

CUTANEOUS TUBERCULOSIS IN AN IMMUNOCOMPETENT TWENTY-ONE-YEAR-OLD MAN

BELMA PARALIJA^{1,2}, ELVIRA ABDIĆ³, JASMINA MUSTAFIĆ PANDŽIĆ¹

¹Department of Lung Diseases and Tuberculosis, University of Sarajevo Clinical Center, Sarajevo, Bosnia and Herzegovina; ²Faculty of Medicine, University of Sarajevo, Sarajevo, Bosnia and Herzegovina; ³Dr Irfan Ljubijankić Cantonal Hospital, Bihać, Bosnia and Herzegovina

Cutaneous tuberculosis is a rare form of tuberculosis. Considering the numerous skin manifestations that differ not only in clinical features but also in the way the infection reaches the skin, cutaneous tuberculosis is a great challenge for diagnosis. We present a case of cutaneous tuberculosis in a 21-year-old male migrant from Pakistan, hospitalized at the Department of Lung Diseases and Tuberculosis, Sarajevo University Clinical Center due to recurrent abscesses, furuncles and carbuncles of the left thigh and right forearm, that persisted for the past year and were treated with various antibiotics. Pus obtained by abscess incision, wound swabs of the left thigh, and skin tissue obtained by biopsy were sent for microbiological and *Mycobacterium (M.) tuberculosis* analysis. Wound swabs and skin tissue culture were positive for *M. tuberculosis* on solid (Löwenstein) and liquid (MGIT) medium. Sputum smear and culture for *M. tuberculosis* were negative. Chest x-ray also was without active pathomorphological changes. Antituberculosis therapy was started with four drugs (isoniazid, ethambutol, pyrazinamide, rifampicin). In addition to antituberculosis therapy, the wound of the left thigh required surgical treatment. The patient was successfully treated with antituberculosis therapy along with surgical treatment of skin changes and their healing. The diagnosis of cutaneous tuberculosis in our patient was established after a long period and after the failure of antibiotic treatment. Proper diagnosis of cutaneous tuberculosis is very important since it can be well treated with common antituberculosis therapy.

Key words: cutaneous tuberculosis, diagnosis, treatment

Address for correspondence: Belma Paralijsa, MD, PhD
Department of Lung Diseases and Tuberculosis
Sarajevo University Clinical Center
Bardakčije 90
71000 Sarajevo
Bosnia and Herzegovina
E-mail: paralijabelma@gmail.com

INTRODUCTION

Cutaneous tuberculosis is a rare form of tuberculosis, occurring in less than 1% of cases, especially in developing countries (1). Considering the numerous skin manifestations that differ not only in clinical features but also in the way the infection reaches the skin, cutaneous tuberculosis is a great challenge for diagnosis (2). *Mycobacterium (M.) tuberculosis* complex, including *Mycobacterium bovis*, as well as Bacillus Calmette-Guérin (BCG) vaccine, are the most common causes of skin changes (3). Mycobacteria are slow-growing aerobic bacilli with a high concentration of lipids in their cell wall, which makes them impermeable to many colors. Because of their ability to retain their color and survive decolorization with acid and alcohol, they are

labelled as acid-fast bacilli (AFB) (4). Numerous factors are associated with an increased risk of getting sick with tuberculosis, the most important of which are the patient's immune status, living conditions, history of previous illnesses, environmental factors, and nutrition (5,6).

CASE REPORT

We present a case of cutaneous tuberculosis in a 21-year-old man, a migrant from abroad, without prior immunocompromising conditions or comorbidities. The patient was admitted to the Department of Lung Diseases and Tuberculosis, Sarajevo University



Figure 1. Skin defect with sutures.



Figure 2. Crusts on the skin after furuncle secretion.

Clinical Center, due to recurrent abscesses, furuncles and carbuncles of the left thigh and foot, as well as the left and right forearm, that had lasted for the past year, along with osteomyelitis of the left foot, which had been treated for a year with various antibiotics. For the previous two years, the patient lived in large refugee camps in different countries with a low level of hygiene, without proper nutrition, and was in contact with tuberculosis patients. On admission, he was communicative, moved with the help of crutches, average osteomuscular constitution, malnourished (body mass index 18.2), afebrile, eupneic, with normal auscultatory findings over the lungs and heart, and hypotensive. BCG vaccination scar was visible on his left upper arm. On examination, in the area of the lateral side of the left thigh, there was a skin defect, neat edges, with sutures present, and slightly moist (Figure 1). There was a visible scar tissue 10 cm long on the right elbow, as well as scar tissue on the left forearm and crusts on the skin of the dorsal part of the left foot after furuncle secretion (Figure 2). Extremities were without edema, regularly palpable pulsations over arteries.

DIAGNOSTIC METHODS

Upon admission, complete laboratory findings were obtained, which indicated a normal number of leukocytes and erythrocytes, with a drop in hemoglobin and hematocrit, slightly elevated D-dimer values, and high C-reactive protein. In differential blood count, a reduced number of lymphocytes and monocytes was found, along with a normal number of neutrophils. Electrolyte status was normal.

Sputum smear and culture for AFB (*M. tuberculosis*) were negative. Chest x-ray was normal, without active pathomorphological changes, and so was bronchoscopic examination. As the bronchoscopic findings and chest radiograph were normal, we decided not to perform computed tomography scan of the chest.

On standard x-rays of the left foot in the dorsoplantar and profile projection, the bone structure and mineralization were reduced, with emphasized reduction of the bone structure and mineralization of the base of the metatarsal III and IV, that according to x-ray characteristics, may have corresponded to osteomyelitis changes (Figure 3).

Pus obtained by abscess incision, wound swabs of the left thigh, and skin tissue obtained by biopsy were sent for microbiological and *M. tuberculosis* analysis. There was no isolation of the usual microbiological agents in the biological samples of our patient. Wound swabs and skin tissue culture were positive for AFB on solid (Löwenstein) and liquid (MGIT) (mycobacteria growth indicator tube) medium. Hepatitis markers were negative. VIKIA and COMBO HIV were negative. Interferon Gamma Release Assay (IGRA) analysis for *M. tuberculosis* was performed. The positive result was obtained by Quantiferon-TB Gold In-Tube (QFT-GIT) analysis conducted at the Biochemical Laboratory, Sarajevo University Clinical Center.

Antituberculosis treatment was administered and started with four drugs (isoniazid, ethambutol, pyrazinamide, and rifampicin) for nine months. General condition of the patient was improving, but there was no adequate healing of the existing wound despite regular wound treatment and antituberculosis therapy admin-



Figure 3. X-ray of the left foot consistent with osteomyelitis.

istered. Wound swabs were positive for AFB on liquid (MGIT) medium after 40 days of the antituberculosis therapy prescribed. Wound dehiscence occurred (Figure 4) and an open wound was bandaged daily with sterile dressings.



Figure 4. Wound dehiscence despite regular wound treatment and antituberculosis therapy.

In addition to antituberculosis therapy, the wound on the left thigh also required surgical treatment. After consultation with an orthopedist, the patient was transferred to the Department of Orthopedics due to the need of surgical treatment of the existing wound. After the wound healing, the patient was discharged for further treatment at the refugee center under the supervision of a resident doctor. Antituberculosis therapy was carried out for 9 months. The patient was successfully treated with antituberculosis therapy along with surgical treatment of skin changes and their healing. The patient recovered, and the wounds and abscesses were healed.

DISCUSSION

Tuberculosis is an infectious disease caused by *M. tuberculosis*, which predominantly affects the lungs, while lymph node involvement is the most common form of extrapulmonary tuberculosis (EPTB), which occurs in 20%-60% of all EPTB cases. Tuberculosis can affect the bones (6% of cases) and central nervous system (3% of cases), while the skin is very rarely involved, occurring in less than 1% of cases (1).

According to the latest data from the World Health Organization, a total of 1.6 million people died from tuberculosis in 2021, including 187,000 people infected with human immunodeficiency virus (HIV). Globally, tuberculosis was the 13th leading cause of death and the second leading infectious cause, right behind COVID-19 and ahead of HIV/AIDS in 2021. As many as 10.6 million people were affected by tuberculosis, of

which 6 million were men, 3.4 million women, and 1.2 million children. In addition, tuberculosis is present in all countries and age groups. However, the 30 most affected countries accounted for 87% of cases. Globally, tuberculosis incidence is decreasing by around 2% annually, which is an overall decline of 11% since 2015 and 2020, but which compares to a 20% decline in the incidence over the same period, according to the End Tuberculosis Strategy, almost half as much as predicted (7).

Factors such as malnutrition, alcoholism, drug addiction, disorders of the immune response, and even poor housing conditions can cause tuberculosis (8). An additional challenge are patients suffering from HIV infection, where *M. tuberculosis* is the most virulent opportunistic pathogen among HIV patients (9,10).

Clinical signs and symptoms of cutaneous tuberculosis may include joint pain, regional lymphadenopathy, painful nodular, and later ulcerating lesions, with or without symptoms of pulmonary tuberculosis (10). Cutaneous tuberculosis can occur as a result of exogenous inoculation, continuous spread from the focus of infection, or hematogenous spread from a distant focus. An additional useful concept of dividing cutaneous tuberculosis is based on the 'bacterial load', where cutaneous tuberculosis is classified into multibacillary and paucibacillary forms (11). Primary tuberculosis inoculation occurs when mycobacteria enter the skin or, less commonly, the mucosa of a person who has not previously been infected or vaccinated against *M. tuberculosis*. As AFB cannot penetrate the normal, intact skin barrier, some form of injury is required to initiate the infection. The entry point for AFB is usually through minor skin scratches, nail wounds, impetigo or ulcers (12). In patients with pre-existing immunity to tuberculosis, post-primary skin inoculation usually occurs, with the development of a hyperkeratotic papule, which eventually becomes a true wart (5,11,12).

Enlargement of the lymph glands as a result of inoculation is seen in patients with primary lesions, while it is absent in persons who have been vaccinated or previously treated for tuberculosis (11). Cutaneous tuberculosis infection may also occur by continuous spread to the skin from a subcutaneous focus (most commonly tuberculous lymphadenitis or tuberculosis of the bones and joints), or may be secondary to tuberculous epididymitis (5,13). In the past, the term scrofuloderma was used to describe this condition. The most commonly affected organs are cervical lymph nodes; children are affected more often than adults (5,11,12).

Cutaneous tuberculosis can be the result of autoinoculation of the mucosa and adjacent openings, which occurs when tubercle bacilli are directly coughed up

or transmitted to immunocompromised patients. Then the tubercle bacilli invade tissue that is normally resistant to infection. In the past, the term orofacial tuberculosis was used to describe this condition (2,5,12).

Lupus vulgaris is an example of cutaneous tuberculosis caused by the hematogenous spread of the causative agent. It is a special type of chronic cutaneous tuberculosis that occurs in individuals previously immunized against *M. tuberculosis*. Occasionally, lupus vulgaris can appear precisely at the sites of primary contact with tuberculosis, such as on the scars of scrofuloderma, or at the sites of repeated BCG vaccination.

The disease presents clinically differently, from psoriasisiform lesions, nasal ulceration, and nasal cartilage destruction to widespread hematogenous dissemination, which is why the disease is often misdiagnosed. In 10.5% of cases, the disease can change malignantly in terms of the development of squamous cell or basal cell cancer up to 25-30 years after infection (2).

A less common, fulminant form of cutaneous tuberculosis, previously known as *TB cutis miliaris disseminata*, occurs in infants or children after acute hematogenous dissemination of *M. tuberculosis*, which is often fatal. Increasingly, it can also be found in individuals with weakened cellular immunity, such as patients with advanced HIV (14). Cutaneous hematogenous dissemination of *M. tuberculosis* can often occur in the form of soft tissue abscesses (in the past the term gumma was used) and nodules (2).

Such presentation of cutaneous tuberculosis was present in our patient, who was not immunocompromised, but was a malnourished person on the move, constantly exposed to poor hygienic conditions and contact with other people suffering from tuberculosis.

Both scrofuloderma and gumma are forms of cutaneous tuberculosis often associated with the involvement of bones and joints (5,11,12) as it was also the case in our patient.

Cases of chronic cutaneous miliary tuberculosis have also been described, a very often forgotten entity, which is also caused by hematogenous spread of the bacilli into the skin, and which is characterized by numerous erythematous, confluent papules and plaques, prone to peeling (14). A group of skin changes that appear in the presence of tuberculosis but do not contain culturable AFB are designated as tuberculids (5,11). Seen histopathologically, they were previously considered an allergic reaction. These conditions included erythema induratum, papulonecrotic tuberculides, and lichen scrofulosorum. They are considered paucibacillary forms of cutaneous tuberculosis infection (5,8,11).

Because most patients with cutaneous tuberculosis have an active systemic infection, treatment consists of standard two months of 4 antituberculosis drugs and then four months of two antituberculosis drugs (15).

Considering that our patient had bone involvement by tuberculosis as well, we administered antituberculosis therapy according to the nine-month regimen, namely isoniazid, rifampicin, ethambutol, and pyrazinamide for two months, followed by another seven months of isoniazid, rifampicin.

CONCLUSION

Taking into account a number of predisposing factors that favor the development of tuberculosis, such as diabetes mellitus, HIV infection, immunocompromising conditions, previous malignant diseases, malnutrition, but also information about previous tuberculosis or immunization against it (BCG vaccine) that can affect the clinical tuberculosis presentation, the importance of taking thorough history data and insight into previous history of the patient's illness is emphasized in order to raise suspicion of this disease.

In the vast majority of cases of cutaneous tuberculosis, the diagnosis of this disease was established only after a long period and after failure of the usual antibiotic regimens for the treatment of skin lesions, as was the case in our patient. Only proper diagnosis established on time and initiation of antituberculosis therapy can prevent further progression of skin changes.

Recurrent abscesses, and the absence of isolation of the usual microbiological agents in the biological samples of our patient ultimately raised suspicion of a cutaneous form of tuberculosis.

Although rare, accounting for less than 1% of cases, cutaneous tuberculosis has a good treatment response rate to common antituberculosis therapy regimens.

Ultimately, this work aims to draw attention to the quite unusual manifestations of tuberculosis and enable patients to have timely access to treatment of this disease.

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S A Ž E T A K

**TUBERKULOZA KOŽE KOD IMUNOKOMPETENTNOG
DVADESETJEDNOGODIŠNJEG MUŠKARCA**

B. PARALIJA^{1,2}, E. ABDIĆ³, J. MUSTAFIĆ PANDŽIĆ¹

¹Klinika za plućne bolesti i tuberkulozu, Klinički centar Univerziteta u Sarajevu, Sarajevo, Bosna i Hercegovina;

²Medicinski fakultet, Univerzitet u Sarajevu, Sarajevo, Bosna i Hercegovina; ³Kantonalna bolnica

“Dr Irfan Ljubijankić”, Bihać, Bosna i Hercegovina

Kožna tuberkuloza je rijedak oblik tuberkuloze. S obzirom na brojne kožne manifestacije koje se razlikuju ne samo po kliničkim karakteristikama, nego i po načinu na koji infekcija dopijeva na kožu, kožna tuberkuloza veliki je izazov za dijagnosticiranje. Prikazujemo slučaj kožne tuberkuloze kod 21-godišnjeg migranta iz Pakistana, hospitaliziranog na Klinici za plućne bolesti i tuberkulozu, Klinički centar Univerziteta u Sarajevu zbog ponavljajućih apscesa, furunkula i karbunkula lijeve natkoljenice i desne podlaktice, koji su trajali jednu godinu i liječeni su različitim antibioticima. Gnoj dobiven incizijom apscesa, brisevi rane lijevog bedra, tkivo kože dobiveno biopsijom poslani su na mikrobiološku analizu i analizu na *Mycobacterium (M.) tuberculosis*. Brisevi rana i kulture kožnog tkiva bili su pozitivni na *M. tuberculosis* na čvrstom (Löwenstein) i tekućem (MGIT) mediju. Razmaz sputuma i kultura na *M. tuberculosis* bili su negativni. Rentgenogram prsnog koša bio je također bez aktivnih patomorfoloških promjena. Antituberkulozna terapija započeta je s četiri lijeka (izonijazid, etambutol, pirazinamid, rifampicin). Uz antituberkuloznu terapiju ukazala se potreba i za kirurškim liječenjem rane lijeve natkoljenice. Bolesnik je uspješno liječen antituberkuloznom terapijom uz kirurško liječenje kožnih promjena i njihovo cijeljenje. Dijagnoza kožne tuberkuloze kod našeg bolesnika postavljena je nakon dužeg vremena i nakon neuspjeha antibiotskog liječenja. Pravilna dijagnoza kožne tuberkuloze vrlo je važna, jer se može dobro liječiti uobičajenom antituberkuloznom terapijom.

Ključne riječi: tuberkuloza kože, dijagnoza, liječenje