TB has now surpassed HIV in global disease-specific mortality, causing 700,000 more deaths than HIV since the HIV pandemic started. More than 1.8 million people worldwide died from TB in 2015, most of which have been due to pulmonary TB and TB/HIV co-infections [2]. Nearly 10% of all adult TB-related infections and 20% of pediatric TB cases are extrapulmonary in nature [3,4]. Cutaneous TB makes up a small proportion of these cases. More commonly found in the developing world, cutaneous TB is rarely reported in the developed countries. It is fairly challenging to diagnose without histological examination. *Mycobacterium tuberculosis* complex, including *M. bovis* and *Bacillus Calmette-Guérin* are the most common causative organisms. Mycobacteria are non-spore-forming, non-motile, non-toxin producing strictly aerobic bacilli [4,5]. Factors such as individual immunity, environmental influences, and type of inoculum are contributory in the natural history of the disease process [4].

TB is most primarily transmitted via an airborne route, with extrapulmonary manifestations including in the skin caused by hematogenous or contiguous spread from a focus of infection.

However, a primary infection can occur through direct inoculation of mycobacteria into the skin or mucosa of a susceptible individual by trauma or injury. In the presence of HIV, intravenous drug use, diabetes mellitus, immunosuppressive therapy, malignancy, end-stage renal disease, or infancy, the risk of infection and disease progression appear to be higher as compared to the immunocompetent individuals [6–8].

In this report, we present an immunocompetent 7-year-old male with a complex medical history that presented with cutaneous TB after multiple VPS revisions. The infection was initially treated with first-line TB therapy based on sensitivity studies. However, after recurrent episodes, the patient had to be maintained on prophylaxis therapy throughout the remainder of his life.

Case Report

The patient was a Caucasian male, ex-24 week premature birth with a medical history significant for hydrocephalus and VPS placement as an infant, chronic lung disease, cerebral palsy and global developmental delay. He was home-based and had no interactions with the outside world. At age 7, he presented to his primary care physician with the chief complaint of an “ingrown hair” that the mother noticed after giving him a haircut. The lesion was noted to be pea-sized and found on the incision site of the shunt on his scalp. The patient had no other complaints including fever, weight loss, and acute respiratory illness. At the time, the PCP felt no further workup was needed and sent the patient home with

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bacitracin ointment. Three days later, the lesion had grown and begun oozing purulent fluid. The patient's mother became concerned and her child was brought to the emergency department (ED).

On initial presentation, the patient was noted to have erosion at the shunt site and part of the shunt tubing could be visualized. The patient's neurosurgeon was contacted and he performed a shunt revision. After an uncomplicated hospital course, the patient was discharged home. Over the subsequent 18 months, similar episodes occurred with the patient requiring multiple VPS revisions.

At age 9, the patient presented to the ED with a much larger lesion that was dime-sized. On physical examination, the patient's pertinent findings included an erythematous, firm, and painless rash on the right side of the neck along the route of the shunt catheter with a central light-colored region of granulose-like base with oozing. He was suspected to have cellulitis as a complication of his latest shunt revision. A bacterial culture was obtained, but after five days there was no growth. Treatment was started with clindamycin and bacitracin ointment for suspicion of *Staphylococcus aureus* or beta-hemolytic streptococci.

After a 10-day course of antibacterials, symptoms persisted with no notable improvement. Neurosurgery and infectious disease were consulted. A biopsy of the lesion and immunological workup was obtained. The patient was continued on the same regimen and was started on dietary supplementation to optimize wound healing, which included vitamin A, vitamin C, vitamin D and zinc. The immunological workup showed normal immunoglobulin counts, normal T and B cell subsets, and normal neutrophils. The biopsy results showed granulomas with a necrotizing neutrophilic infiltrate with numerous acid-fast bacilli (AFB). A chest radiograph was unremarkable. A Mantoux tuberculin skin test was performed, which showed a 17 mm induration. Based on the findings, the patient was diagnosed with primary cutaneous tuberculosis.

Culture studies from the biopsy were performed and grew *Mycobacterium tuberculosis*. Sequencing identification of the pathogen by the CDC matched that of patient zero, a transient adult male that lived in the same city and was the source of multiple exposures. In the case of our patient, epidemiological studies showed that he was likely exposed to TB on an ED visit when he was 6 years old and was being seen for chronic lung disease exacerbation.

The patient was started on isoniazid, rifampin, pyrazinamide, and ethambutol. However, during the first two weeks of treatment, he began to have feeding difficulties and developed jaundice. Alanine transaminase (ALT) and aspartate aminotransferase (AST) were five times the normal range. All TB medications were stopped until ALT and AST returned to normal. Rifampin was restarted, but the patient again developed jaundice and elevated liver enzymes. We determined that he could not tolerate rifampin and placed him on double therapy of isoniazid and ethambutol for 24 months. The patient performed well with therapy whereby there were resolution of granulation tissue and no AFB found on post-treatment biopsy.

Three months after the completion of treatment, the patient underwent a VPS revision without complications during the procedure. However, six months later, he developed a new erythematous, non-pruritic rash with oozing at the site of incision of the shunt revision on the scalp. A new biopsy was obtained which showed multiple AFB, thereby resulting in his diagnosis of recurrent cutaneous TB. Due to the hepatotoxicity of the first treatment plan, the patient was placed on intravenous amikacin, oral cycloserine, and oral ethionamide for three months and subsequently, amikacin was replaced with levofloxacin. The triple therapy was maintained for 18 months with resolution of the

lesion. Given the recurrent nature of the patient's TB, he was placed on prophylaxis isoniazid and ethambutol with no documented recurrence TB throughout the remainder of his life. He succumbed from unrelated complications of his chronic disease.

Discussion

Our patient was initially diagnosed to have cellulitis due to either *Staphylococcus aureus* or beta-hemolytic streptococci. Failure of clindamycin, histologic findings on skin biopsy, and negative bacterial cultures resulted in the diagnosis. Cutaneous granulomas with necrotizing neutrophilic infiltrate with numerous AFB was consistent with primary cutaneous TB (CTB).

While clinically similar, individual CTB lesions can present with different development, progression, and prognosis. There are commonly two well-used classification systems (Table 1). The first is based on the mechanism of propagation—exogenous versus endogenous dissemination. An exogenous propagation consists of an infected individual inoculating a new susceptible host, while endogenous dissemination results in a new skin inoculation from an already infected individual. The second scheme is based on the concept of bacterial load, which is used to differentiate between the paucibacillary form whereby identification of bacilli in culture and histological tissue is very difficult; and multibacillary where the organism is easily found and identified [4].

Currently, the frequency of CTB worldwide has been variable and according to some studies, lupus vulgaris is the most common with 55% of all presentations, followed by scrofuloderma which is seen in 25% of patients, and then by orificial tuberculosis, tuberculosis verrucosa cutis, papulonecrotic tuberculid, and erythema induratum with 5% in each [3,9,10]. However, studies performed in Brazil, which is an endemic country for TB, show that scrofuloderma is the most common presentation and in one statewide retrospective study, erythema induratum of Bazin is found to be the most common type [11,12].

There have been some individual case reports suggestive of rare presentations of CTB. For instance, as a metastatic tuberculous abscess, where it was presented as two distinct swellings on the anterior chest wall that grew at different points in time. Another rare presentation was that of a facial skin involvement with ulceration, which was initially suspected to be a cutaneous leishmaniasis that did not respond to standard treatment [6,7].

Table 1
Classifications for Cutaneous Tuberculosis.

Classification I		
Mechanism of Propagation	Dissemination	Type of Lesion
Exogenous		Lupus vulgaris Tuberculous chancre Tuberculosis verrucosa cutis
Endogenous	Contiguous	Orificial tuberculosis Scrofuloderma
	Hematogenous	Acute miliary tuberculosis Lupus vulgaris Metastatic tuberculous abscess Papulonecrotic tuberculid
	Lymphatic	Lupus Vulgaris
Classification II		
Form	Type of Lesion	
Multibacillary	Active miliary tuberculosis Metastatic tuberculous gumma Tuberculous chancre Tuberculosis orificialis	
Bacillary	Lupus vulgaris Tuberculids Tuberculosis verrucosa cutis	

Table 2
First-line Medications for Cutaneous Tuberculosis.

Medication	Adult Dosing	Children Dosing	Adverse Reactions
Isoniazid	5mg/kg daily, max 300 mg	10–15 mg/kg daily	Elevated liver enzymes, peripheral neuritis, hypersensitivity
Rifampin	15 mg/kg TIW 10 mg/kg daily, max 600 mg	15–20 mg BIW daily or BIW	Orange discoloration of secretions or urine, staining of contact lenses, hepatitis, thrombocytopenia, pruritus, influenza-like reaction, oral contraceptives may be ineffective
Pyrazinamide	10 mg/kg TIW, max 600 mg 20–25 mg/kg daily, max 1600 mg	30–40 mg/kg daily 50 mg BIW	Hepatotoxic effects, hyperuricemia, arthralgia, gastrointestinal tract upset, pruritus, rash
Ethambutol	25–35 mg/kg TIW, max 2400 mg 40–50 mg/kg BIW, max 400 mg 15–20 mg/kg daily, max 1600 mg	15–25 mg/kg daily 50 mg/kg BIW	Optic neuritis, decreased red-green color or discrimination, gastrointestinal tract disturbances, hypersensitivity

TIW = three times a week. BIW = two times a week.

It has always been challenging to diagnose and promptly treat TB due to a variety of clinical presentations, but the prescribed guidelines for TB diagnosis have been revised to consistently address this fundamental problem. As per the diagnostic guidelines quantiferon (TB GOLD), tuberculin skin test, chest X-ray and sputum staining for AFB are used for the screening of TB. However, recent guidelines recommend more accurate and rapid tests for TB screening and detection as Xpert MTB/RIF, which also detects rifampin resistance [13]. Absolute positive testing of DNA-PCR techniques including a dry and wet culture are needed, which are confirmatory of TB [14].

As per the updated treatment guidelines according to the CDC and ISDA (2016), the aim of the treatment is to help cure the individual patient, decrease the risk of death and disability, reduce transmission of *Mycobacterium tuberculosis* to other individuals, and prevent the development of drug resistance. The mainstay treatment for drug-susceptible TB, in absence of HIV infection, remains the 2-month intensive therapy with isoniazid, rifampicin, pyrazinamide, and ethambutol followed by four months of maintenance therapy with isoniazid and rifampin (Table 2) [16]. It is recommended to use directly observed therapy (DOT) for all forms of TB [13]. One of the most common adverse events is the development of liver enzyme elevations. In the first two months of treatment, an asymptomatic liver enzyme elevation can be observed in a small subset of patients that is followed by complete spontaneous resolution with no clinical manifestations and without the need to disrupt or change the therapeutic regimen. However, treatment should be stopped if liver enzyme levels are greater than three times the normal value such as in our reported case. Once liver enzyme levels normalize and there is resolution of symptoms, the reintroduction of the basic scheme is indicated as follows: rifampin + ethambutol, followed by isoniazid and lastly, pyrazinamide with an interval of 3–7 days between them. If the patient again has abnormal liver enzyme levels, then an alternate scheme for hepatic insufficiency must be utilized as follows: ethambutol, streptomycin and another drug such as isoniazid, rifampin or ofloxacin [15].

This case of cutaneous TB in an immunocompetent patient is remarkable in its uncharacteristic presentation with no obvious source of TB infected contacts or travel history. In a review of the literature, there have been no similarly described cases in the past. The patient likely had an unfortunate exposure while in the emergency department where an individual with active TB transmitted the infectious bacillus to him.

CRedit Author Statement

Alvaro Galvis: Conceptualization, Visualization, Writing-Original draft preparation.

Vidyasagar Jaiswal: Writing-Original draft preparation.

Iris Pecson: Writing-Reviewing, Editing, Resources.

Craig Nakamura: Supervisor.

Dena Austin: Resources.

Conflict of Interest

All authors have no conflict of interest to disclose.

Informed Consent

Written informed consent was obtained from the patient's family for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

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