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Tuberculosis verrucosa cutis in a patient with pulmonary tuberculosis: A case report

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Case Report

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ABSTRACT

Cutaneous tuberculosis is a skin disorder caused by *Mycobacterium tuberculosis*, commonly classified according to its spreading route into endogenous, exogenous, and hematogenous, with distinct skin morphology and histopathological findings. Tuberculosis verrucosa cutis is a classification form of cutaneous tuberculosis, a paucibacillary disease caused by exogenous reinfection (inoculation) after sensitization on an immunocompromised individual. Management of cutaneous TB is generally similar to the management of pulmonary TB. In this paper, we presented a case of 62 years old male with a purplish rough patch on the right dorsum of the foot that began 1,5 years. There is a history of trauma and pulmonary TB. On the right dorsum of the foot, we identified a verrucous lesion with a livid base, irregular with the size of 6x3 cm. The diagnosis is established based on clinical features and histopathology evaluation. The patient received treatment with antituberculosis medication, topical mupirocin ointment 2%, and vaseline petroleum jelly. Improvement of the lesions was observed after the patient completed the intensive phase in two months of treatment with antituberculosis drugs.

Tuberkulosis kutis (TBC kulit) adalah penyakit kulit yang disebabkan oleh Mycobacterium tuberculosis yang dapat diklasifikasikan berdasarkan rute penyebaran sebagai penyebaran endogen, eksogen, dan hematogen, yang memiliki morfologi gambaran kulit dan temuan histopatologi yang berbeda. Salah satu bentuk dari tuberkulosis kutis adalah tuberkulosis kutis verukosa yang merupakan penyakit pausibasiler yang disebabkan oleh reinfeksi eksogen (inokulasi) setelah adanya sensitisasi pada orang dengan imunitas lemah. Pengobatan TBC kulit secara umum hampir sama dengan pengobatan TBC paru. Dalam tulisan ini, kami mempresentasikan seorang laki-laki 62 tahun, dengan plak keunguan kasar di dorsum pedis kanan, sejak 1,5 tahun lalu. Terdapat riwayat trauma, disertai dengan tuberkulosis paru. Pada regio dorsum pedis dekstra ditemukan lesi verukosa dengan dasar livide bentuk ireguler ukuran 6×3 cm. Diagnosis ditegakkan berdasarkan gambaran klinis dan pemeriksaan histopatologik. Pasien selanjutnya mendapatkan tatalaksana dengan antituberkulosis dan salep mupirosin 2% dan jeli vaselin petroleum topikal. Perbaikan lesi terlihat setelah pasien menyelesaikan fase intensif selama dua bulan pengobatan dengan obat anti tuberkulosis.

INTRODUCTION

Tuberculosis (TBC) is an infectious disease caused by a bacteria called *Mycobacterium tuberculosis*. Tuberculosis continues to be a huge problem, especially in developing countries.[1,2] About a quarter of the global population has been infected with M. tuberculosis.[3] Although most TBC cases are in the lungs, TBC potentially involves other organs, for example, the skin.[4] Cutaneous tuberculosis is more commonly found in the tropics.[2] Meanwhile, in the last decade, the incidence of cutaneous tuberculosis is decreased in the United States and Northern Europe, in line with the decreased rate of pulmonary tuberculosis after the development of Bacillus Calmette-Guerin vaccination and the effective implementation of anti-tuberculous drugs.[5]

The reported prevalence of cutaneous tuberculosis is only 1%–2% of all tuberculosis cases.[5,6] At the Dr. Cipto Mangunkusumo Hospital,

scrofuloderma is the most common form of cutaneous tuberculosis (84%), followed by tuberculosis verrucosa cutis (13%), and the rests are uncommon.[7]

Based on the route of infection, cutaneous TB classification includes exogenous, endogenous, lymphogenic, and hematogenic spread.[7] The clinical features of cutaneous tuberculosis are widely varied according to the infection route, the immune status of the patients, and the presence of prior infection or sensitization by previous tuberculosis bacteria.[8] *Tuberculosis* verrucosa cutis is classified as a form of cutaneous tuberculosis, a paucibacillary disease caused by exogenous reinfection (inoculation) after sensitization on the immunocompromised individual.[7,9,10,11]

In Europe, the lesions are commonly found on the arms, while in Asia, the lesions are in the ankles and glutes. The lesions are initially present as a wart-like papule that is progressively expanding. Involution may be found at the center, becoming an atrophic scar. The lesion may be purplish, erythematous, and or brownish in colour. The consistency is generally hard or solid with the occasional soft area, crusts, and exudation.[12,13] Diagnosis of cutaneous TBC commonly requires several additional work-ups, including histopathological examination that commonly reveals a tuberculoid granuloma with lymphocytes. These findings are often variable as they depend on the severity of cutaneous TB and the patient's immunological reaction.[14] In the case of cutaneous TBC, there might be coinfection on other organs. Cases of cutaneous TBC usually respond well to anti-tuberculous drugs such as rifampicin, isoniazid, pyrazinamide, ethambutol, or streptomycin.[7,9,12]

CASE DESCRIPTION

A 62-year-old male, a farmer, came to the dermatology clinic of RSUD Dr. Zainoel Abidin Banda Aceh general hospital with a complaint of an ulcerating wound on the dorsum of his right foot, unresolved for 1,5 years, sometimes itchy and painful. Initially, there was an abrasion due to his habit of scratching the dorsum of his right foot. However, the wound healed without any other complaints. Six months later, there were small red spots in the previous location, with the itchy sensation of the red rash leading to scratching that caused the rupture, oozing blood, and pus from the lesion. After a while, the lesion was getting larger in size and became thickened. The patient went to the primary care doctor and got treated with oral medication and ointment, but the lesion was not resolved, even getting worse until recently.

Additionally, the patient also complained about a recurring cough for six months. Fever, night sweats, and decreased appetite are all denied. The patient has had a history of diabetes mellitus for seven years and was controlled with insulin within the last six months. He denies any close contact with people with chronic coughs. There are no other family members with a similar complaint as he has. He does not remember the history of BCG vaccination. He works as a farmer and rarely uses boots at work.

Vital signs showed a blood pressure of 130/80 mmHg, a pulse of 88 bpm, RR 20x/min, and a temperature of 36,9° C. Anthropometry measurements showed that his body weight and height were 52 kg and 155 cm, respectively. The patient's Body mass index (BMI) is 21.6, a normal nutritional status. On physical examination, there is no lymphadenopathy. The dermatological evaluation revealed a verrucous patch on the dorsum of the right foot, with a purplish erythematous base, solitary, irregular, well-defined margin, with a violaceous halo with a size of 6 cm x 3 cm, covered by a brownish-yellow crust.

Laboratory test reveal: Hb: 14,4 g/dL, leukocyte: 8010/mL, hematocrit: 42 %, Erythrocyte sedimentation rate (ESR): 30 mm/h, fasting blood glucose (FBG): 304 mg/dL, blood glucose 2 hours postprandial: 539 mg/dL, HbA1C: 12%, urea: 28 mg/dL, creatinine: 0.58 mg/dL, AST: 10 U/L, ALT: 11 U/L, complete urine tests are within normal limit. Chest X-ray revealed a feature of pulmonary TBC. Histopathological examination from the dorsum of the right foot revealed skin tissue with hyperkeratosis, acanthosis, dilated blood vessels, and polymorphonuclear (PMN) inflammatory cell infiltration along with Langhans giant cells. There was no malignancy found. The conclusion of the histopathological examination on this patient suggests features commonly found in tuberculosis verrucosa cutis.

Based on the history, physical, and supporting examination, the patient is diagnosed with tuberculosis verrucosa cutis. The after-planning is to explain the disease and its treatment to the patient and to encourage the patient to take

Figure 1. The clinical feature on the initial visit. (a verrucous patch on the dorsum of the right foot, with a purplish erythematous base, solitary, irregular, well-defined margin, with a violaceous halo with a size of 6 cm x 3 cm, covered by a brownish-yellow crust (arrow))

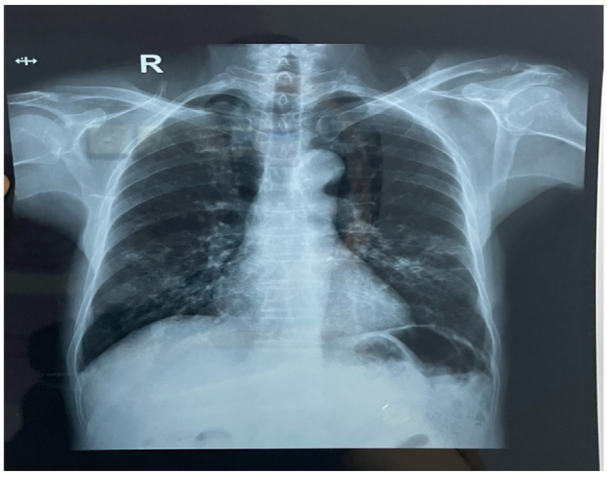

Figure 2. Chest x-ray (18th May 2022) suggesting pulmonary TB

medication regularly. The primary care referred him to a pulmonologist for multidisciplinary management. The patient received the first category of anti-tuberculous drugs with a Fixed-dose combination (FDC) consisting of rifampicin 150 mg, isoniazid 75 mg, ethambutol 275 mg, and pyrazinamide 400 mg given four tablets daily for two months in the intensive phase. Subsequently, the regimen was continued with a maintenance phase for the next four months. In the maintenance phase, two tablets of FDC drugs, each consisting of 75 mg of isoniazid and 150 mg of rifampicin, were given three times a week, for the next four months. In addition, the dermatologist also administered Mupirocin ointment 2% and Vaseline petroleum jelly.

After four weeks of the anti-tuberculosis, the skin lesion is improving, the thick crust has resolved, and the verrucous patch is getting thinner with a size of 6 × 3 cm and an erythematous base. After the patient completed the intensive phase, there was significant regression of the lesion, with a thickness of 0,1 mm, size of 6x3 cm, with a violaceous erythematous base.

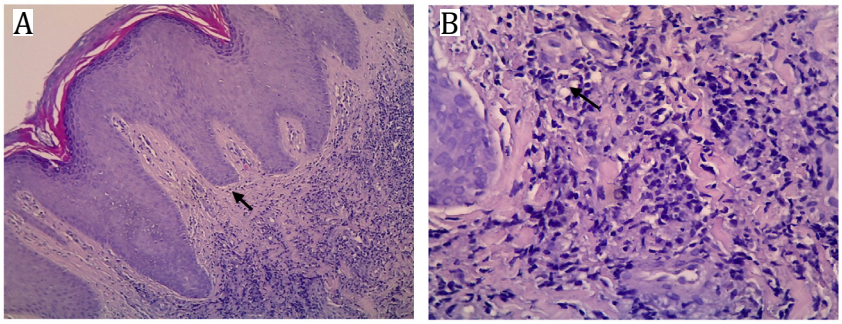

Figure 3. Histopathological result showed (A) showed a hyperkeratosis and acanthosis (H & E, 10 X) and (B) lymphocyte and neutrophil (H & E, 40 X)

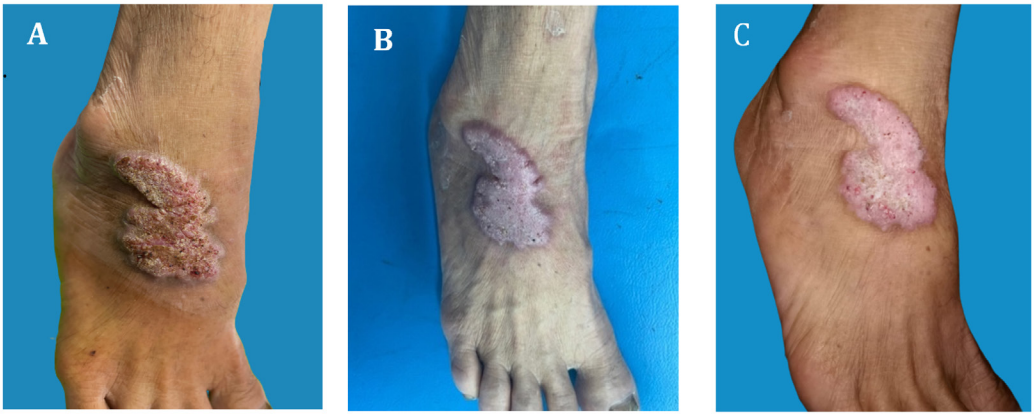

Figure 4. The clinical feature of patient after anti-tuberculosis treatment
Description: (A) After one week of anti-tuberculosis are given, the thick crust is getting thinner (30th May 2022) (B) After one month of anti-tuberculosis are given, the verrucous patch is getting thinner (27th June 2022) (C) After two months of treatment, the verrucous patch was getting thinner (thickness: 0,1 mm) sized 6x 3 cm, with a violaceous erythematous base (27th July 2022)

DISCUSSION

Based on the history taking, and physical and supporting examinations, the patient is diagnosed with skin tuberculosis verrucosa initiated by his previous trauma. Human skin is an organ of the body that protects from physical, mechanical, thermal, chemical, and infectious disorders.[7] When disruption of the protective function occurs, such as during trauma, a broken barrier may facilitate bacterial entrance and inoculation in the traumatic area. Tuberculous verrucosa cutis occurs exogenously, which means *M. tuberculosis* directly enters through the micro wound or abrasion to create inoculation forming papules or nodes, usually solitary but also can be multiple, which further become hyperkeratotic, resembling warts (warty papule) on an erythematous base, without pain and systemic symptoms.[5-7,9,15,16] This disease is generally found in areas prone to trauma, such as extremities.[17] This disease often occurs in health workers, laboratory workers, farmers, butchers, and infected children through contact with contaminated soil.[10]

TBC commonly infects the lungs, so in patients with tuberculosis verrucosa cutis, a chest x-ray is required to look for focal infection.[7,15] In this patient, the chest X-ray showed pulmonary TBC and Diabetes Mellitus (DM), shown by the result of HbA1c and FBG tests. Diabetes is one of the most common risk factors for pulmonary TBC. The frequency of DM in a patient with pulmonary TBC is as high as 10-15%, and the prevalence of this infectious disease is 2-5 times higher in diabetic compared to non-diabetic patients.[4]

Cutaneous tuberculosis can be diagnosed using blood examination, especially an increased ESR, which suggests the presence of damaged tissue. Moreover, the test is more beneficial for

patient follow-up during the treatment. The bacteriological, histopathology, and tuberculin tests might also be required to determine the etiology, as well as histopathological examination and tuberculin tests.[6,7,18] The tuberculin test was not carried out in this case, as the test was only meaningful at the age of 5 years or younger. A positive result only means a current or a history of tuberculosis infection.[7]

The gold standard to determine the causative agent is the detection of *Mycobacterium tuberculosis* in the cultured skin biopsy specimen or cytology view or the of Mycobacterium spp. DNA with molecular evaluation.[4] However, most cases of cutaneous TBC contain small amounts of bacteria and commonly yield a negative result, with only 21.7% showing positive results. Besides, bacteriological examination with culture needs roughly eight weeks.[7]

In this patient, the differential diagnosis includes chromoblastomycosis, and squamous cell carcinoma, which can be excluded by histopathological examination. The histopathological appearance of tuberculosis verrucosa cutis showed hyperkeratosis, papillomatosis, and acanthosis. Acute inflammatory infiltrates are found beneath the epidermis. Tuberculoid structures with moderate amounts of necrosis are usually present in the mid-dermis.[8,19] The histopathological picture in our case showed hyperkeratosis, acanthosis, dilated blood vessels in the epidermis, and PMN inflammatory cells with Langhans giant cells without any malignancy. The diagnosis of chromoblastomycosis can be ruled out in this case, as the histopathological examination does not reveal any fungal cells, either sclerotic cells or brownish-round muriform cells. Besides, histopathology showed no signs of malignancy, and Squamous Cell Carcinoma can be ruled out.[12]

Diagnosis of cutaneous tuberculosis is quite challenging due to the high rates of negative results with microbiological and molecular tests. Therefore, pathognomonic finding on every type of cutaneous TBC on histopathological examination is crucial to establish an accurate diagnosis.[5] Topical medication for cutaneous TBC is mainly applied to resolve pathological skin conditions, including ulceration, to prevent further infection of the skin structure.[14] This patient was given topical medications such as Mupirocin ointment 2% and Vaseline petroleum jelly.

Specifically for cutaneous TBC, anti-tuberculosis should be given for at least two months after the skin lesions have entirely resolved.[4,8] The principle of cutaneous tuberculosis management is similar to the management of pulmonary tuberculosis. The anti-tuberculosis drugs available in Indonesia are shown in the table below. INH (H), rifampicin (R), pyrazinamide (Z), and streptomycin (S) are all bactericidal drugs, while ethambutol (E) is bacteriostatic.[4,7,20] Tuberculosis treatment consists of 2 phases; the initial phase (intensive phase) and the advanced phase (maintenance). The initial phase of treatment is to kill the actively multiplying bacteria as much and as fast as possible using bactericidal drugs. Meanwhile, the advanced stage is a sterilization step to kill the slow-growing bacteria.[4,20]

Table 1. Recommended Dose of First Line Anti-tuberculosis for Adults (Kemenkes RI)[4]

Drugs	Daily recommended dose		Dose of 3 times per week	
	Dose (mg/kgBW)	Maximum (mg)	Dose (mg/kgBW)	Maximum (mg)
Isoniazid	5 (4-6)	300	0 (8-12)	900
Rifampicin	10 (8-12)	600	10 (8-12)	600
Pyrazinamide	25 (20-30)	-	35 (30-40)	-
Ethambutol	15 (15-20)	-	30 (25-35)	-
Streptomycin	15 (12-18)	-	15 (12-18)	-

The patient received the first category of antituberculosis drugs with Fixed Dose Combination (FDC) consisting of Rifampicin 150 mg, Isoniazid 75 mg, Ethambuthol 275 mg, and Pyrazinamide 400 mg given 4 tablets daily for 2 months in the intensive phase.

CONCLUSION

Tuberculosis verrucosa cutis is caused by an exogenous inoculation of M. tuberculosis into the skin through an open wound or abrasion on the previously sensitized individual. The diagnosis of cutaneous tuberculosis can be established based on the history to find the risk factors of tuberculosis infection, and physical examination of the lesion, supported by additional supporting tests. Improvement of the lesions was seen after the patient completed the intensive phase in two months of treatment with anti-tuberculous drugs.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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