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Case Report

Tuberculous Primary Complex of the Skin on The Face of a Patient with Rheumatoid Arthritis Report on an Entity of an Unaccounted Nature

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Abstract: Cutaneous tuberculosis is dangerous. The *M. tuberculosis* complex causes 1.5–3% of extrapulmonary cases. This chronic illness needs long care. Tuberculous primary complex, commonly known as primary inoculated tuberculosis, is a rare (1%) clinical and histological diagnosis. To provide a histopathological case of primary skin tuberculosis with an unusual clinical presentation and immunization mechanism, to emphasize the significance of early detection to minimize sequelae and infections. A 52-year-old man has rheumatoid arthritis and systemic hypertension. It started with a unilateral localized dermatosis affecting the head in the left malar region characterized by an erythematosus papule of 2 mm in diameter, which at 2 weeks evolved into a 3 mm ulcer accompanied by pain and edema. The injury evolved every month to malar region, eyelids and left atrial pavilion consisting of a 15 cm erythematous myxedematous plate, was evaluated and treated with multiple antimicrobials without improvement, trauma was ruled out, skin biopsy was taken in the presence of two alcohol-resistant acid bacilli and by computed tomography infection by mycobacteria was excluded, skin tuberculosis was diagnosed of the primary skin complex type and treatment was initiated showing clinical improvement at 4 weeks and resolution at 8 months of treatment. The diagnosis of cutaneous tuberculosis presents a significant challenge owing to the diverse range of morphological manifestations. The manifestations observed in these cases have the ability to imitate various skin diseases, encompassing both infectious and non-infectious conditions. Moreover, it is imperative to exclude the existence of systemic tuberculosis in every instance.

Keywords: Cutaneous tuberculosis, Face, Tuberculous primary complex of the skin, Tuberculous chancre, Primary inoculation, Rheumatoid arthritis.

INTRODUCTION

Cutaneous tuberculosis represents a growing threat to public health (Chen l *et al*., 2019) and is caused by the Mycobacterium tuberculosis complex, rarely, can be caused by *M. bovis* or BCG bacillus (an attenuated *M. bovis strain*) (Kaul S *et al*., 2022).

Extra-pulmonary tuberculosis constitutes between 8-24% of cases. Cutaneous tuberculosis accounts for about 1.5-3% of extra-pulmonary cases. As infection of the skin is an uncommon, often insidious manifestation that has myriad possible morphologies, a chronic course, and the need for prolonged treatment (Kaul S *et al*., 2022).

The classification of cutaneous tuberculosis (Table 1) is complex and depends on several factors, including the route of infection, immune status, prior tuberculosis exposure[2] so the infections are more prevalent in men (56%), followed by women (32%), and children (12%) (Global Tuberculosis Report 2021). Based on bacillary load, it can be multibacillary or paucibacillary, based on the route of infection (Kaul S *et al*., 2022), it is categorized as exogenous or primary infection and endogenous or secondary by contiguity or autoinoculation and hematogenous dissemination (Charifa A *et al.*, 2022).

Table 1: Classification of cutaneous tuberculosis

Classification	Infection source and pathogenesis	Subtypes
True cutaneous tuberculosis	Exogenous	• Tuberculous chancre / tuberculosis of primary inoculation. • Verrucosa tuberculosis cutis.
	Endogenous	• Scrofuloderma. • Orifice tuberculosis. • Lupus vulgaris. • Tuberculous gumma. • Acute miliary tuberculosis.
Tuberculids	Hypersensitivity reaction to bacterial antigens.	• Papulonecrotic tuberculid • scrofulous lichen • Bazin's indurated erythema

In general, cutaneous Tuberculosis is divided into true tuberculosis and tuberculids. True cutaneous tuberculosis has demonstrable *Mycobacterium tuberculosis* in the lesions, by conventional (microscopy and culture) or molecular diagnostic methods (PCR). Tuberculids are hypersensitivity reactions ("id" reaction) to mycobacterial antigens, indicate a strong immune response, and do not have any detectable lesional mycobacteria. However, rarely PCR may be positive (Kaul S *et al*., 2022).

The Tuberculous chancre or primary inoculation TB, it is a rare form (0 – 1% of all cutaneous tuberculosis) and occurs after mycobacterial entry via an injury that is often unnoticed. About 2-4 weeks later, a brown-red asymptomatic papule develops at the site of entry, which can form a friable painless ulcer with undermined edges. Regional lymphadenopathy may or may not be present. If left untreated, it can progress to scrofuloderma, lupus vulgaris, disseminated TB, or exceptionally resolve with scarring (Kaul S *et al*., 2022).

Case Presentation

A 52-year-old male, with a 10-year history of rheumatoid arthritis diagnosed on treatment with tacrolimus, methotrexate, and leflunomide; Systemic arterial hypertension with a 2-year diagnosis and treatment with irbesartan and hydrochlorothiazide.

He started with a localized unilateral dermatosis that affects the head in the left malar region, characterized by a 2-mm diameter erythematous papule, which evolved into a 3-mm ulcer 2 weeks later (Fig 1), accompanied by pain and edema. After a month, the lesion evolved to the malar region, eyelids, and left auricular pavilion consisting of a 15 cm erythematous edematous plaque (Fig 2).

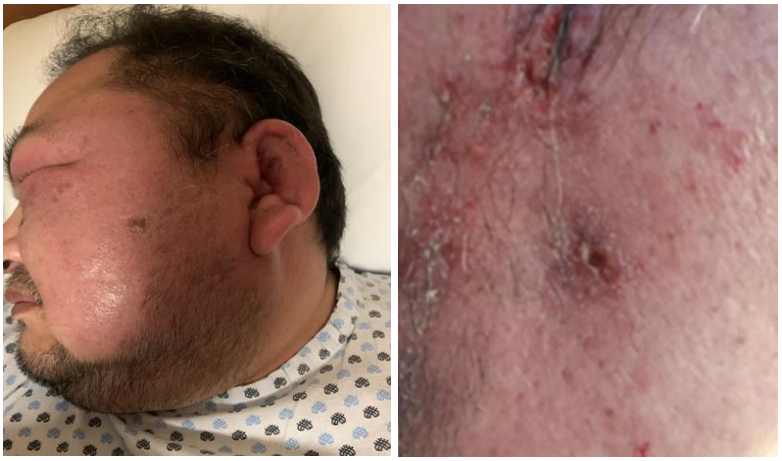

Fig. 1: Unilateral localized dermatosis affecting the head in the left malar region characterized by a friable ulcer with undermined and irregular edges, and a fibrin-filled background, 2 weeks after the initial papule

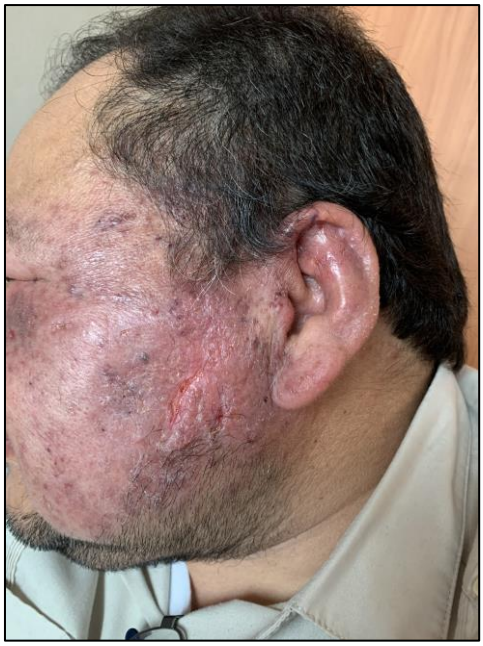

Fig. 2: Erythematous edematous plaque (++) measuring 15 cm, with ill-defined irregular borders, exulcerations, and bloody crusts on its surface

He was assessed and treated with multiple antimicrobials (clindamycin, trimethoprim-sulfamethoxazole, and levofloxacin) for 3 months without improvement. Traumatisms were ruled out, only regular beard shaving. In the hospital, he received intravenous meropenem and linezolid with partial improvement, for which a skin biopsy was taken with the presence of two acid-fast bacilli (Fig 3), a culture of bacteria, fungi, and mycobacteria were negative. Computed tomography of neck, thorax, abdomen, and pelvis was performed, showing no evidence of nodules, adenopathies, ascites, or any other radiographic manifestation suggestive of infection at those levels by mycobacteria. With the above, cutaneous tuberculosis of the primary tuberculosis complex type was diagnosed and treatment was started, the intensive phase (bactericide) with 600mg rifampicin, 1200mg ethambutol, 300mg pyrazinamide, and 900mg isoniazid for 2 months (Dotbal) from Monday to Saturday and 9 months phase of support (sterilant) with rifampicin 800mg and isoniazid 600mg three times a week, showing notable clinical improvement at 4 weeks and resolution at 8 months of treatment (Fig 4).

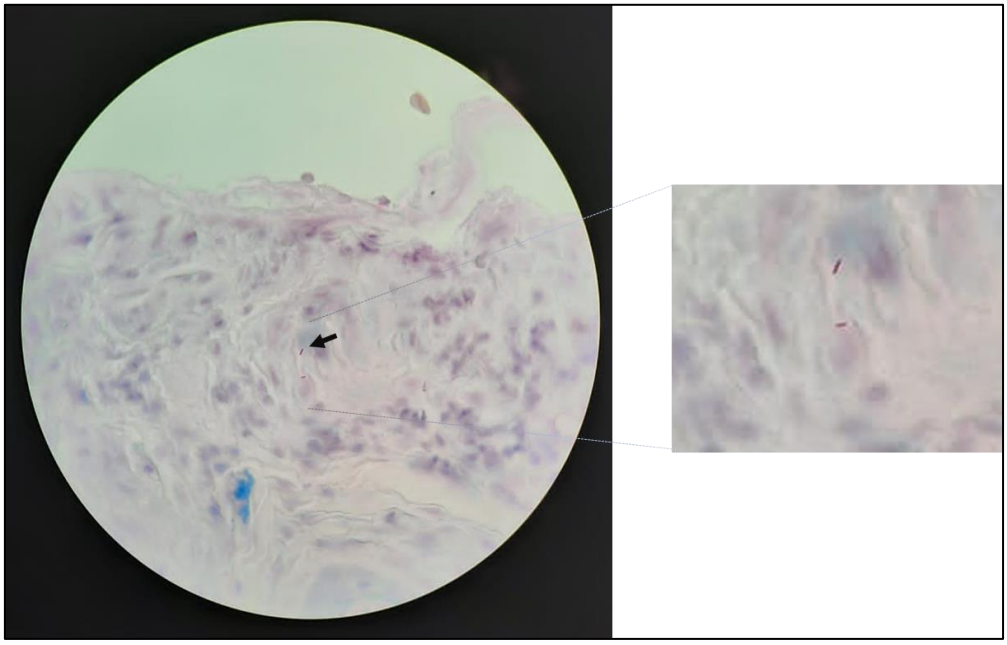

Fig. 3: Spindle skin biopsy with pseudoepitheliomatous hyperplasia of the epidermis, hyperkeratosis, and a dense infiltrate of inflammatory cells with neutrophils, lymphocytes, and giant cells, as well as granulomatous infiltrates, with the presence of 2 acid-fast bacilli

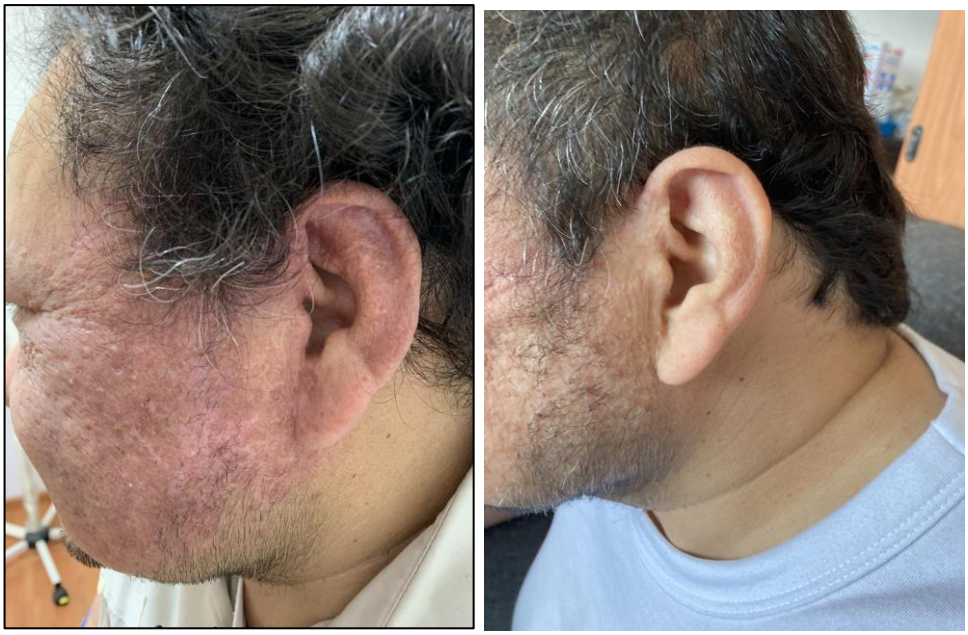

Fig. 4: Resolution of dermatosis 8 months after the start of treatment

DISCUSSION

Cutaneous tuberculosis is uncommon, that has a varied presentation, the diagnosis is challenging as lesions mimic other more common conditions and microbiological confirmation is often not possible (Kaul S *et al*., 2022).

It is important to differentiate between the types of tuberculosis cutaneous, mainly if the first exposure to TB leads to a disease manifestation, it is termed a "primary" infection as in the case of this patient, without prior exposure to tubercle bacilli, which can be confused with lupus vulgaris in those with partial immunity, and tuberculosis verrucosa cutis in those with a robust immune response (Kaul S *et al*., 2022).

Tuberculous primary complex of the skin or tuberculous chancre requires a breach of the normal barrier function of the skin from a minor abrasion or injury (Kim JK *et al*., 2010), allowing entry of the tubercle bacilli, therefore the primary inoculation tuberculosis has been reported in Illegal Acupuncture (Kim JK *et al*., 2010), after vaccination with bacillus Calmette-Guérin (BCG) (Lew W *et al*., 1990), intralesional steroid injection (Kim JC *et al*., 1991), needle stick injury (You DO *et al*., 2002), blepharoplasty (Kim MG *et al*., 2006), contaminated milk (Tappeiner G *et al*., 2003), following tattooing, circumcision, ear-piercing and tooth extraction (Wong HW *et al*., 2005). In this case we did not determine a primary focus with regard to the cause of the hematogenic or lymphatic spread in our patient and we suspected that a minor trauma by shaving of the beard and possible contact in his work activity in a funeral as a balsamator, were the mechanisms of entry that favored the infection.

Because of the above, its localization is predominant in the face and limbs, characterized by an initial injury consisting of a painful nodule that ulcerates quickly, leaving at 3-8 weeks a regional adenopathy that heals in 2-5 months (Arenas R *et al*., 2019). In our case due to late diagnosis and treatment, the dermatosis evolved over 3 months, compromising more areas of extension, causing after its healing significant post-inflammatory residual lesions.

For this reason, the diagnosis is mainly based on clinical appearance, microscopic and histopathological features are characterized by marked pseudoepitheliomatous hyperplasia of the epidermis with hyperkeratosis and dense inflammatory cell infiltrate consisting of neutrophils, lymphocytes, and giant cells. The presence of granulomatous infiltrates is a cardinal sign (Vora RV *et al*., 2016).

The clinical diagnosis is a challenge, because of its morphological variants, so carrying out a differential diagnosis with other medical conditions such as leishmaniasis, chronic vegetative pyoderma, drug reactions, granulomatosis with polyangiitis, atypical mycobacterial infection, nodular vasculitis and cellulitis is fundamental to avoid error in diagnosis and treatment, as observed in this patient who at its beginning presented characteristics similar to those of a piogenic cellulite, which caused difficulty at the time of diagnosis.

We have no evidence or case reports of patients with primary inoculated tuberculosis associated with the use of immunosuppressive therapy (Wedy GF *et al*., 2021), such as tacrolimus or methotrexate as indicated in this case for rheumatoid arthritis, but we can suggest that the drugs used are a risk factor for their presentation.

The treatment is performed in two phases, the intensive phase of therapy lasts about 8 weeks and the continuation phase is designed to eradicate remaining bacteria and lasts for 9 to 12 months (Charifa A *et al*., 2022). Mycobacteria coexists with the patient for a long period of time, coming into contact with different classes of drugs that can promote the appearance of resistant strains (Wedy GF *et al*., 2021), so the cure of skin tuberculosis requires strict adherence to treatment, noting that the results of treatment depend on the immunity of a patient, the stage of the disease, the type of cutaneous lesions, duration of treatment, and any side effects experienced (Charifa A *et al.*, 2022).

CONCLUSIONS

The diagnosis of primary inoculated skin tuberculosis in the present case involved a thorough clinical evaluation, histopathology studies, and tissue cultures. This case is notable for its unusual clinical presentation and inoculation mechanism. The findings underscore the significance of early diagnosis in order to prevent complications and associated infections. The diagnosis of skin tuberculosis presents a significant challenge due to the diverse range of morphological manifestations it exhibits. These manifestations can mimic various infectious and non-infectious dermatoses, further complicating the diagnostic process.

The diagnosis of this condition is frequently delayed due to the need for a heightened level of suspicion. This is because the progression of the disease is gradual and persistent when proper treatment is not provided. Therefore, it is crucial to rule out the presence of tuberculosis in each individual case, whether it is localized or systemic in nature.

At the international scale, a dearth of clinical research is observed owing to the relatively low incidence of cutaneous tuberculosis, thereby impeding the capacity to effectively suspect and diagnose this condition. Consequently, there exists a dearth of information pertaining to the clinical trajectory of the ailment and its corresponding reaction to therapeutic interventions.

Conflict of Interest: The authors declare that there are no conflicts of interest at the time of publication of this article.

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