

# Papulonecrotic Tuberculid: A Rare Form of Cutaneous Tuberculosis

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*We describe a case of papulonecrotic tuberculid, a rare form of cutaneous tuberculosis, in a 25-year-old Philippino woman who had immigrated to Canada 8 years previously. The patient presented with a 3-week history of tender left cervical adenopathy; 1 week later, she developed multiple ulcerated erythematous nodules and emboluslike lesions scattered over her fingers. Results of a biopsy performed on the lymph node revealed granulomatous lymphadenitis, and Mycobacterium tuberculosis grew from the lymph node. Histopathologic analysis of an ulcerative finger lesion demonstrated nonnecrotizing granulomas with dense lymphocytic inflammation of the superficial dermis; however, results of acid-fast staining, mycobacterial culture, and polymerase chain reaction for M tuberculosis complex were all negative. Different conditions can mimic papulonecrotic tuberculid. Therefore, the diagnosis can be difficult unless M tuberculosis is isolated from a site other than the skin, because stain and culture results from skin biopsy specimens are typically negative and the polymerase chain reaction is positive in only 50% of cases. We review the epidemiology, clinicopathologic features, and differential diagnosis of papulonecrotic tuberculid. Awareness of this entity is important to distinguish it from other conditions and to institute appropriate therapy in a timely fashion.*

*Cutis.* 2005;75:341-346.

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Accepted for publication June 3, 2004.

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The authors report no conflict of interest.

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**T**uberculosis is an important global health problem. It infects one third of the world's population (1.86 billion people), causes 8 million new cases annually, and is responsible for 1.9 million deaths per year.<sup>1,2</sup> Although typically manifested as chronic pneumonia, 15% to 20% of all tuberculosis cases present in an extrapulmonary form. Cutaneous tuberculosis is relatively rare and makes up approximately 1% of all cases of extrapulmonary tuberculosis.<sup>3</sup> A study conducted in a tertiary care hospital in India between 1975 and 1995 reported that 0.1% of all dermatology patients had cutaneous tuberculosis.<sup>4</sup>

Cutaneous tuberculosis can present in many morphologic forms, including macules, papules, nodules, gummas, abscesses, papules, and hyperkeratotic lesions. The condition arises from either direct inoculation of *Mycobacterium tuberculosis* from endogenous spread of infection to the skin (scrofuloderma, acute miliary tuberculosis, tuberculous gumma, orificial tuberculosis, and lupus vulgaris) or from an exogenous source (tuberculous chancre, warty tuberculosis, and occasionally lupus vulgaris). The tuberculids (papulonecrotic tuberculid, erythema induratum of Bazin, and lichen scrofulosorum) are a rare form of cutaneous tuberculosis and are thought to be caused by an immune reaction to endogenous tuberculosis infection.<sup>5-7</sup>

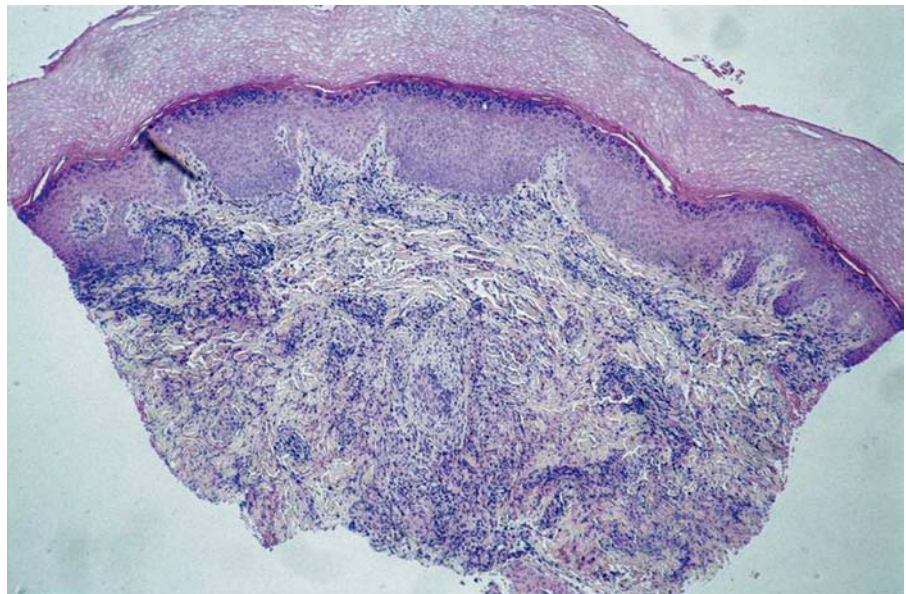
## Case Report

A 25-year-old previously healthy Philippino woman presented with a 3-week history of a progressively enlarging tender left cervical mass associated with 3 days of fever, chills, and night sweats. She had emigrated from the Philippines to Canada 8 years prior but had not traveled recently and did not report infectious contacts. The patient denied weight loss, recent dental procedures, or recent pharyngitis. One week after presentation, she developed multiple lesions on the fingers of both hands.

Results of a physical examination revealed a nontoxic, afebrile, young woman in no distress. There was a 3×5-cm, firm, fixed, nontender left



**Figure 1.** Ulcerated erythematous nodules on the dorsal aspect of the fingers.



**Figure 2.** Dense lymphocytic inflammation in the superficial dermis, with lymphocytic venulitis and perivascular granulomas (H&E, original magnification  $\times 20$ ).

supraclavicular mass and multiple, dusky, erythematous nodules scattered over the palmar and dorsal surfaces of the fingers of both hands. A few of these lesions showed evidence of superficial ulceration (Figure 1).

Results of laboratory investigations revealed mild anemia (hemoglobin level, 114 g/L), normal leukocyte and platelet counts, and an elevated C-reactive protein level of 17.9 mg/L. Results of blood cultures for routine bacteria and mycobacteria

were negative, as were the results for human immunodeficiency virus serology. Results of a computed tomography scan of the neck and chest demonstrated a 7 $\times$ 2.5-cm necrotic mass in the left supraclavicular region and a small 5-mm nodule in the lower lobe of the right lung. Tuberculosis adenitis was suspected based on these findings, and the patient was started on a standard 4-drug anti-tuberculous regimen (isoniazid, rifampin, pyrazinamide, and ethambutol).

Table 1.

**Clinical Presentation of Cutaneous Tuberculosis<sup>3,8</sup>**

Type of Infection	Lesion	Route of Infection	Clinical Presentation	Common Location
Primary (exogenous)	Tuberculous chancre	Direct inoculation, previously non-infected host	Painless red-brown papule or chancre, ulceration, lymphadenopathy	Site of exposure; anywhere
	Tuberculosis verrucosa cutis	Direct inoculation, previous immunity	Papule, hyperkeratotic and verrucous plaque with reexposure	Distal extremities
	Lupus vulgaris (some cases)	Direct inoculation, Bacillus Calmette–Guérin vaccine	Gelatinous plaque with ulceration or necrosis, soft hypertrophic nodule	Head or lower limbs
Secondary (endogenous)	Orificial tuberculosis	Autoinnoculation of mucosa adjacent to the orifice draining infection	Small yellow nodules with progression into painful ulcerations	Oral, pharyngeal, genital and/or anal orifices, viscera
	Scrofuloderma	Contiguous involvement of skin over the focus	Firm, mobile subcutaneous nodules; ulceration and pus or caseous discharge	Skin overlying lymph node
	Miliary tuberculosis	Hematogenous	Discrete purpuric macules or papules	Dissemination to all areas of body
	Metastatic tuberculous abscess (gummatous tuberculosis)	Hematogenous	Nontender subcutaneous abscesses with ulceration and fistulas	Trunk, extremities, and head
	Lupus vulgaris (most cases)	Hematogenous, lymphatic, or contiguous	Gelatinous plaque, soft hypertrophic nodule, papule with ulceration, necrotic ulcer	Typically head and neck
Tuberculids (eruptive)	Lichen scrofulosorum	Hematogenous	Lichenoid papules	Perifollicular distribution
	Erythema induratum of Bazin	Hematogenous	Erythrocyanotic indurated nodules, occasional ulceration	Lower extremities
	Papulonecrotic tuberculid	Hematogenous	Asymptomatic, dusky-red papules; crust; ulceration	Acral distribution
	Nodular granulomatous phlebitis	Hematogenous	Subcutaneous nodules without ulceration	Lower extremities

Table 2.

**Papulonecrotic Tuberculid: Clinical and Histologic Features\***

Reference	No. of Patients	Clinical Presentation	Significant Histologic Findings	TB Culture and PCR
Jordaan et al, 1994 <sup>7</sup>	15	Children and adults, 10 females; presumptive diagnosis of TB in 5 patients; response to anti-TB Tx in weeks; positive TST results in 13/15 (87%) patients	Dermal necrosis; poorly formed granulomatous infiltrate; vasculitis, perivascular spongy edema, and follicular necrosis	Culture not mentioned; results of all AFB stains were negative
Jordaan et al, 1996 <sup>6</sup>	8	Case series—children only, 6 females; 7 (88%) had clinical pulmonary TB (abnormal chest x-ray), positive TST results, and response to anti-TB Tx within weeks	Ulceration and dermal necrosis; granulomatous inflammation; superficial and deep lymphocytic infiltration; no vasculitis	All culture and AFB stain results were negative; 1 (13%) positive for TB PCR
Morrison and Fourie, 1974 <sup>5</sup>	91	Young adults and children; 2/3 of cases <30 y old; 86 African, 5 white; rapid response to anti-TB Tx; focus of TB found in 35 (38%): lymph glands (17), lungs (11), vertebrae/joints (4), urogenital (3)	Leukocytoclastic vasculitis; swelling of the arteriole-capillary endothelium with intraluminal accumulation of polymorphs/fibrin; epithelioid and giant cells around the cone of necrotic cells with mononuclear cell infiltrate	Not mentioned
Wilson-Jones and Winkelmann, 1986 <sup>14</sup>	12	Young adults and children; cutaneous lesions for a mean of 4 y; 6 patients with presumptive clinical TB; all had positive TST results; resolution of cutaneous lesions over 3–12 wk after anti-TB Tx	Subacute lymphohistiocytic vasculitis, thrombosis, and destruction of small dermal vessels; central zone of necrosis with surrounding inflammation in the superficial to the deep dermis	Culture results not mentioned; all AFB stain results were negative; PCR not done
Kullavanijaya et al, 1991 <sup>19</sup>	11	Adults 17–33 y old, 9 females; cutaneous lesions for 2 mo–12 y; 7 (64%) with preexisting history of TB, 5 (45%) with cervical adenitis, 3 (27%) household contacts of TB; positive TST result; resolution of lesions over several weeks after starting anti-TB Tx	Superficial dense infiltration of lymphoid cells, histiocytes, and eosinophils; and granulomatous changes deeper with associated vasculitis	Not mentioned

\*TB indicates tuberculosis; PCR, polymerase chain reaction; Tx, treatment; TST, tuberculin skin test; AFB, acid-fast bacilli.

The pathology result from the fine-needle aspiration biopsy specimen of the cervical lymph node revealed granulomatous lymphadenitis, and *M tuberculosis* grew from the aspirated material. Histopathologic analysis of the biopsy specimen from one of the finger lesions revealed a small nonnecrotizing granuloma in a perivascular position, dense lymphocytic inflammation confined to the superficial dermis, lymphocytic venulitis, and granular collagen degeneration (Figure 2). Results of acid-fast staining were negative, as were the polymerase chain reaction and culture for *M tuberculosis*. The clinicopathologic features were suggestive of a papulonecrotic tuberculid reaction form of cutaneous tuberculosis. Within 2 weeks of commencing antituberculous therapy, the cutaneous lesions resolved and the lymphadenitis decreased in size.

### Comment

Cutaneous tuberculosis can be caused by several mycobacterial species, including *M tuberculosis*, *Mycobacterium bovis*, Bacillus Calmette–Guérin vaccine, and *Mycobacterium avium-intracellulare*.<sup>8-10</sup> Cutaneous tuberculosis lesions can present with several nonspecific morphologies, including papules, nodules, abscesses, plaques, and ulcerations. The clinical presentation of cutaneous tuberculosis is largely dependent on the route of mycobacterial inoculation (ie, exogenous, endogenous, autoinoculation) and the immune status of the host. Several types of cutaneous tuberculosis are summarized in Table 1 and are reviewed in depth elsewhere.<sup>3,8</sup> Exogenous cutaneous tuberculosis can be classified into primary inoculation tuberculosis, tuberculosis verrucosa cutis, and some variants of lupus vulgaris<sup>4,8,9,11,12</sup>; endogenous cutaneous tuberculosis includes orificial tuberculosis, scrofuloderma, miliary tuberculosis, metastatic tuberculosis abscess (tuberculous gumma), and other variants of lupus vulgaris.<sup>4,8,11,12</sup>

The concept of tuberculids was first introduced by Darier<sup>13</sup> in 1896. Tuberculids are thought to be due to a cutaneous hypersensitivity reaction to mycobacteria or their breakdown products lodged in small vessels.<sup>5-7,14</sup> An etiologic link between *M tuberculosis* and tuberculid skin lesions has become more convincing because fragments of *M tuberculosis* DNA have been found by polymerase chain reaction testing in some lesions; in addition, the link is supported by the often rapid resolution of the cutaneous lesions after institution of antituberculous therapy.<sup>15-17</sup>

True tuberculids include papulonecrotic tuberculid, erythema induratum of Bazin, lichen scrofulosorum, and recently identified nodular

granulomatous phlebitis.<sup>8</sup> Papulonecrotic tuberculid and erythema induratum of Bazin account for most tuberculid reactions. The 2 entities have, in fact, been suggested to be part of a clinicopathologic continuum and are characterized by immunologic response to lodged mycobacterial products in superficial vessels in papulonecrotic tuberculid and in larger deeper vessels in erythema induratum of Bazin<sup>7</sup>; the 2 entities also have been reported to occur simultaneously.<sup>7,16,18</sup>

Clinicopathologic features of papulonecrotic tuberculid have been consistently documented in several case series and are summarized in Table 2.<sup>5-7,14,19</sup> Papulonecrotic tuberculid usually occurs in children and young adults, of which 38% to 75% of cases have an extracutaneous focus of tuberculosis.<sup>5-7,14,19</sup> In one case series of papulonecrotic tuberculid, a focus of tuberculosis was found in 38% of cases, with the extracutaneous sites affected with the following frequency: cervical lymph glands (19%), lungs (12%), vertebrae and joints (4%), and urogenital areas (3%).<sup>5</sup> Lesions of papulonecrotic tuberculid are typically symmetrical, erythematous, ulcerating papules on the extensor aspects of the arms, legs, and ears; in addition, the lesions may be long-term, lasting from weeks to several years.<sup>6</sup> The lesions usually undergo necrosis, become crusted, and, once healed, often leave atrophic scars.<sup>5-7,14</sup> The histology of papulonecrotic tuberculid is characterized by granulomatous inflammation, variable lymphohistiocytic vasculitis with necrosis in the superficial dermis, and destruction of superficial small dermal vessels.<sup>4,7,14</sup>

Erythema induratum of Bazin typically presents as erythrocyanotic indurated nodules with occasional ulceration, typically on the calves of both legs. The pathologic changes, though similar to those in papulonecrotic tuberculid, occur in the deeper dermis.<sup>20</sup> The combination of clinical and histologic features of our patient's case (ie, symmetrical papules on the fingers and involvement of the superficial dermis) are more consistent with the diagnosis of papulonecrotic tuberculid.

Cutaneous lesions in conditions such as pityriasis lichenoides et varioliformis acuta, popular urticaria, septicemia, papulopustular syphilis, granuloma annulare, and allergic granulomatoses can mimic papulonecrotic tuberculid. A definitive diagnosis can be difficult unless *M tuberculosis* is isolated from a site other than the skin because results of acid-fast stains and mycobacterial cultures from cutaneous biopsy specimens are usually negative, and polymerase chain reaction for *M tuberculosis* is positive in only 50% of cases.

Awareness of this entity is important to distinguish it from other conditions and to institute appropriate antituberculous therapy in a timely fashion.

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