Tuberculosis verrucosa cutis (TVC) is a form of cutaneous tuberculosis that results from accidental inoculation of Mycobacterium tuberculosis in a previously infected or sensitized individual with a moderate to high degree of slowly evolving cell-mediated immunity. TVC usually begins as a solitary papulonodule following a trivial injury or trauma on one of the extremities that soon acquires a scaly and verrucous surface. The lesion, which is usually persistent, expands slowly over several months or years with or without central clearing and atrophy. We report a case of TVC in a 15-year-old girl that was undiagnosed for 10 years. The diagnosis was confirmed by a positive mycobacterial culture and characteristic histopathologic findings of the biopsy specimens. The patient responded well to antituberculous therapy (ATT), and the lesion resolved with residual scarring.

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GOAL
To understand cutaneous tuberculosis to better manage patients with the condition

OBJECTIVES
Upon completion of this activity, dermatologists and general practitioners should be able to:
1. Recognize the morphologic features of cutaneous tuberculosis.
2. Describe the histopathologic characteristics of cutaneous tuberculosis.
3. Explain the treatment options for cutaneous tuberculosis.

CME Test on page 320.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: October 2006.

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Drs. Janjua, Khachemoune, and Guillen report no conflict of interest. The authors discuss off-label use of ethambutol, isoniazid, pyrazinamide, and rifampicin. Dr. Fisher reports no conflict of interest.

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Case Report

A 15-year-old girl presented with a 10-year history of a slowly enlarging asymptomatic warty plaque over the right knee. The lesion started as a small asymptomatic red papule following a trivial injury and slowly progressed over several months to form a large warty plaque covered with a thick scale. The patient and her mother reported that the lesion also would get tender, intermittently discharging yellowish exudate. The lesion initially was treated with home remedies and later with topical steroids and oral antibiotics prescribed by local physicians, but the lesion continued expanding slowly to involve a large area of the right knee and upper leg. There was neither a family history of nor any known contacts with tuberculosis.

Results of a physical examination revealed a 4×7-cm, large, well-defined, verrucous, thick, scaly, linear plaque situated over the right knee with involvement of the lower aspect of the anterior thigh and the right anterior upper aspect of the leg. Central clearing with atrophy gave the lesion a somewhat annular shape (Figure 1). Diascopy results did not show an apple jelly–brown color. Regional lymph nodes were not palpable.

The remainder of the physical examination showed unremarkable findings. A bacillus Calmette-Guérin vaccination scar could be identified on the left deltoid. Routine blood and urinalyses results were within reference range. Purified protein derivative test results were strongly positive (≥15 mm of induration after 72 hours). Findings from a chest x-ray revealed no evidence of pulmonary disease.

Histopathologic examination results of a biopsy specimen taken from the lesion revealed marked epidermal hyperkeratosis, acanthosis, pseudoepitheliomatous hyperplasia, and multiple well-formed tuberculous granulomas in the dermis (Figure 2). Each of the granulomas consisted of large numbers of lymphocytes, neutrophils, histiocytes, and Langhans giant cells (Figure 3). However, caseation necrosis was not present, and acid-fast bacilli could not be found. *Mycobacterium tuberculosis* was cultured from the biopsy specimen.

Daily oral antituberculous therapy (ATT) (rifampicin 450 mg/d, isoniazid 300 mg, and pyrazinamide 1200 mg) was recommended for 3 months (Figure 4). The patient responded well to the treatment and there was perceptible regression of the skin lesion. Treatment was continued with rifampicin 450 mg/d and isoniazid 300 mg/d for
another 6 months, resulting in complete regression of the lesion with residual scarring.

Comment
Tuberculosis is a serious public health concern in developing countries due to lower socioeconomic status, malnutrition, and overcrowding; additionally, the morbidity and mortality rates of the disease are increasing rapidly in these countries. The incidence of tuberculosis also is on the rise in developed countries, including the United States and United Kingdom, both of which were previously considered free of this disease.\(^1\,^2\)

Systemic tuberculosis was well-documented in ancient medical scriptures, but its first intelligent description, phthisis (to waste away), was given by Hippocrates (circa 460–376 BC).\(^3\) Cutaneous tuberculosis makes up only a small proportion of the cases of extrapulmonary tuberculosis. Children and immunocompromised adults are at increased risk of developing this form of the disease.\(^3\)

Cutaneous tuberculosis may present in a number of diverse clinical forms (Table). The 4 major categories of cutaneous tuberculosis that have been described in the literature include: (1) inoculation from an exogenous source (ie, tuberculous chancre, tuberculosis verrucosa cutis [TVC]); (2) endogenous cutaneous spread either contiguous or by autoinoculation (ie, tuberculosis cutis orificialis, scrofuloderma); (3) hematogenous spread (ie, lupus vulgaris, acute miliary tuberculosis, tuberculosis ulcer/gumma/abscess); and (4) tuberculids (ie, erythema induratum [Bazin disease], papulonecrotic tuberculids, lichen scrofulosorum).\(^4,^5\)

TVC is a form of cutaneous tuberculosis that results from accidental inoculation of *M. tuberculosis* into the skin through open wounds or abrasions in previously infected or sensitized individuals with a moderate to high degree of immunity,\(^6\) as opposed to tuberculosis chancre, which occurs in uninfected or unsensitized individuals. Individuals vaccinated with the bacillus Calmette-Guérin vaccine have been sensitized and carry a higher risk of developing TVC.\(^7\) In low socioeconomic environments, children can be infected by playing on ground contaminated with tuberculous sputum.\(^8\) Autoinoculation of a wound with a patient’s own tuberculous sputum rarely causes TVC.\(^7\) The sites of predilection for inoculation tuberculosis in children are the lower extremities (ie, knees, thighs, and buttocks) because these areas are most likely to be traumatized. In adults, fingers and hands frequently are involved. The historically well-known “prosector’s wart” is considered a prototype of TVC and is caused by accidental inoculation during autopsy.\(^4\)

The diagnosis of TVC should be based on history and evolution of the disease, cardinal morphologic features, histopathologic characteristics, and mycobacterial culture of the biopsy specimen. The lesions of TVC typically are asymptomatic.
<table>
<thead>
<tr>
<th>Mode of Infection</th>
<th>Type of Cutaneous Tuberculosis</th>
<th>Clinical Presentation</th>
<th>Status of Sensitivity/Transmission</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exogenous</td>
<td>Tuberculous chancre</td>
<td>Painless brown papule 2–4 wk after inoculation; may progress to nodule, plaque, or ulcerate; children typically affected; face and extremities are commonly involved; may follow BCG vaccination; regional lymphadenopathy 3–8 wk after infection</td>
<td>Nonsensitized; negative TB test</td>
<td>Sporotrichosis, blastomycosis, histoplasmosis, coccidioidomycosis, nocardiosis, syphilis, leishmaniasis, yaws, tularemia, atypical mycobacterial infection, pyogenic granuloma, cat scratch disease</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis verrucosa cutis</td>
<td>A small papule progressing to hyperkeratotic plaque (can resemble a wart), peripheral expanding, with or without central clearing; dorsi of fingers or hands in adults, ankles and buttocks in children; regional lymphadenopathy only if secondary bacterial infection present</td>
<td>Sensitized; strongly positive TB test</td>
<td>Atypical mycobacterial infection, North American blastomycosis, Majocchi granuloma, chromoblastomycosis, verruca epidermal nevus, hypertrophic, L.P. iododerma, bromoderma, verruca vulgaris</td>
</tr>
<tr>
<td></td>
<td>Mucocutaneous cutis orificialis</td>
<td>Mucocutaneous border of the nose, mouth, anus, urinary meatus, and vagina; mucous membrane of the mouth or tongue; lesions ulcerate from the beginning (soft punched out ulcers with undermined edges) and extend rapidly, with no tendency to heal</td>
<td>Variable sensitivity; underlying active visceral tuberculosis (larynx, lungs, intestines, and genitalurinary tract); variable TB test</td>
<td>Gossitis, aphthosis, deep fungal infections</td>
</tr>
<tr>
<td>Mode of Infection or Transmission</td>
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<td>Status of Sensitivity/Previous Infection</td>
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<tr>
<td>Endogenous—autoinoculation</td>
<td>Tuberculosis</td>
<td>Previously infected and sensitized</td>
<td>Direct extension from the underlying tuberculous lymphadenitis; subcutaneous masses enlarge to form nodules with central suppuration; cervical lymph nodes commonly involved, also may occur over involved bones or joints; healing with cordlike scars</td>
<td>Atypical mycobacterial infection, sporotrichosis, actinomycosis, coccidioidomycosis, lymphogranuloma venereum</td>
</tr>
<tr>
<td>Hematogenous</td>
<td>Lupus vulgaris</td>
<td>Sensitized; positive TB test</td>
<td>Typically single plaque composed of red-brown papules with overlying adherent scale; ulceration frequently occurs, and involution leaves deforming scars; 90% of lesions occur on head and neck; lymphangitis and lymphadenitis may be associated</td>
<td>Colloid milia, acne vulgaris, sarcoidosis, rosacea, tertiary syphilis, chronic discoid LE, leprosy, systemic mycoses, leishmaniasis</td>
</tr>
<tr>
<td>Acute miliary tuberculosis</td>
<td>Tuberculosis</td>
<td>Fulminant tuberculosis of the lungs or meninges present; negative TB test</td>
<td>Generalized erythematous macules or papules, pustules, subcutaneous nodules, and purpuric lesions that most commonly affect immunocompromised hosts; ulceration may occur</td>
<td>Drug reactions</td>
</tr>
<tr>
<td>Tuberculosis ulcer/gumma/abscess</td>
<td>Tuberculosis</td>
<td>Sensitized; primary focus of infection usually present; positive TB test</td>
<td>Firm nontender erythematous nodules that soften, ulcerate, and form sinuses; may present as chronic mastitis with abscess and sinus formation</td>
<td>Syphilitic gumma; hidradenitis suppurativa</td>
</tr>
<tr>
<td>Mode of Infection or Transmission</td>
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<tr>
<td>Tuberculids</td>
<td>Erythema induratum (Bazin disease)</td>
<td>Sensitized; positive TB test</td>
<td>Predominantly affects middle-aged women; tender, erythematous, 1–8-mm subcutaneous nodules on lower posterior calves; lesions resolve with or without ulcerations over several months</td>
<td>Erythema nodosum, nodular vasculitis, polyarteritis nodosa, tertiary syphilis, other infectious and inflammatory panniculitides</td>
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<tr>
<td>Papulonecrotic tuberculids</td>
<td>Sensitized/Evidence of prior or active disease present in one third to two thirds of cases, especially in lymph nodes; strongly positive TB test</td>
<td>Symmetrically distributed, 2–3-mm, firm, inflammatory papules, becoming pustular or necrotic and appearing in crops; lesions resolve slowly with varioliform scarring; may appear in association with erythema nodosum and scrofuloderma</td>
<td>Papulopustular secondary syphilis, pityriasis lichenoides et varioliformis acuta, Churg-Strauss granuloma, lymphomatoid papulosis, perforating GA, perforating collagenosis, necrotizing vasculitis</td>
<td></td>
</tr>
<tr>
<td>Lichen scrofulosorum</td>
<td>Sensitized and infected, involving bones or lymph nodes; positive TB test</td>
<td>Groups of indolent, minute keratotic, discrete 2–4-mm, yellowish-pink to reddish-brown papules; lesions arranged in discoid groups over the trunk</td>
<td>Lichen nitidus, LP, secondary syphilis, sarcoidosis</td>
<td></td>
</tr>
</tbody>
</table>

*TB indicates tuberculin; BCG, bacillus Calmette-Guérin; LP, lichen planus; LE, lupus erythematosus; GA, granuloma annulare.
and start as small papules that slowly progress to verrucous or hyperkeratotic plaques over several months to years. Superficial scaling and fissuring with subsequent intermittent purulent discharge may occur. There may be central clearing with scarring and atrophy, as seen in this case. The disease usually runs a prolonged course with persistent verrucous lesions, especially if left untreated. Regional lymph nodes commonly are not enlarged unless there is superadded bacterial infection. Other organs, including the lungs, bone, and kidneys, do not appear to be affected in TVC, which differs from other forms of cutaneous tuberculosis. TVC is only locally invasive and usually does not cause any deformity or functional impairment of the affected extremity, but exceptions can occur.

Differentiation from infection with atypical mycobacteria may prove to be difficult and usually requires culture of the causative organism. Other unusual infections such as North American blastomycosis, chromoblastomycosis, Majocchi granuloma, and fixed sporotrichosis may need to be differentiated from TVC by histopathology. Inflammatory dermatoses, including psoriasis, lichen simplex chronicus, hypertrophic discoid lupus erythematosus, and hypertrophic lichen planus, also may mimic TVC but are differentiated on the basis of characteristic clinical findings and histopathology.

The histopathologic features of TVC include a pseudoepitheliomatous epidermal hyperplasia with hyperkeratosis and a dense dermal infiltrate of neutrophils, lymphocytes, and giant cells arranged in multiple well-formed tuberculous granulomas. Acid-fast bacilli rarely are seen and typical tuberculous foci with caseation necrosis are uncommon. Case reports in the literature indicate the usefulness of polymerase chain reaction for the detection of M tuberculosis in cutaneous tuberculosis. Polymerase chain reaction has not been found to be very helpful in the paucibacillary forms of cutaneous tuberculosis such as TVC. In cases for which the clinician has strong suspicion but negative laboratory test results, it might be possible to use the dramatic response to ATT as a diagnostic criterion. A study of patients with equivocal laboratory results noted 100% clinical improvement in all patients taking ATT for 20 days, and it has been proposed that response to treatment in 4 weeks can be used to support the diagnosis.

Standard multidrug ATT is the treatment of choice and most lesions resolve after 4 to 5 months. An intensive phase of ATT consists of rifampicin, isoniazid, and pyrazinamide used for 2 months, with rifampicin and isoniazid continued for an additional 4 to 10 months. In cases of isoniazid resistance, ethambutol may be added to the regimen. The intensive-phase treatment should result in perceptible regression of the lesion, prompting the treating physician to continue the treatment through the continuation phase. Surgical excision of the isolated lesion also is useful.

Our case of cutaneous tuberculosis remained undiagnosed for an unusually long period of 10 years. Although cutaneous tuberculosis may be regarded as a rare finding in the United States and other developed countries, it is not uncommon in countries with endemic tuberculosis. Delay in referral may lead to long-standing extensive lesions, as in this case. Physician awareness and education of early diagnosis and management of cutaneous tuberculosis are key to reducing the number of cases similar to ours.

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REFERENCES


