

A Rare Enigmatic Case of a 24-Year Old Female with Cutaneous Tuberculosis (Lupus Vulgaris) Arising on Burn Scar Lesion *

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ABSTRACT

Cutaneous tuberculosis, a rare dermatologic condition with a wide spectrum of clinical findings depending on the source and immune status of patient. The common subtype is Lupus Vulgaris which is extremely chronic and progressive type

Objective: To discuss the summary of the case, management options and outcomes of the management options.

Case Summary (Methods): Herein a case of a 24-year-old female presenting with two year history of gradual appearance of pruritic and tender erythematous plaque on the left forearm arising on scald burn lesions sustained twenty years ago. Patient is generally healthy with no history of pulmonary tuberculosis (PTB) nor exposure to close contacts. Skin punch biopsy showed caseating tuberculoid granulomas in the dermis consistent with cutaneous tuberculosis. Other work up for tuberculosis such as tissue culture, GeneXpert, PCR, tuberculin skin test and chest x-ray were all negative. Patient was started with a therapeutic trial of standard treatment regimen for tuberculosis.

As part of multidisciplinary care, the patient was referred to ophthalmology service due to complaints of blurring of vision which started one month after treatment initiation. She was managed as a case of TB Uveitis and was given Oral Prednisone with unrecalled dosage. She was likewise referred to plastic surgery and infectious disease for co-management of hypertrophic scars and tuberculosis.

Conclusion: Treatment of cutaneous tuberculosis is anti-Koh's (HRZE) medication and requires a multi-specialty approach. After 12 months of treatment, patient noted 80% improvement which greatly contributed to her increased self-esteem and patient satisfaction. The highlight of this case was to report a rare clinical manifestation of cutaneous tuberculosis arising on burn scar lesion which is the first case report in the Philippines.

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INTRODUCTION

Cutaneous tuberculosis or TB of the skin is a rare manifestation which presents with a wide array of clinical findings depending on the source of infection: Endogenous or Exogenous route of infection and the immune status of the patient.^[2] Tuberculosis is highly endemic especially in our country. It is estimated that 14% of TB patients present the extrapulmonary form of the disease and 1–2% of these have cutaneous presentation.^[1,2,8]

Lupus vulgaris, a subtype of cutaneous tuberculosis, is the most common form of cutaneous tuberculosis comprising of 64%.^[1,3] It is a chronic, progressive, endogenous paucibacillary form of cutaneous tuberculosis which presents primarily in a previously sensitized individual.^[1] Various types of lupus vulgaris include plaque, ulcerative, mutilating, vegetative, papular or nodular and hypertrophic forms. Of the different types, the most common of which is the plaque form which presents with irregular borders, surface with can either be smooth or covered with psoriasiform scales. Initial lesions would present as brownish to red, soft, solitary plaque, having a centrifugal growth which eventually coalesce to form plaques. The most common location of Lupus Vulgaris are the lower half of the body involving the legs, thigh and feet however, unusual locations like the extremities and face can also be affected.^[5,6] The epidemiology greatly affects female with a 2:3 ratio to males.^[1] The average prevalence of 0.37% among the general skin patients.^[7]

The diagnosis of this disease is a crucial factor since there are numerous published cases that were often misdiagnosed due to variations in clinical presentation. Most of the diagnostic methods for cutaneous tuberculosis confer lower sensitivity and specificities.^[3] There are numerous evidence supporting the role of therapeutic trial when diagnostic work up resulted to a negative result. If left untreated, this disease can cause extensive destruction and disfigurement which eventually can lead to development of squamous

cell carcinoma. The aim of this paper is to impart the importance of a good clinical correlation with a histological and diagnostic work up results in a multidisciplinary approach among inter-professional team members to optimize outcome results for our patients.

CASE REPORT

We are presented with a 24-year-old female, Filipino, housewife, from Bulacan city. Her chief complaint was the appearance of erythematous plaques arising on burn scar lesions that occurred twenty years ago. History started two years prior to consult when the patient noted appearance of few erythematous plaque on the left arm associated with pruritus. Patient self-medicated with topical application of BL cream (clobetasol + ketoconazole) applied once a day which provided temporary relief of pruritus with partial resolution of erythematous skin lesions on affected areas. In the interim, the patient noted gradual progression of similar lesions now with pustules and erosions specifically confined on areas of burn scar lesions on the right arm, trunk, left inner thigh, back and face associated pruritus and tenderness. Patient had no history of PTB nor exposure to close contacts with PTB. She denies weight loss, fever and night sweats. There was no history of non-resolving wound, and exposure to UV radiations. Numerous consults were done with different physicians wherein diagnosis was not disclosed and was prescribed with fourteen days of unrecalled dosage of oral antibiotics wherein the patient noted no resolution of skin lesions. This led the patient to sought consult in our institution for further evaluation and work up.

The review of systems was generally unremarkable. Patient had a history of a 3rd degree scald burn lesion at three years of age. The patient was hospitalized in a tertiary hospital with unrecalled management and disposition. Family history revealed a history of Pulmonary tuberculosis – completed six months of treatment on the maternal side, there was no exposure to

relatives who had PTB at the course of the disease. The patient is a non-smoker, non-alcoholic beverage drinker and denies illicit drug use. The patient claims to be compliant with sunscreen use and sun protective clothing prior sun exposure. There was no history of exposure to UV radiation.

Physical examination was generally unremarkable except for BMI of 28.1- overweight. No palpable lymph nodes were noted on the body. Cutaneous examination revealed multiple, well

defined, irregularly shaped, erythematous coalescing plaque topped with scaling, some with hemorrhagic crusts and excoriations on the bilateral side of the face, chest, abdomen, back, bilateral upper extremity and inner thigh. Dermoscopy examination showed Irregular dilated vessels, yellow to orange areas with follicular plugging, hemorrhagic crust and scales on the right and left side of the face, chest, abdomen, arms and back. Diascopy examination was negative for apple jelly sign.



Figure 1 A-C. Multiple, well defined, irregularly shaped, erythematous coalescing plaque topped with scaling on the face and shoulders



Figure 2 A-B. Multiple, well defined, irregularly shaped, erythematous coalescing plaque topped with scaling some with hemorrhagic crusts and excoriations on the chest, abdomen and back.



Figure 3 A-B.



Figure 4 A-B. Multiple, well defined, irregularly shaped, erythematous coalescing plaque topped with scaling on the bilateral upper extremity.

A 4mm skin punch biopsy was done which showed tuberculoid granulomas in the dermis with caseation necrosis, dermal lymphocytic infiltrates

and several Langhans type multinucleated giant cells. These findings were consistent with cutaneous tuberculosis.

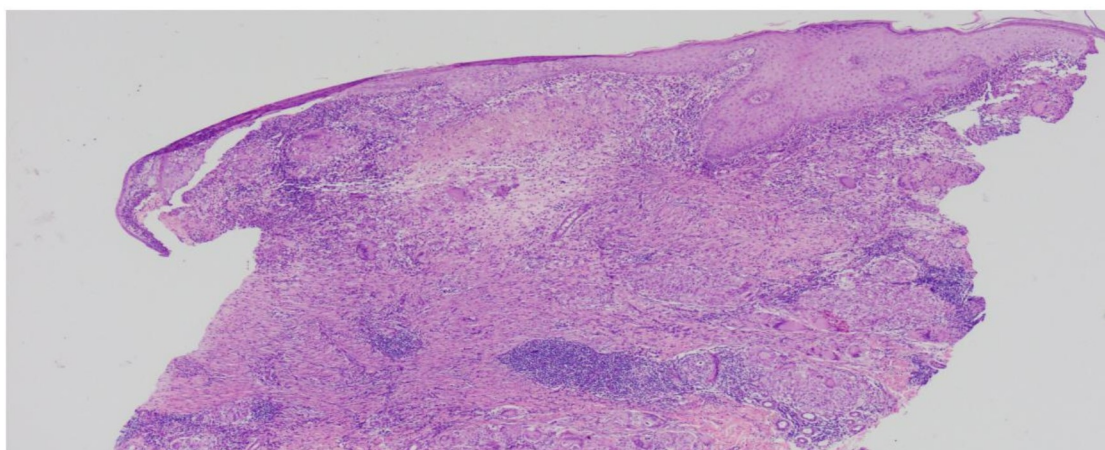


Figure 5. Histopathology (H & E stain) of the patient's skin showing tuberculoid granulomas in the dermis, lymphocytic infiltrates and Langhans type multinucleated giant cells in LPO.

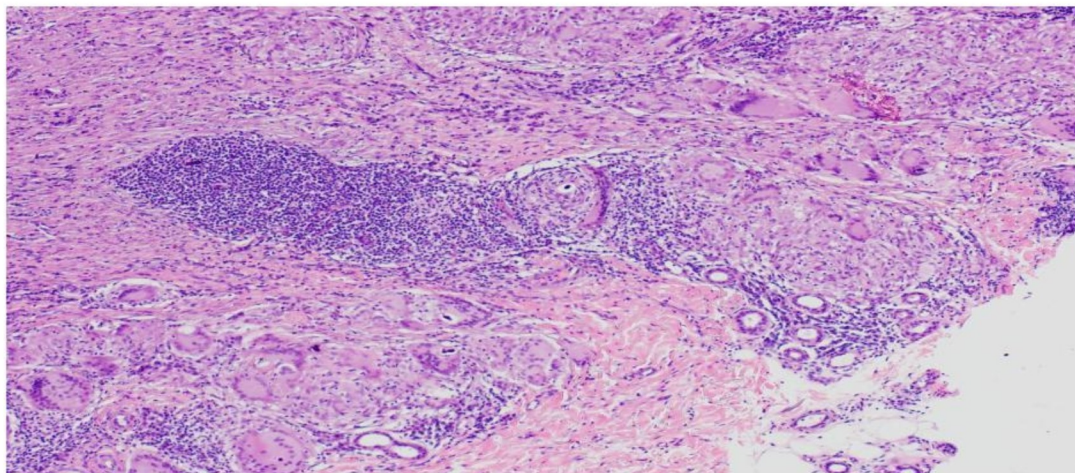


Figure 6. Histopathology (H & E stain) of the patient's skin showing tuberculoid granulomas in the dermis, lymphocytic infiltrates and Langhans type multinucleated giant cells in HPO

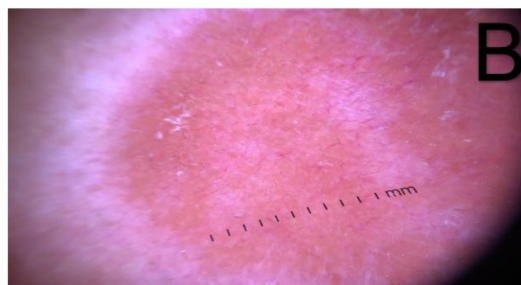


Figure 7 A-B. Dermoscopy examination of the Left (A) and Right(B) side of the face showing linear branching vessels, yellow to orange areas with white scales

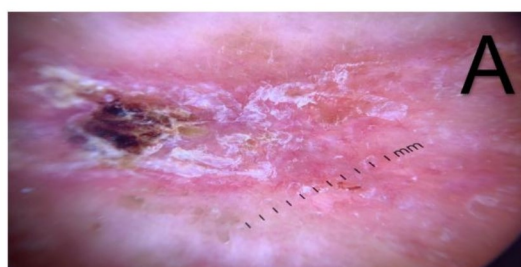


Figure 8 A-B. Dermoscopy examination of the chest showing linear branching vessels, yellow to orange areas with follicular plugging and hemorrhagic crust and white scales on the chest



Figure 9 A-B. Negative apple jelly sign as depicted by the diascopy examination of the abdomen (A) and left side of the face (B)

Other ancillary tests such as complete blood count showed monocytosis, eosinophilia and thrombocytosis, Blood chemistry showed a mildly elevated liver enzymes. Urinalysis and Chest Xray was generally unremarkable. Results of the slit skin smear showed no evidence of bacilli; fite faraco stain was negative. Fungal culture showed no fungus isolated after 4 weeks incubation. Gram staining of the wound tissue showed moderate pus cells, few epithelial cells with no organisms seen. Cutaneous tuberculosis work up such as tissue GeneXpert, sputum GeneXpert, tissue culture and PCR all yielded a negative result.

The patient was started with anti-tuberculosis medications: intensive phase consisting of Rifampicin 450mg/day, Isoniazid 300mg/day, Pyrazinamide 1500mg/day and Ethambutol 750mg/day and maintenance phase consisting of Rifampicin 600mg/day and Isoniazid 600mg/day. Patient was also given zinc + copper + sucralfate cream BID on affected lesions and mild soap for daily bathing. The patient was then referred to the service of ophthalmology, infectious disease and plastics surgery for co-management.

The patient noted an 80% improvement overall with noted decrease in the appearance of erythema and scaling all over the body. The plastic surgery service appraised the patient for possible excision and local advancement flap to address contractures on the sternal and back area. One month after initiation of treatment, patient developed blurring of vision and is being managed by Ophthalmology service as a case of Anterior Uveitis probably TB Uveitis; intermediate uveitis bilateral eye and is currently maintained on prednisone eye drops and on tapered oral prednisone.

DISCUSSION

Lupus vulgaris, a subtype of cutaneous tuberculosis, is the most common form of cutaneous tuberculosis.^[1] It is an extremely chronic, progressive, endogenous paucibacillary form of cutaneous tuberculosis which occurs primarily in the previously sensitized individual especially that tuberculosis is highly endemic in our country. Lesions present as brownish to red, soft, solitary plaque, having a centrifugal growth which eventually coalesce into a plaque. The plaques grow peripherally with serpiginous borders accompanied by central discoloration and atrophy.^[3] Progression is characterized by elevation,

a deeper brownish and formation of a plaque. The most common location of Lupus Vulgaris are the lower half of the body involving the legs, thigh and feet, however, the extremities and the face can also be affected as seen in our patient. Spontaneous involution may occur, and new lesions may arise within old scars as depicted by the patient. Female are more likely to be affected 2 to 3 times as often as males.^[1] According to the Philippine Dermatological Society, there are a total of 260 cases of cutaneous tuberculosis, of the 260 cases diagnosed since 2011, 129 cases of which are lupus vulgaris type. Based from the data provided, there is a predominance of female genders presenting with the disease most commonly at second to third decade of life, however, it can occur at an early age. In our institution, we have a total of 9 cases of biopsy proven cutaneous tuberculosis since 2015. However, there are no other data supporting appearance of cutaneous tuberculosis on burn scar in our local setting, hence an enigmatic presentation.

The pathophysiology of CTB is attributed to Mycobacterium tuberculosis- occasionally M. bovis or BCG vaccination and can be contracted either primarily by direct inoculation of the bacilli or at the site of previous BCG vaccination individuals with moderate immunity or secondarily by hematogenous and lymphatic spread from an underlying distal focus.^[1,3] After infection, the macrophages in the infected tissues are first activated to eliminate the bacilli at the infected site. Monocytes, lymphocytes, neutrophils, and dendritic cells are then recruited by the chemokines and cytokines released by macrophages which eventually lead to granuloma formation.^[4] The host characteristics, the load and pathogenicity of the bacillus strain, and the method of infection determine the clinical outcome of CTB.^[4]

The diagnosis of cutaneous tuberculosis can either be bacteriologically confirmed or clinically diagnosed. For bacteriologically confirmed cases, patient with a smear/culture/rapid diagnostic test from a biological specimen in an extra pulmonary site positive for AFB or MTB complex and for clinically diagnosed cases, patient with histological and or clinical or radiologic evidence consistent with active extra pulmonary tuberculosis. The absolute criteria consist of finding of M. tuberculosis from tissue culture, inoculation on guinea pig, or positive result on PCR. The relative criteria are based on history taking and clinical manifestations which supported for the diagnosis of cutaneous TB, active TB found on other organs, finding of AFB on lesions, finding of tuberculous granuloma on histopathological examination, positive tuberculin test, and responsiveness toward anti-TB medications.^[8]

The differentials for Cutaneous tuberculosis includes the following:

Squamous cell carcinoma, the second most common skin cancer after basal cell carcinoma and the most common skin cancer in immunosuppressed organ transplant recipients worldwide. SCC was initially considered as a differential due to the typical clinical finding of skin-colored to erythematous plaques with marked hyperkeratosis on sun-exposed areas of the skin such as the face and the forearm which was present in the patient, however, was ruled out since lesions depicted by the patient are not seen on a background of pre-invasive tumors or in situ tumors such as actinic keratosis or Bowen's disease which are characteristic of SCC. Risk factors attributed to the growth of SCC involves increasing age, red hair, blue eye, white complexion, and increased sun/ UV exposure. All aforementioned risk factors and dermoscopy findings such as white

structureless area, looped vessels and central keratin were not presented in the patient, hence this disease is less likely.

Hansen's disease, a chronic granulomatous disease affecting mainly the skin and nerves caused by the obligate intracellular pathogen, mycobacterium leprae which infects mucous cutaneous tissues and peripheral nerves leading to loss of sensation of the skin. Hansen's disease was considered as a differential in this patient due to the presence of erythematous plaques on the body, however, was ruled out since Hansen's disease usually presents with loss of sensation in lesions associated with hypohidrosis, alopecia and nerve enlargement which is not present in the patient. The evolution of Hansen's disease which usually starts with hypopigmented macules or patches and dermoscopy finding yellow white areas, distorted pigment network, widened skin furrows/ chrysalis-like structures, slight diminution of appendageal structures and hairs were not depicted by the patient, hence this disease entity was ruled out.

Treatment options for Cutaneous tuberculosis following the standard regimen of WHO recommendation consists of Isoniazid, Rifampicin, Pyrazinamide and ethambutol are the first line treatment for all types of cutaneous tuberculosis. The minimum duration of treatment is 6 months- 2 months of intensive phase consisting of Rifampicin 450mg/day, Isoniazid 300mg/day, Pyrazinamide 1500mg/day and Ethambutol 750mg/day and 4-months of maintenance phase consisting of Rifampicin 600mg/day and Isoniazid 600mg/day. The patient was initially given a course of 6 months duration of anti- tuberculosis medications.

In 2018, Akinola et al reported a case of a 13 year old female who presented to Ear, Nose and Throat (ENT) clinic with a non-healing wound on the

tip of the nose extending on the bridge for 4-years duration. Despite a negative result for tuberculosis work up, the patient was given quadruple anti-tuberculosis medication for 7 months wherein resolution of lesions were noted. This was the basis for the treatment plan to our patient with marked improvement of skin lesions.^[1,10]

In 2019, Mann et al emphasized the importance of the histopathology (52.0%) as a diagnostic tool in Cutaneous Tuberculosis^[2], since in a significant portion of cases, the cultures are negative which is similar to our patient. Another study published 2018 by Khadka et al, claimed that a negative culture would be attributed to a decreased bacillary load and that a negative PCR/GeneXpert is linked to an unevenly microbial distribution in paucibacillary forms of cutaneous tuberculosis, specifically lupus vulgaris.^[3,5] The negative result from the tissue culture, the atypical localization of the lesion and its characteristic were factors which contributed to the diagnostic dilemma in our case similar to various journals published.

A case by Hagiwara et al presented with a similar clinical presentation to our patient. A 66-year old Japanese woman with squamous cell carcinoma arising from lupus vulgaris on an old burn scar on the left lower extremity was given a therapeutic trial of HRZE medications despite negative diagnostic work up. Resolution of lesions were noted after imitiation of medications.^[10]

Lupus Vulgaris is a long term disorder, and without appropriate therapy it can progress over many years often misdiagnosed. This disease entity can lead to extensive destruction and disfigurement which impairs functions of daily living and eventually if left untreated can develop carcinoma, most specifically squamous cell carcinoma and basal cell carcinoma.



Figure 10 A-F. Showed marked improvement in terms of erythema and scaling on the face and shoulders after twelve months of treatment.



Figure 11 A-B. Showed marked improvement in terms of erythema and scaling all over the body after twelve months of treatment.

CONCLUSION

Lupus Vulgaris arising on a burn scar lesion is an enigmatic presentation of cutaneous tuberculosis due to its diverse clinical manifestations and ambiguity in diagnosis. This case exhibits that a therapeutic trial of medications can be initiated in instances where diagnostic work up yielded negative results despite histological features consistent with cutaneous tuberculosis, specifically lupus vulgaris. The decision to extend treatment regimen would depend on correlation of clinical features and histopathologic findings. This study recommends the accessibility and availability of diagnostic work up for cutaneous tuberculosis in our country and lastly, impart the importance of treatment response as a means to clinically clinch the diagnosis despite a negative diagnostic work up due to the endemicity of tuberculosis in our country.

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