

Cutaneous tuberculosis in the pediatric population: A review



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Importance: Tuberculosis (TB) is a significant health concern, affecting over 1.5 million people annually worldwide, with the incidence increasing in the United States from 2020 to 2021. The pediatric population is particularly vulnerable to TB. Extrapulmonary manifestations of TB include cutaneous tuberculosis (CTB).

Observations: There are 8 forms of CTB. Lupus vulgaris (LV) is the second most common form of pediatric CTB which presents nontender plaques or nodules with ulceration that progress to well-defined, scaly plaques. Tuberculous chancre results from exogenous inoculation and lesions contain large amounts of acid-fast bacilli (AFB). Clinically, tuberculous chancre presents as erythematous papules which form firm nontender ulcers. Tuberculosis verrucosa cutis (TVC) presents as small papules surrounded by inflammation that develops into a wart-like lesion. Periorificial lesions are rare and present as painful ulcers in the oral or perineal regions. Scrofuloderma is the most common form of pediatric CTB and presents as nodules that ulcerate, forming purulent sinus tracts. Tuberculosis miliaris cutis disseminate presents as widespread papules and crusted vesicles. Metastatic abscesses present as multiple nodules that may ulcerate or form draining sinus tracts. Lastly, tuberculid forms include lichen scrofulosorum (LS), which presents as lichenoid papules which may form plaques and scale, and papulonecrotic tuberculid, which presents as necrotic papules. All forms of cutaneous tuberculosis can be treated with the standard 6-month, four-drug anti-tuberculosis treatment (ATT). Some cases of CTB may require debriding and surgical management in addition to ATT.

Conclusions and Relevance: Determining the type of CTB can be challenging clinically. Histopathology is needed to make the diagnosis. Chest x-ray and a review of systems should be obtained for CTB patients to determine if there are other extrapulmonary manifestations of TB. All types are treated with 6 months of ATT. (JAAD Int 2023;12:105-11.)

Key words: cutaneous tuberculosis; pediatric; review; scrofuloderma.

INTRODUCTION

The pediatric population is particularly vulnerable to *Mycobacterium tuberculosis* (TB) infections because of the immaturity of their immune system.¹ Additionally, *Mycobacterium tuberculosis* is a part of the microbiome of asymptomatic premature infants in the NICU.² In the United States in 2020, 7174 tuberculosis (TB) cases were reported to the Center for Disease Control (CDC), of which 317 (4%) were

among children 14 and younger (38% of pediatric cases were among toddlers aged 1-4).³ There was a 9.5% increase in TB cases in the U.S. from 2020 to 2021³ due to an increase in immigrants from endemic areas and the rise of resistant TB.^{4,5}

Tuberculosis is endemic to many countries such as China, Asia, and Africa.⁶ In Europe, Asia, and Africa, 11.4, 12.2, and 12.8% of children had probable latent TB in addition to 3.4, 4.3, and 2.6% with

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confirmed TB, respectively.⁷ An estimated 20% of international children adopted into the US with negative tuberculin skin tests (TST) upon arrival subsequently tested positive within the following 3 months.⁸ Therefore, TST are no longer accepted for immigrant and refugee TB screening; interferon gold assays are required.⁹

Cutaneous tuberculosis (CTB) is an extrapulmonary manifestation of TB which occurs in 1% to 2% of TB cases.¹⁰ CTB results from exogenous inoculations of the skin, endogenous and hematogenous sources of TB, and hypersensitivity reactions (Table I). CTB can be caused by *M. tuberculosis*, *M. ovis*, and the Calmette–Guerin bacillus (BCG) vaccine.^{11,12} CBT's clinical manifestation and severity depend on many host factors such as immunosuppression, nutritional status, and socioeconomic status.^{1,13,14} The purpose of this review is to synthesize the current knowledge of pediatric CTB.

Lupus vulgaris

In India, lupus vulgaris (LV) is the most common CTB overall and amongst adults.^{15,16} In pediatric patients, LV is the second most common form of CTB.^{15,17} It is also more common among female patients.¹⁸ LV is chronic and progressive, resulting from exogenous or endogenous sources of TB.¹⁹ Risk factors for the exogenous spread of LV in children break the skin barrier such as ear piercings and tattoos.^{20,21} LV has also been reported as occurring concomitantly with scrofuloderma.¹¹

The BCG vaccination also provides an exogenous source for LV. A 2013 case report documented a 15-year-old male with lupus vulgaris following BCG vaccination. He presented with painless lesions on the face and multiple lumps on the neck. Histologically, multiple caseating granulomas with AFB were appreciated. Complete resolution was achieved within 6 months of anti-tuberculosis therapy (ATT).²²

Clinically, lesions present on the face or neck when acquired from hematogenous spread and present on the extremities when exogenously reinoculated.^{18,23,24} On exam, the lesions are non-tender plaques or nodules with ulceration²⁵ and are characterized as apple jelly nodules on diascopy.¹⁸ Lesions may progress to well-defined, scaly,

erythematous plaques.²³ Lymphadenopathy in the cervical and supraclavicular regions may also be appreciated.²³ Histology generally shows nonspecific findings; granulomas, giant cells, and caseous necrosis may be present,²³ and TST will be positive.^{18,23} Lesions heal as hyperpigmented plaques.²⁵

Lesions may develop significant sequelae. In a 2015 case report, a 10-year-old, immunocompetent, Indian boy presented with LV of the face. His lesions were erythematous crusted plaques on the nose and cheeks. Intranasally, the cavity was narrowed due to scaly plaques. TST was positive, and the patient started ATT. After 8 weeks of therapy, there was significant resolution at which point a large septal perforation requiring surgical reconstruction was appreciated.²⁶

CAPSULE SUMMARY

- This review synthesizes the various pathogeneses, presentations, and histology of the subtypes of cutaneous tuberculosis in the pediatric population.
- Assessing the current literature on cutaneous tuberculosis in pediatric patients may assist dermatologists in diagnosing and treating pediatric patients with these forms of extrapulmonary tuberculosis.

Tuberculous chancre

Tuberculous chancre, a primary inoculation of TB, results from exogenous inoculation via broken skin in an individual with no prior TB immunity. Risk factors include minor traumas such as piercings, tattoos, and unsterilized surgical instruments.^{27,28} Tuberculous chancre is considered a multibacillary form, meaning there is a high bacterial load. Children may become exposed to TB-contaminated materials if they are exposed to or live with a person suffering from pulmonary TB.^{18,29}

Clinically, lesions present as erythematous papules³⁰ which progress to firm non-tender ulcers frequently occurring on the upper²⁹ and lower limbs.³⁰ There is 1 report of primary cutaneous tuberculosis occurring on the breast which presented with chronic ulcerations and abscesses with purulent discharge.³¹ On physical exam, lymphadenopathy may be noted.³⁰

Histologically, granulomatous inflammation with caseous necrosis and AFB are appreciated.²⁹ TST is positive.^{30,32} Six months of anti-tuberculosis therapy is appropriate.³¹ Tuberculous chancre can resolve within 4 weeks of starting therapy, and abscesses heal via calcification.³³ However, if lesions chronically relapse, lifetime anti-TB medication may be necessary.²⁹

The BCG vaccination can also cause tuberculous chancre. These lesions present as ulceration and pruritis over the site of vaccination. Similarly, on histology, granulomatous dermatitis is present, and

Abbreviations used:

AFB:	acid-fast bacilli
ATT:	anti-tuberculosis therapy
BCG:	Calmette-Guerin bacillus vaccine
CDC:	Centers for Disease Control
CTB:	cutaneous tuberculosis
LS:	lichen scrofulosorum
LV:	lupus vulgaris
PNT:	Papulonecrotic tuberculid
TB:	<i>Mycobacterium tuberculosis</i>
TST:	tuberculin skin test
TVC:	Tuberculosis verrucosa cutis

staining for *Mycobacteria bovis* is positive.³⁴ Surgical debulking of the area may be necessary in addition to 6 months of anti-tuberculosis drugs.³⁴

Tuberculosis verrucosa cutis

Tuberculosis verrucosa cutis (TVC), warty tuberculosis, occurs due to exogenous reinfection and is considered a paucibacillary form.¹⁸ A recent study in India showed that 80% of TVC occurred in adults compared to children aged 14 and younger.¹⁵ These lesions most commonly occur on the bottoms of the feet.¹⁸ TVC develops as a small papule surrounded by inflammation that progresses to an asymptomatic wart-like lesion.³⁵ Histologically, hyperkeratosis and tuberculoid granulomas in the dermis have been reported.³⁶ AFB are not visualized on histology, but TST is typically positive.³⁶ Standard ATT therapy is recommended, and lesions respond well within 4 weeks.³⁶

TVC may present in addition to other forms of TB. A 2017 case report demonstrated TVC with concomitant scrofuloderma in an 11-year-old boy in India. He presented with multiple swellings in the groin area which ulcerated and drained serosanguinous fluid. Additionally, the child had a plaque on the dorsum of the foot. Histology of both lesions demonstrated epithelioid cell granuloma with giant cells and lymphocytic infiltrate.³⁷

Periorificial

Periorificial CTB is auto-inoculated into orifices by secretions during coughing. These lesions present as tender ulcers in the oral or perineal regions.³⁸ Histologically, granulomatous inflammation with caseous necrosis and acid-fast bacilli are present.³⁸ These lesions almost exclusively affect the elderly.³⁸ There are no case reports in the last 10 years documenting a pediatric case of periorificial CTB.

Scrofuloderma

Scrofuloderma, a cervical tuberculous lymphadenitis, is the most frequent CTB in tropical countries¹⁹

and in India.¹⁵ In a study from Morocco, scrofuloderma accounted for 57% of CTB cases.³⁹ The pathophysiology of scrofuloderma involves the contiguous spread of TB from deeper structures, frequently lymph nodes, to the skin, creating sinus tracts.⁴⁰

Clinically, scrofuloderma presents a palpable firm nodule that ulcerates, creating a sinus tract oozing pus.⁴¹ These lesions commonly form on the neck and face.³⁹ Cervical and postauricular lymphadenopathy can also be appreciated on exam.⁴¹ Histology reveals granulomatous inflammation with caseous necrosis; acid-fast bacilli are present. Treatment with 6 months of ATT resolves scrofuloderma.³⁹ Good resolution may be achieved within 4 weeks of starting therapy.¹¹ Scrofuloderma frequently leaves scars behind.⁴²

Scrofuloderma may present with other forms of CTB as well as other extrapulmonary forms of TB. A 2016 case report documented osteomyelitis of the mandible and TB meningitis concomitant with scrofuloderma in a 5-year-old male child in India. The patient presented with nontender submandibular and axillary lymphadenopathy in addition to red-brown erythematous lesions and discharging sinuses over the mandible. The patient received ATT at a 12-month follow-up; all skin lesions had resolved.⁴³

There were 5 pediatric cases of multidrug-resistant scrofuloderma documented in a 2015 case report from India. The children ranged in age from 12 to 18, and only 1 was male. Despite being on ATT for 6-12 months, they continued to develop new scrofuloderma lesions. Therefore, they were started on kanamycin IM 250 mg/day, prothionamide PO 250 mg/day, cycloserine or terizidone 250 mg/day, and levofloxacin 500 mg/day. Kanamycin was discontinued after 6 months, and the other drugs were continued for a year. The lesions began to resolve after 6 weeks of therapy and eventually scarred.⁴⁴

Tuberculosis miliaris cutis disseminate

Disseminated miliary tuberculosis often occurs in immunocompromised individuals and results from acute dissemination of TB from a primary focus. Patients are normally very ill and present with constitutional symptoms.¹⁴ On exam, lesions are widespread papules and crusted vesicles.⁴⁵ There is nonspecific inflammation with necrotizing vasculitis on histology, and AFB are visualized.¹⁴ ATT for 6 months resolves lesions that may heal as scars.⁴⁵

A 2019 case report from Colombia documented disseminated miliary tuberculosis in a malnourished, afebrile, 5-year-old female child who was otherwise immunocompetent. She presented with a painless skin ulcer and supraclavicular and cervical

Table I. Classifications of cutaneous tuberculosis

Source of TB	Route of spread	Type of CTB
Exogenous		Lupus vulgaris Tuberculous chancre Tuberculosis verruccose cutis
Endogenous	Contiguous	Periorificial Scrofuloderma
	Hematogenous	Tuberculosis miliaris cutis disseminate Lupus vulgaris Metastatic abscess Tuberculid
	Lymphatic	Lupus vulgaris

lymphadenopathy and hepatomegaly. Histology showed necrosis with granuloma formation and AFB. Further, on polymerase chain reaction, TB was detected. She was started on 11 months of anti-TB therapy (2 months 4 drug therapy and 9 months 2 drug therapy), and her CTB resolved in 2 months.⁴⁶

Rarely, disseminated CTB can result from the BCG vaccine in immunocompetent individuals.⁴⁷ These lesions present with widespread papules over the site of the BCG immunization. Anti-tubercular treatment for 6 months has been sufficient in previous cases.⁴⁶ Disseminated BCG occurring in children with a primary immunodeficiency is more common and may show dense dermal infiltration by foamy macrophages full of AFB or spindle-cell pseudotumors full of AFB on skin histology.⁴⁸

Metastatic abscess

Metastatic abscess is also known as tuberculous gumma. These lesions result from subacute hematogenous dissemination in the immunocompromised.^{49,50} Clinically, it presents as multiple nodules that can ulcerate, forming draining sinus tracts. Several case reports document abscesses forming on the anterior chest wall.^{51,52} Cervical lymph nodes may be palpable on exam.⁵³ On histology, granulomatous inflammation with caseous necrosis and AFB are present.⁴⁹ Treat patients with standard anti-TB drugs. Abscesses may resolve and scar 3 months following therapy.⁵³

Importantly, malnourishment is a cause of immunosuppression. A malnourished, HIV-negative 14-year-old girl was reported in 2013 to have tuberculous gumma with pulmonary tuberculosis in India. She presented with multiple painless, mobile masses which softened and ruptured, draining yellow material. She improved 4 weeks after beginning ATT.³⁶

Tuberculid

Tuberculid forms of CTB are the result of a hypersensitivity reaction to *M. tuberculosis* in other areas of the body which are not true infections of CTB.⁵⁴ Biopsies of tuberculids do not reveal AFB.

Lichen scrofulosorum. Over 80% of lichen scrofulosorum (LS) cases occur in the pediatric setting.⁵⁵ While the incidence is not known, it is estimated from a case series in India to represent 7.6% of CTB cases.⁵⁵ These lesions have been documented in conjunction with BCG-induced LV.⁵⁶

On exam, lesions present as nontender lichenoid papules which can coalesce to form plaques with fine scales.⁵⁷ These plaques may mimic pityriasis rosea by forming an annular pattern with overlying fine scales.⁵⁸ Lesions typically occur in a bilateral and symmetrical distribution on the trunk and lower extremities.⁵⁹ Cervical lymphadenopathy may also be appreciated.⁶⁰ Histologically, granulomatous inflammation without caseation with a parakeratotic epidermis may be appreciated, but no AFB will be seen with staining.^{60,61} TST is positive.⁵⁹ Anti-tuberculosis drugs for 6 months is the standard of care.⁶⁰ Lesions resolve in 8-12 weeks on average without scarring.^{59,62}

For example, a 2016 case report documented LS occurring in a 9-year-old female with disseminated tuberculosis in India. The child was malnourished, presenting with popular lichenoid erythematous, nonpruritic lesions with a fine scale. On histology, granulomas were appreciated. ATT was started for 6 months, and the skin lesions resolved within 4 weeks.⁶³

Papulonecrotic tuberculid. Papulonecrotic tuberculid (PNT) is another form of tuberculid CTB. Lesions present as necrotic, crusted papules on extensor surfaces.⁶⁴ On histology, necrosis and granulomatous inflammation can be appreciated; no AFB will be visualized.^{65,66} Standard ATT therapy is appropriate.⁶⁵

A 2016 case report from Korea documented a 13-year-old girl with PNT. Following the inception of ATT, she presented with erythematous papules and pustules on the upper extremities extensors. Several crusted dusky ulcers were appreciated. Histopathology showed granulomas with necrosis. ATT was continued for 6 months.⁶⁵

BCG-induced PNT was reported in a 6-month-old boy in Japan in 2020. The boy presented to the emergency department 35 days following BCG vaccination due to several papulonecrotic lesions on the upper limb, trunk, and face. Histology demonstrated pyogenic granulomatous inflammation without AFB. The lesions spontaneously resolved in 2 months.⁶⁶

Table II. Summary of the clinical presentation, histology and tuberculin skin test for the subtypes of cutaneous tuberculosis

Form of CTB	Clinical presentation	Histology and TST
Lupus vulgaris	Nontender plaques or nodules with ulceration Progress to well-defined, scaly plaques Located on face or neck (hematogenous spread) or extremities (exogenous reinoculation) Cervical and supraclavicular lymphadenopathy	Paucibacillary Granulomas, giant cells, and caseous necrosis Positive TST
Tuberculous chancre	Erythematous papules Progress to firm non-tender ulcers Upper and lower limbs +/- Lymphadenopathy	Multibacillary Granulomatous inflammation with caseous necrosis TST is positive.
Tuberculosis verrucosa cutis	Small papules surrounded by inflammation that develops into a wart-like lesion	Paucibacillary Hyperkeratosis and tuberculoid granulomas in the dermis Positive TST
Periorificial lesions	Painful ulcers in the oral or perineal regions	Multibacillary Granulomatous inflammation with caseous necrosis
Scrofuloderma	Firm nodules which ulcerate, forming purulent sinus tracts Cervical and postauricular lymphadenopathy	Multibacillary Granulomatous inflammation with caseous necrosis
Tuberculosis miliaris cutis disseminate	Widespread papules and crusted vesicles Immunocompromised patient	Multibacillary Nonspecific inflammation with necrotizing vasculitis
Metastatic abscesses	Multiple nodules that may ulcerate or form draining sinus tracts +/- Cervical lymphadenopathy	Multibacillary Granulomatous inflammation with caseous necrosis
Tuberculid forms	Lichenoid papules which may form plaques and scale	Paucibacillary; TST positive
Lichen Scrofulosorum	Bilateral and symmetrical distribution	Granulomatous inflammation without caseation with a parakeratotic epidermis
Papulonecrotic Tuberculid	Necrotic papules	Necrosis and granulomatous inflammation

Diagnosis and treatment

Patients presenting with suspicion for CTB should undergo a biopsy with Ziehl–Neelsen (ZN) stain for AFB and TB culture.⁶⁷ Clinical presentations and histological findings are summarized in Table II. Additionally, a TST or INF- γ assay can support the diagnosis of TB infection. A 2017 Indian study determined the sensitivities of DNA PCR, culture, and histopathology to be 24.5, 16.3, and 91.8%, respectively.⁶⁸ Diagnosing CBT should prompt a review of symptoms and chest x-ray to determine if there are other manifestations of extrapulmonary tuberculosis in the patient.⁶⁷ Anti-tuberculosis therapy typically consists of 6 months of therapy. The first 2 months consist of isoniazid, rifampin, pyrazinamide, and ethambutol followed by isoniazid and rifampin for 4 months.⁶⁹

Conflict of interest

None disclosed.

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