CASE PRESENTATION

Tuberculosis vulgaris

Hiba Adnan Hammed[a], Mohammad Yahya Abdulrazaq[b], Abbas Farhood Hussein[c]

ABSTRACT

Extra pulmonary tuberculosis constitutes about 20% - 40% of all tuberculosis (TB) cases and cutaneous tuberculosis (CTB) makes up around 0.5-1% of them, despite prevention programs all over the world, tuberculosis is still progressing in the endemic form in developing countries.

A 43-year-old female presented to the Dermatology Department in Bagdad teaching hospital with unilateral plaque lesions below the left ear lobe associated with fever, weight loss, and loss of appetite, there was no history of trauma or ear piercing, lesion remained unhealed after antibiotic treatment, a biopsy was taken and genxpert test for Mycobacterium tuberculosis complex was positive. The patient was diagnosed as a case of skin tuberculosis and treated successfully with anti-tubercular therapy.

Key words: Extrapulmonary tuberculosis, cutaneous tuberculosis, lupus vulgaris.

INTRODUCTION

About 10.6 million people were estimated to have tuberculosis (TB) infection in 2021. The TB incidence rate (new cases per 100 000 population per year) increased by 3.6% between 2020 and 2021. The burden of drug-resistant TB (DR-TB) is estimated to be 450 000 new cases of rifampicin-resistant TB (RR -TB) in 2021. Globally, the success rate for people treated for TB in 2020 was 86%.[1]

Extrapulmonary tuberculosis constitutes about 20%- 40% of all tuberculosis cases, and around 1% of them are cutaneous. Despite prevention programs, tuberculosis is still endemic in developing countries.[2] It can also arise after endogenous or exogenous inoculation or as a complication of Bacillus Calmette–Guérin (BCG) vaccination.[3]

Bacillus Calmette-Guérin (BCG) is derived from an attenuated strain of Mycobacterium bovis and is employed beneficially as a relatively safe vaccination in countries where the prevalence of tuberculosis is high. However, BCG vaccination may produce complications, including lupus vulgaris. A similar phenomenon has been described after immunotherapy with BCG vaccination. Re-infection (secondary) inoculation, cutaneous tuberculosis may also occur due to BCG vaccination, producing either lupus vulgaris or tuberculosis varicose cutis, probably depending upon the patient's degree of cell-mediated immunity.[4]

Cutaneous tuberculosis has various clinical manifestations, including lupus vulgaris, scrofuloderma, TB verrucosa cutis, orificial TB, tuberculous gumma, tuberculous chancre, and acute cutaneous miliary TB.[5]

Cutaneous tuberculosis can also be classified into two broad categories depending on the load of the pathogens on the skin. The multibacillary forms, when the bacilli are easily detected in cutaneous tissue. These include tuberculous chancre, scrofuloderma, orificial tuberculosis, acute miliary tuberculosis, and tuberculous gumma. And the paucibacillary forms, when they are sparse in the lesions. These include TB verrucosa cutis, tuberculoid, and lupus vulgaris. [6]

Diagnosis of cutaneous tuberculosis is complicated and requires a full work-up, including a

a: MBChB, FIBMS; Family medicine specialist. National Tuberculosis Institute, Baghdad, Iraq. b: CABM, FIBMS, FRCP; Consultant pulmonologist & Consultant Internist, National Tuberculosis Institute. Baghdad, Iraq. c: MBCHB, FIBMS; Family medicine specialist. National Tuberculosis Institute, Baghdad, Iraq.

*Corresponding Author: **Hiba Adnan Hammed**, E mail: **drhibaadnan85@gmail.com**.*

detailed history and physical examination, careful consideration of clinical presentation, skin biopsy with histological analysis, and special staining methods for identification of acid-fast bacilli (AFB), in addition to other diagnostic tests, such as chest X-ray and sputum culture for diagnosis of associated pulmonary TB.[7]

Lupus vulgaris (LV) is often misdiagnosed because of its heterogeneous clinical manifestations in atypical disease sites. Moreover, the fact that LV is a pauci bacillary form of cutaneous TB often prevents successful culture testing. The disease predominantly affects individuals who have built up a moderate-to-high degree of immunity against tuberculosis.[8] There is a diversity of morphological forms and unusual clinical presentation with involvement of the face, nose, conjunctiva, and buttocks. Lupus vulgaris is the most common form of cutaneous TB, characterized by slowly enlarging plaque with a slightly elevated border, central atrophy, and "apple jelly" crusting.[9] Lupus vulgaris spreads through the blood or lymphatic system from an internal focus or, more rarely, infects exogenously by direct inoculation in a susceptible patient.[10]

CASE PRESENTATION

A 43-year-old housewive woman was referred from the dermatology department in Baghdad Teaching Hospital to National Tuberculosis Institute in Baghdad in January 2023 as a case of tuberculosis vulgaris

The condition started as a slowly growing lesion, over weeks, below the left ear lobe. The lesion was not discharging, painless, with red discolouration. The patient reported a history of fever, loss of appetite and significant weight loss. The patient was not a cigarette smoker, had no significant medical illnesses, and had no history of trauma to the ear lobe, including an ear piercing. She reported no history of pulmonary tuberculosis and exposure to a patient with TB in the family.

The systematic examination was not revealing, but local examination showed a soft yellow-to-purple papule, forming an infiltrative erythematous plaque with a sharp margin below the patient's right ear lobe, see **figure 1A**. The lesion was not tender for palpation, and no cervical lymph node enlargement was detected.

At first, the patient consulted a general surgeon, who prescribed a ceftriaxone injection of 1 g daily for a month without a significant clinical response; on the contrary, the mass had enlarged. The patient was seen by a dermatologist who took a biopsy for histopathological examination. The biopsy showed non-caseating granulomatous tissue reaction with scattered Langhans giant cells. Ziehl-Neelsen staining was negative; however, the genxpert test for Mycobacterium tuberculosis complex was positive. Other baseline investigations like complete blood counts, renal function, and liver function tests were within normal. The test for HIV, chest X-ray, and sputum for AFB were negative.

We started the standard TB therapy; isoniazid 300 mg, rifampicin 600 mg, pyrazinamide

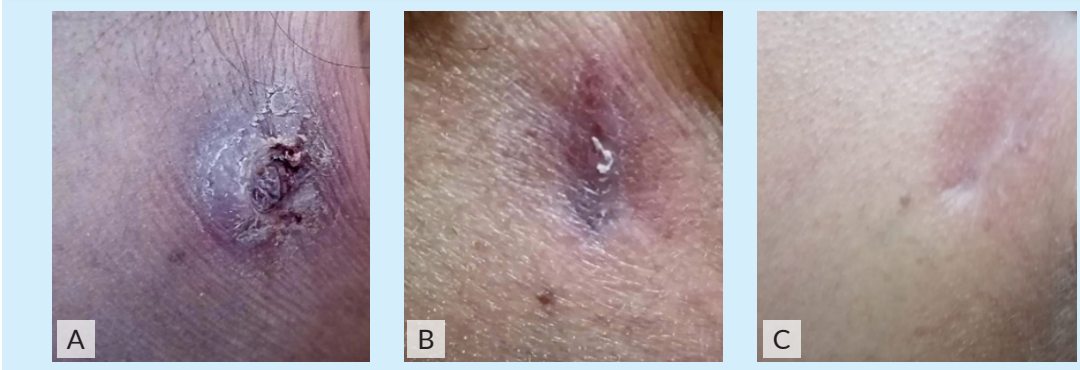

Figure 1 | **A:** Soft, yellowish-to-purple papules forming an infiltrative erythematous plaque with sharp margins below the patient's right earlobe. **B:** The lesion two months after tretament. **C:** Healing with some atrophic scarring after end of therapy.

1600 mg, and ethambutol 1100 mg daily. After two months, the lesion responded to the treatment, **figure 1B**. We continued isoniazid 300 mg and rifampicin 600 mg once daily for four months to complete the course of the treatment. After the end of the course of the anti-TB treatment, the lesion showed a satisfactory response, leaving some atrophic scarring, as seen in **figure 1C**.

DISCUSSION

TB is a curable and preventable disease. About 85% of people with TB can be successfully treated with antituberculous drugs for six months, while 1–6 months can be used to treat TB infection (latent). From the mid-twentieth century onwards, the disease was resurgent, with the main causes being the increased incidence of HIV-positive patients, the emergence of multidrug-resistant tuberculosis and the growing number of patients receiving immunosuppressive treatments.[11]

Cutaneous tuberculosis is a rare extrapulmonary tuberculosis primarily occurring in developing countries. The recent increase in the incidence of tuberculosis, especially due to human immunodeficiency virus (HIV) infections, has also led to a resurgence of extrapulmonary forms of this disease.[12] The occurrence of ulcerative skin TB is believed to be caused by the hematogenous spread of a preexisting TB infection in another organ or tissue. Mycobacteria are released into the blood and lymph circulation. Infection occurs when the immunity of the patient is decreased (or) M. tuberculosis is directly implanted into the mucosa, further forming an ulcer when further infected with enteric bacteria.[13] All age groups are equally affected, and the male-to-female ratio for true Cutaneous TB was 1.86:1.[14,15]

LV is a slowly progressing disease affecting patients previously infected by M. tuberculosis with moderate or high immunity against the bacterium,[16] and the predilection sites for LV are the face, neck, lower arms, chest, trunk, and leg.[17] This explains the slowly progressing of our young patient's symptoms throw the two months, which began with a slow-growing lesion below the left ear lobe

lupus vulgaris has five major clinical variations, including plaque, hypertrophic or vegetation, tumour-like, papular or nodular, and ulcerative types.[18] Our patient had soft, yellowish-to-purple papules with sharp margins on the patient's left ear lobe. Clinical features, especially on the face, may lead to confusion as lesions may look like cutaneous leishmaniasis, sporotrichosis, or chromoblastomycosis.[19] Our patient was misdiagnosed as having a simple skin infection and received antibiotics for one month ineffectively.

The diagnosis of skin TB mainly depends on the followings: clinical manifestations, skin PPD test, smearing and culture of M. tuberculosis, histopathological biopsy, history of TB in other systems or organs, and PCR method. Histopathological biopsy remains to be the gold standard for diagnosing TB. However, the examination period was relatively long, which limited its clinical application.[20] The comprehensive application of the PCR technique helps diagnose skin TB with higher efficiency; higher diagnostic sensitivity, and specificity than other traditional acid-fast staining smear tests. Rapid and accurate diagnosis of skin TB can be made by PCR utilizing chip diagnostic technology.[21] In our patient, histopathology showed non-caseating granulomas with scattered Langhans giant cells. Although the Ziehl-Neelsen stain was negative, the genxpert test for Mycobacterium tuberculosis complex was positive, confirming the diagnosis.

We made a chest X-ray for our patient before the therapy to exclude active pulmonary involvement, [22] which was normal.

Four anti-TB drugs regimen is the standard treatment for lupus vulgaris but patients still have scars once the treatment is completed. A positive outcome observed on TB treatment is sometimes the only argument supporting lupus vulgaris diagnosis.[23]

An empirical trial of triple anti-tuberculosis therapy, isoniazid, rifampicin, and pyrazinamide, may be considered in difficult cases. A clinical response would be expected within 4-6 weeks.

[24] Standard TB therapy (isoniazid 300 mg, rifampicin 600 mg, pyrazinamide 1600 mg, and ethambutol 1100 mg daily) was immediately initiated. The lesion responded nicely after two months of the treatment as showed in **figure 1B**. Then she was kept on isoniazid 300mg and rifampicin 600mg once daily for four months to complete the course of the treatment. After 6 months of anti-TB therapy, the clinical response was satisfactory, but with some atrophic scarring remains, **figure 1C**.

CONCLUSION

TB should be suspected for non-healing ulcers and kept in mind and a full course of anti-TB regimen is mandatory, it is important for clinicians to recognize the many clinical variants of cutaneous TB to prevent missed or delayed diagnoses.

REFERENCES

1. Global tuberculosis report 2022. WHO 2022.
2. Puri N. A clinical and histopathological profile of patients with cutaneous tuberculosis. *Indian journal of dermatology*. 2011 Sep;56(5):550.
3. Tan HH, Seow CS. A review of cutaneous granulomas and lupus vulgaris following BCG vaccination in a skin hospital in Singapore. *Annals of the Academy of Medicine*, Singapore. 2002 Sep 1;31(5):663-5
4. Solis AH, González NE, Cazarez F, Pérez PM, Diaz HO, Escobar-Gutierrez A, Ortiz IC, González HG, Reding-Bernal A, Sabido RC. Skin biopsy: a pillar in the identification of cutaneous Mycobacterium tuberculosis infection. *The Journal of Infection in Developing Countries*. 2012 Aug 21;6(08):626-31
5. Gunawan H, Achdiat PA, Hindritiani R, Essary ED, Ningtias LD, Siregar EP, Sori PR, Febrina D. Various cutaneous tuberculosis with rare clinical manifestations: A case series. *The International Journal of Mycobacteriology*. 2018 Jul 1;7(3):288-91.
6. Abebe F, Bjune G. The protective role of antibody responses during Mycobacterium tuberculosis infection. *Clinical & Experimental Immunology*. 2009 Aug;157(2):235-43.
7. Halle A, Lombart F, Chaby G, Bendamman M, Lok C, Hamdad F. An Erythemato-papular and Nodular Lesion on the Earlobe. *Clin Infect Dis*. 2020 Nov 5;71(8):1969-1972. doi: 10.1093/cid/ciaa154. PMID: 33151326; PMCID: PMC7643730.
8. Santos JB, Figueiredo AR, Ferraz CE, Oliveira MH, Silva PG, Medeiros VL. Cutaneous tuberculosis: epidemiologic, etiopathogenic and clinical aspects-part I. *Anais brasileiros de dermatologia*. 2014 Mar;89:219-28.
9. Shah AA, Pande AA, Vora IM, Ogale SB. Primary lupus vulgaris of the pharynx (a case report). *Journal of Postgraduate Medicine*. 1990 Apr 1;36(2):106.
10. Sehgal VN, Srivastava G, Bajaj P, Sengal R. Reinfection (secondary) inoculation cutaneous tuberculosis. *International journal of dermatology*. 2001 Mar;40(3):205-9.
11. Global tuberculosis report 2021. WHO 2021.
12. Granado J, Catarino A. Cutaneous tuberculosis presenting as lupus vulgaris. *International Journal of Infectious Diseases*. 2020 Jul 1;96:139-40.
13. Bravo FG, Gotuzzo E. Cutaneous tuberculosis. *Clinics in dermatology*. 2007 Mar 1;25(2):173-80.
14. Pai VV, Naveen KN, Athanikar SB, Dinesh US, Divyashree A, Gupta G. A clinico-histopathological study of lupus vulgaris: A 3 year experience at a tertiary care centre. *Indian Dermatology Online Journal*. 2014 Oct;5(4):461.
15. Choudhury AM, Ara S. Cutaneous tuberculosis--a study of 400 cases. *Bangladesh Medical Research Council Bulleti*n. 2006 Aug 1;32(2):60-5.
16. Bhutto AM, Solangi A, Khaskhely NM, Arakaki H, Nonaka S. Clinical and epidemiological observations of cutaneous tuberculosis in Larkana, Pakistan. *International journal of dermatology*. 2002 Mar;41(3):159-65.
17. Østerlind A, Hou-Jensen K, Møller Jensen O. Incidence of cutaneous malignant melanoma in Denmark 1978-1982. Anatomic site distribution, histologic types, and comparison with non-melanoma skin cancer. *British journal of cancer*. 1988 Sep;58(3):385-91.
18. Pai VV, Naveen KN, Athanikar SB, Dinesh US, Divyashree A, Gupta G. A clinico-histopathological study of lupus vulgaris: A 3 year experience at a tertiary care centre. *Indian Dermatology Online Journal*. 2014 Oct;5(4):461.
19. Solis AH, González NE, Cazarez F, Pérez PM, Diaz HO, Escobar-Gutierrez A, Ortiz IC, González HG, Reding-Bernal A, Sabido RC. Skin biopsy: a pillar in the identification of cutaneous Mycobacterium tuberculosis infection. *The Journal of Infection in Developing Countries*. 2012 Aug 21;6(08):626-31
20. Yeboah-Manu D, Asante-Poku A, Asan-Ampah K, Ampadu ED, Pluschke G. Combining PCR with microscopy to reduce costs of laboratory diagnosis of Buruli ulcer. *The American journal of tropical medicine and hygiene*. 2011 Nov 11;85(5):900.
21. Guo Y, Zhou Y, Wang C, Zhu L, Wang S, Li Q, et al. Rapid, accurate determination of multidrug resistance in M. tuberculosis isolates and sputum using a biochip system. *The International journal of tuberculosis and lung disease*. 2009 Jul 1;13(7):914-20
22. El Fekih N, Fazaa B, Kerkeni N, Sfia M, Zeglaoui F, Zermani R, Bouacha H, Kamoun MR. Le lupus tuberculeux. *Medecineet maladies infectieuses*. 2009 Jun 1;39(6):409-12.
23. Zahaf A, Turki H, Masmoudi A. Lupus tuberculeux [Tubercular lupus]. *Ann Dermatol Venereol*. 2004 May;131(5):503-7. French. doi: 10.1016/s0151-9638(04)93652-6. PMID: 15235546.

Abbreviations Acid-fast bacilli (**AFB**), Bacillus Calmette–Guérin (**BCG**), Drug-resistant TB (**DR-TB**), Human Immunodeficiency Virus (**HIV**), Lupus vulgaris (**LV**), Polymerase Chain Reaction (**PCR**), Rifampicin-resistant TB (**RR -TB**), Tuberculosis (**TB**).

Conflict of interest: Author has nothing to disclose.

Funding: Nothing apart from self-funding.