

“Were-Wolf” Cutaneous Tuberculosis^{1, †}

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ABSTRACT

Lupus vulgaris is a variant of cutaneous tuberculosis. Its more destructive and mutilating clinical forms have become rarer in consonance of a general decline of cutaneous tuberculosis. It is rarely seen now in developed countries due to stringent control measures, improved quality of living and effective therapeutic regimens. Misdiagnosis, neglect, or late diagnosis may result in severe, ulcerative and mutilating “wolf eaten” skin lesions.

This paper describes four such cases of “were-wolf” cutaneous tuberculosis. Early diagnosis and treatment is important to prevent much of the disfigurement.

RÉSUMÉ

Le lupus vulgaire est la variante la plus commune de la tuberculose cutanée. Ses formes cliniques plus destructives et plus mutilantes sont devenues rares, en relation avec un déclin général de la tuberculose cutanée. Il est rarement observé maintenant dans les pays développés où il existe des mesures rigoureuses de contrôle, une qualité de vie améliorée et des traitements efficaces. Des erreurs de diagnostic, des négligences ou encore un diagnostic tardif peuvent résulter en des lésions cutanées ulcéreuses et mutilantes dites ‘en morsure de loup.’

Cet article décrit quatre de ces cas de tuberculose cutanée dite ‘de loup.’ Un diagnostic précoce et un traitement sont importants afin d’éviter que le patient ne soit défiguré.

RESUMEN

Lupus vulgaris es una variante común de la tuberculosis cutánea. Sus formas más destructivas y mutilantes han llegado a ser muy raras, en consonancia con la disminución general de la incidencia de la tuberculosis cutánea. Actualmente se observa raramente en los países desarrollados debido a las estrictas medidas de control, al mejoramiento en la calidad de vida y a los regímenes terapéuticos efectivos. El diagnóstico equivocado, el descuido, o el diagnóstico tardío, favorecen el desarrollo de lesiones dérmicas severas, ulcerativas y mutilantes, conocidas como “mordidas de lobo.”

Este artículo describe 4 casos de tuberculosis cutánea tipo “mordida de lobo.” El diagnóstico y tratamientos tempranos son importantes en la prevención de esta condición clínica desfigurante.

Lupus vulgaris (L V) is a chronic, progressive form of cutaneous tuberculosis occurring in individuals with a moderate to high degree of immunity. The characteristic lesion is a plaque composed of reddish brown nodules, which on diascopy reveals an “apple jelly” color. The disease process

is usually associated with scarring and atrophy causing considerable tissue destruction over many years. The common clinical forms include papular, nodular, plaques, ulcerative and tumid lesions but atypical morphology is becoming more common. Uncommon forms, such as frambosiform, gangrenous or ulcero-vegetating type of lesions too have been documented (³). The term “lupus” means wolf; perhaps the name alludes to the appearance of a face that has been chewed by a wolf (¹). Such “wolf eaten” appearance is uncommon and seen only in the severe, ulcerative, mutilating type of lupus vulgaris of the face.

The more destructive and mutilating forms have become rarer, at least in immunocompetent patients, due to better awareness, effective treatment regimens

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FIG. 1. Mutilating facial lesions of lupus vulgaris. **Note:** Parrot-beak nose and cicatricial ectropion.

and better access to health care facilities. However, the diagnosis of LV may often be delayed when the index of suspicion is low, especially in the developed countries, where the disease has become very rare (¹⁵). As the disease has potential to mutilate when left untreated, leaving deforming scars and disfigurement, an early diagnosis is of paramount importance.

We present here four cases of this disease that is not so rare in developing countries where the importance of high clinical suspicion, early diagnosis and treatment can not be over emphasized.

Case 1. This 24-yr-old male patient presented with multiple, asymptomatic, and slowly progressive facial lesions and deformed nose. History revealed that about 10 yrs earlier he had developed a nodulo-plaque lesion over right submandibular area. Similar new lesions continued to appear all over the face in the next 4 to 5 yrs. He had also developed deformity of the tip of the nose and right eye during this period. There was no history of any major systemic

illness any time during the course of his disease. For his cutaneous lesions, various medical practitioners had treated him at different times during his illness, but to no avail.

Cutaneous examination showed (Fig. 1) multiple, multicentric, papulo-nodulo-plaque lesions of variable size and shapes over both cheeks, the malar area of face, nose and upper lip. The lesions were discrete, but had coalesced at places to form bigger lesions. A few lesions also showed subtle, adherent scales. There was loss of both *alae nasi* (more loss on the left), contractures of the right upper eyelid with cicatricial ectropion, loss of eyelashes and partial destruction of lid margins. The eyelashes of the left eye were partially absent due to lesions over lid margins. Both nasolacrimal ducts were blocked resulting in epiphora. A few lesions showed healing with atrophic, paper-thin scars. Examination of the nasal cavity revealed partial destruction of the nasal septum and extension of facial lesions inside. There was no re-



FIG. 2. Destruction of the tip of the nose and nasal septum.

gional lymphadenopathy . Oral mucosa, hair, nails, and other systemic examination were normal.

Laboratory investigations, including complete blood counts, ESR, blood sugar , hepatorenal function tests, x-ray films for chest and paranasal sinuses, ultrasonography of abdomen, HIV serology, urinalysis, and sputum examination for acid-fast bacilli (AFB), did not show any abnormality. The Mantoux test was positive, measuring 15×20 mm. Histopathology from one of the lesions showed an unremarkable epidermis, a few epitheloid cell granulomas with Langhan's giant cells in the dermis and at places small areas of necrosis. No acid-fast bacilli (AFB) could be demonstrated either in direct smears, histopathologic sections or from culture of biopsy specimen on Loewenstein-Jensen (LJ) medium.

Treatment with rifampicin 450 mg/day , isoniazid 300 mg/day , ethambutol 800 mg/day and pyrazinamide 1250 mg/day was

effective within a month in checking the progress of the disease and further tissue destruction. This treatment was continued for one month more. During the continuation phase of the next four months the patient received only rifampicin and isoniazid. All the lesions healed completely but with disfiguring scarring.

Case 2. This 40-yr-old male patient was hospitalized with progressive loss of his nose tip associated with foul smelling discharge. He stated that a year earlier he had an erythematous, papulo-nodulo-plaque lesion over the tip of the nose associated with swelling of the nose and surrounding area. The lesion was progressive in size and had resulted in loss of tip of the nose during this period. He had no associated systemic symptoms at any time during the course of his disease. Treatment from local practitioners had not been helpful.

Cutaneous examination (Fig. 2) revealed destruction of the tip of the nose and nasal



FIG. 3. Infiltrated, fissured, crusted and hemorrhagic lesions of lupus vulgaris involving nostrils, lips and surrounding skin.

septum, exposing a nasal cavity full of foul smelling exudate. There was erythema and edema of surrounding skin. An ill defined, erythematous, infiltrated, and locally crusted plaque involved the philtrum, nose, left cheek, and nasal bridge. A few small and isolated plaques were also present on the forehead and left infra-orbital area. There was no regional lymphadenopathy. Examination of oropharynx, hair, nails and other systems did not reveal any abnormality.

A high ESR (70 mm in 1st hr) and negative Mantoux test were the only abnormalities found in the various laboratory investigations carried out. Histopathology was consistent with lupus vulgaris. AFB could not be demonstrated in direct smears, histopathology or culture.

The patient was treated with rifampicin 450 mg/day, isoniazid 300 mg/day, ethambutol 800 mg/day, and pyrazinamide 1250 mg/day for the initial two months. Lesional erythema and induration subsided within the first month of treatment. The treatment with rifampicin 450 mg/day and isoniazid 300 mg/day was continued for next four months. All lesions healed with scarring and disfigurement at the end of treatment.

Case 3. This 16-yr-old girl was hospitalized with a large, ulcerated, crusted lesion involving the nostrils and lips, of four years duration. It had started as a small nodulo-plaque lesion over the upper lip that progressively enlarged to involve the nearby areas. She had no other associated systemic symptoms.

Cutaneous examination showed a large ulcerated lesion involving *alae nasi*, nostrils, and the entire upper and lower lips. It was covered with thick hemorrhagic crusts, with fissuring and a tendency to bleed. There was diffuse erythema, edema, and infiltration of surrounding skin extending irregularly beyond the central crusted lesion (Fig. 3). Examination of the oral cavity showed irregular, erythematous, granulating patches over the hard palate. The nasal cavity could not be examined due to exudates and bleeding from the lesions. The nasopharynx did not show any lesions.

Laboratory investigations did not reveal any abnormalities. The Mantoux test was positive, measuring 20 × 24 mm. Histopathology showed features of lupus vulgaris. AFB could not be demonstrated in any of the specimens.



FIG. 4. A disfigured ear lobe.

The lesions showed healing after four weeks of rifampicin 450 mg/day, isoniazid 300 mg/day, ethambutol 600 mg/day and pyrazinamide 1000 mg/day. After two months of intensive treatment with these drugs she showed further improvement. Treatment was continued for four months with rifampicin 450 mg/day and isoniazid 300 mg/day. Scarring and cicatricial microstomia remained afterwards.

Case 4. This 28-yr -old female patient presented to us with almost complete loss of right earlobe. It had started about 10 yrs prior, following a cosmetic ear piercing, which had developed into an asymptomatic, slowly progressing non-healing ulcerative lesion having intermittant purulent discharge. Slowly and steadily her earlobe was lost as the tissue eroded (Fig. 4).

Cutaneous examination revealed an absent right earlobe almost extending to the cartilage. The residual part had ragged edges, erythematous and granulomatous infiltration and crusting in places. There was no regional lymphadenopathy. Hair, nails, and mucous membranes were normal.

There were no associated systemic symptoms. Systemic examination did not reveal any abnormality.

Laboratory investigations, carried out as in other cases, did not demonstrate any abnormality. Histopathology showed a normal epidermis, but the dermis had a few ill-formed epithelioid cell granulomas. The dense inflammatory lymphoplasmacytic infiltrate extended into and involved the subcutaneous tissue. Staining for AFB was positive. The Mantoux test could not be carried out due to non-availability of tuberculin at the time. Culture of the biopsy specimen on LJ medium did not show growth of mycobacteria.

She was lost to follow-up after initiation of antituberculosis treatment.

DISCUSSION

Cutaneous tuberculosis has declined after the introduction of highly effective antituberculosis treatment regimens. In an Indian study (¹¹), cases of cutaneous tuberculosis comprised only 0.15% of all dermatology out-patients compared to previously re-

ported incidence of 0.25% and 0.59%^(9, 13). Lupus vulgaris is the most common variant of cutaneous tuberculosis, accounting for nearly 59% of secondary skin tuberculosis cases in India with an average prevalence of 0.37% among general dermatology patients^(7, 12). It has become so rare in USA that "Lupus," unqualified, means lupus erythematosus and not lupus vulgaris⁽¹⁾.

Lupus vulgaris is acquired exogenously by direct inoculation of the bacilli or endogenously via hematogenous or lymphatic spread from associated tuberculosis of other organs. Primary inoculation tuberculosis comprises 0.14% of all primary tuberculous lesions, i.e., tuberculous chancre and the primary tuberculous complex⁽¹⁴⁾. The latter is a cutaneous analog of as the Ghon complex primary pulmonary tuberculosis and evolves into inoculation lupus vulgaris. Although primary inoculation lupus vulgaris has been reported^(8, 10) it is not very frequent. The disease shows a predilection for the face and almost 80% of the lesions are seen over the head and neck. On the face it tends to involve the nose, earlobes, upper lip and frequently extends to the contiguous mucosal surfaces.

Nasal lesions start as nodules that bleed easily and then ulcerate, sometimes destroying the cartilage. Destruction of the whole nose may occur leaving only orifices and the posterior parts of septum and turbinate visible. The upper-lip, when involved, becomes swollen, thickened, and fissured having adherent crusts and a tendency to bleed. Granulating, vegetating, or ulcerative lesions of the buccal mucosa, palate, gingiva, or oropharynx may occur from direct extension or by lymphatic spread from nasal lesions.

Spontaneous healing may occur but not without scarring, atrophy, contractures, and tissue destruction. On the face, such mutilations and scarring leads to "parrot-beak" nose, ectropion and atrophied lips that may eventuate in a "were-wolf" appearance.

Sarcoidosis and rosacea may sometimes simulate early lupus vulgaris. Histopathology and tissue culture studies may also be required as clinical differentiation from several diseases is often difficult, including tertiary syphilis, chronic discoid lupus erythematosus, deep mycoses (sporotrichosis, blastomycosis, chromoblastomycosis), leishmaniasis,

and—more commonly—leprosy. It is important that biopsies taken are deep enough to be representative.

Demonstration of a classical tubercular granuloma on histopathology is diagnostic but caseation necrosis is usually sparse or absent⁽⁶⁾. Demonstration of AFB in Ziehl-Neelson stained tissue smears, or their recovery in culture on LJ medium is disappointing in most instances. AFB were present in only 5% patients of lupus vulgaris in a recent study⁽⁸⁾. Scattered, non-caseating, compact epithelioid cell granulomas sparsely surrounded by lymphocytes are characteristic of sarcoidosis. Tuberculoid leprosy is differentiated by neural and perineural granulomatous inflammation. Tertiary syphilis shows more pronounced vascular changes and plasma cell infiltrates. Non-specific tuberculoid infiltrates without formation of typical tubercles is seen in rosacea. Demonstration of causative organisms in histologic sections or cultures will be diagnostic in leishmaniasis and deep mycoses.

The diagnostic value of a positive Mantoux test is ambiguous if the patient has had BCG vaccination or other mycobacterial exposure. A strongly positive test is significant but the sensitivity decreases with advancing age, early treatment, and conditions that reduce delayed hypersensitivity. Other than these factors and technical errors (e.g., subdermal injection of tuberculin), about 5% of patients do not react to ordinary intermediate strength of tuberculin used, for reasons unknown⁽⁴⁾.

Polymerase chain reaction (PCR) provides rapid, specific and sensitive testing for *M. tuberculosis*. In polymerase chain reactions (PCR), discrete fragments of DNA are specifically amplified from specimens in cutaneous tuberculosis. A specific *M. tuberculosis* genome fragment, mtp 40, has been identified that allows prompt differentiation from atypical mycobacteria⁽¹⁶⁾. The high cost and need of expertise, however, limit its routine use.

All of our patients exhibited classic features of lupus vulgaris. An early diagnosis and specific treatment would have prevented much of the mutilation. It is baffling that all these patients neglected themselves or could not be diagnosed for years especially in this era of diagnostic and therapeutic advancements. It seems that in the absence of symp-

toms such as disfigurement (even of the face) remains of little consequence in view of the high cost of treatment or specialized consultations. We feel that a high index of clinical suspicion is of foremost importance in the diagnosis of cutaneous tuberculosis during the early stage of the disease. This is particularly true for areas where the disease is seen rarely. Nevertheless tuberculosis remains a disease of great importance as it can be treated effectively.

In view of emerging drug resistant strains only multi-drug chemotherapy is now recommended for all forms of tuberculosis, and a strict compliance to the regimen is imperative. It needs no modification in dermatological practice. The standard regimen consists of rifampicin (10 mg/kg, up to 600 mg/day), isoniazid (5 mg/kg, up to 300 mg/day), ethambutol (15 mg/kg/day) and pyrazinamide (15–30 mg/kg, up to 2 gm/day) given for initial 2-months in the intensive phase. This is then followed by treatment with rifampicin and isoniazid during the continuation phase for next 4-months. The reported incidence of *M. tuberculosis* resistance, to one or more first line drugs, is 10–14% in the U.K. and the U.S.A. (3).

It is now possible to detect drug resistance by molecular means or by using the light-producing enzyme Luciferase, the gene for which has been added to mycobacteriophage (2), instead of more time consuming culture and sensitivity techniques. Because the drug resistance patterns vary at a given time and place it is advisable to consult local specialists well-versed in this particular problem, as well as for their expertise in managing difficult cases and drug intolerance.

REFERENCES

1. ARNOLD, H. L. JR., ODOM, R. B., and JAMES, W. D. Mycobacterial diseases: Lupus vulgaris. In: *Andrews Diseases of the Skin*, 8th edn. Philadelphia: WB Saunders Co., 1990. pp. 377–379.
2. FRANCK, N., and CABIE, A. The reemergence of tuberculosis and atypical mycobacterial diseases. *Curr. Opin. Dermatol.* (1995) 249–253.
3. GAWKRODGER, D. J. Mycobacterial infections. In: *Textbook of Dermatology*, 6th edn. Oxford: Blackwell Science, 1998. pp. 1181–1214.
4. KAKAKHEL, K. U., and FRITSCH, P. Cutaneous tuberculosis. *Int. J. Dermatol.* **28** (1989) 355–362.
5. KAUR, C., SARKAR, R., and KANWAR, A. J. How safe is nose-piercing? Inoculation cutaneous tuberculosis revisited. *Int. J. Dermatol.* **42** (2003) 645–646.
6. LEVER, W. F., and SCHAUMBERG-LEVER, G. Bacterial diseases. In: *Histopathology of the Skin*, 7th edn. Philadelphia: J. B. Lippincott, 1990. pp. 318–351.
7. RAMESH, V., MISRA, R. S., and JAIN, R. K. Secondary tuberculosis of the skin. *Int. J. Dermatol.* **26** (1987) 578–581.
8. RAMESH, V., SAMUEL, B., and MISRA, R. S. *In-situ* characterization of cellular infiltrates in lupus vulgaris indicates lesional T cell activation. *Arch. Dermatol.* **126** (1990) 331–335.
9. SATYANARAYANA, B. V. Tuberculosis: a brief review together with statistical analysis and observation. *Indian J. Dermatol. Venereol. Leprol.* **29** (1963) 25–40.
10. SEHGAL, V. N. Inoculation lupus vulgaris. *Int. J. Dermatol.* **19** (1992) 58–60.
11. SEHGAL, V. N., JAIN, V. K., and SRIVASTAVA, G. Changing pattern of cutaneous tuberculosis: a prospective study. *Int. J. Dermatol.* **28** (1989) 231–236.
12. SEHGAL, V. N., SRIVASTAVA, G., K. HURANA, V. K., SHARMA, V. K., BHALLA, P., and BEOHAR, P. C. An appraisal of epidemiologic, clinical, bacteriologic histopathologic and immunologic parameters in cutaneous tuberculosis. *Int. J. Dermatol.* **26** (1987) 521–526.
13. SINGH, G. Lupus vulgaris in India. *Indian J. Dermatol. Venereol. Leprol.* **40** (1974) 257–260.
14. TAPPEINER, G., and WOLFF, K. Tuberculosis and other mycobacterial infections. In: *Fitzpatrick's Dermatology in General Medicine*, 5th edn. New York: McGraw Hill, 1999. pp. 2274–2292.
15. WARIN, A. P., and WILSON-JONES, E. Cutaneous tuberculosis of the nose with unusual clinical and histological features leading to delay in the diagnosis. *Clin. Exp. Dermatol.* **2** (1977) 235–242.
16. WEI, C. Y., LEE, C. N., CHU, C. H., HAWANG, J. J., and LEE, C. P. Determination of the sensitivity and specificity of PCR assays using different target genes for the detection of *Mycobacterium tuberculosis*. *Kaohsiung J. Med. Sci.* **15** (1999) 396–405.