*** no patient handout*

Cutaneous tuberculosis

Synopsis

Tuberculosis (TB) is a mycobacterial infection most commonly caused by *Mycobacterium tuberculosis*. TB is distributed worldwide, and it is estimated that one-third of the world's population is infected (most without apparent disease). The majority of incidence cases come from India, Indonesia, China, Nigeria, Pakistan, and South Africa. Global incidence is on the decline since 2014, yet TB remains a top 10 cause of death worldwide. Risk factors for TB include poverty, homelessness, unemployment, crowding, and human immunodeficiency virus (HIV) infection. Most morbidity and mortality is seen in developing countries in tropical climates and in HIV-infected individuals. The risk of active TB in HIV-infected patients is 3%-8% per year with a lifetime risk of over 50%.

Cutaneous tuberculosis (CTB) is caused by *M. tuberculosis*, *Mycobacterium bovis*, and the Bacillus Calmette–Guérin (BCG) vaccine. It is exceedingly rare, only occurring in 1%-2% of extra-pulmonary tuberculosis cases. CTB is more common in children, pregnant women, and HIV-infected persons. Cutaneous manifestations of TB can be subclassified into 4 categories.

Exogenous Sources: Primary inoculation TB occurs at sites of trauma, abrasions, or wounds or at mucous membranes.

- In patients with no immunity against TB, a scab or chancre forms at the wound site and can be associated with regional lymphadenopathy after several weeks. Lymph nodes can eventually suppurate, abscesses can form, and fever and pain can develop.
- In previously sensitized individuals, primary inoculation can lead to tuberculosis verrucosa cutis (warty tuberculosis) and is not usually associated with systemic symptoms.

Endogenous spread (hematogenous, lymphatic, or contiguous spread to skin):

- Scrofuloderma results from involvement of skin overlying a contiguous TB focus, usually a lymph node, bone, joint, or lacrimal gland. It is the most common form of CTB in children.
- Orificial TB is a rare mucosal autoinoculation TB from pulmonary, genitourinary, or intestinal disease shedding organisms that seed the adjacent orifices.
- Lupus vulgaris results from hematogenous spread and is a progressive form of CTB seen in individuals with prior sensitivity and low immunity.
- Tuberculous gumma (metastatic tuberculous abscess) is a rare form of hematogenous TB.

- Acute miliary TB is a rare but life-threatening form of hematogenous TB seen in patients with low immunity.

Tuberculids: Tuberculids are presumed to be a hypersensitivity reaction to the TB organism and occur in patients with high immunity. There are 3 forms:

- Micropapular (lichen scrofulosorum)
- Papular (papulonecrotic tuberculid)
- Nodular (**erythema induratum**). Erythema nodosum can be also seen in pulmonary TB. Lesions are typically asymptomatic but may be painful. Localized adenopathy may occur.

Tuberculosis due to BCG vaccination: Lupus vulgaris, scrofuloderma, erythema induratum, papulonecrotic tuberculids, and lichen scrofulosorum have all been described.

All forms of CTB including tuberculids require systemic treatment. Without treatment, lesions can persist for months to years. The prognosis of miliary TB is often poor.

Codes

ICD10CM:
A18.4 – Tuberculosis of skin and subcutaneous tissue

SNOMEDCT:
66986005 – Cutaneous tuberculosis

Look For

Inoculation TB:
A small papule evolving into an ulcer with ragged, red-blue, undermined edges. Also look for thick adherent crusts in older, larger lesions and regional adenopathy.

Tuberculosis verrucosa cutis:
Look for one or more large verrucous plaques (often on the hands).

Scrofuloderma:
A nodule, frequently overlying cervical lymph nodes, breaks down into an ulcer, which may have numerous fistulae and scarring.

Orificial TB:
Red nodules break down into shallow, painful ulcers that are smaller than 2 cm (oral, genital, perianal).

Miliary TB:
Multiple papules, vesicles, pustules, or purpuric lesions.

Tuberculous gumma:
Firm nodule or abscess, with single or multiple lesions, usually on the extremities.

Lupus vulgaris:
Red-brown plaque, sometimes with ulceration and scar, central clearing over time, sometimes nodular. "Apple jelly" has been used to describe the characteristic yellow-brown color under diascopy. Usually single, on the head and neck, or around nares in adults. More common on the buttocks or extremities in children.

Lichen scrofulosorum:
0.5-3 mm grouped, crusted papules, usually on the trunk and proximal extremities. Ears are further sites of predilection.

Papulonecrotic tuberculid:
Crops of firm, red papules that crust or ulcerate, leaving varioliform scars, usually on the extensor extremities and buttocks.

Erythema induratum:
Nodules typically on the posterior legs that may ulcerate, more often in women.

Diagnostic Pearls

Given its clinical heterogeneity, consider the diagnosis of CTB for any nonhealing nodule, ulcer, plaque, or draining lymph node in patients from endemic TB areas or with AIDS.

Differential Diagnosis & Pitfalls

Non-tuberculous mycobacterial infection (ie, ***Mycobacterium marinum***, ***Mycobacterium avium* complex** [MAC]) can be clinically indistinguishable from CTB.

Primary inoculation TB

- Deep fungal infection
- **Nocardiosis**
- **Pseudomonal folliculitis**
- **Primary syphilis**
- Leishmaniasis (**Old World** and **New World**)
- **Yaws**
- **Tularemia**
- **Bartonellosis**

- **Cat-scratch disease**
- **Impetigo**
- **Ecthyma**
- **Cellulitis**

TB verrucosa cutis

- **Blastomycosis**
- **Chromoblastomycosis**
- **Tertiary syphilis**
- **Verrucous epidermal nevus**
- Hypertrophic **lichen planus**
- Halogenoderma
- **Verruca vulgaris**
- **Prurigo nodularis**

Scrofuloderma

- **Sporotrichosis**
- **Actinomycosis**
- **Coccidioidomycosis**
- **Mycetoma**
- **Lymphogranuloma venereum**
- **Acne conglobata**
- **Hidradenitis suppurativa**

Orificial TB

- **Aphthous ulcers**

- Syphilis (all stages) (see **secondary syphilis**)
- **Lymphogranuloma venereum**
- **Blastomycosis**
- **Rhinoscleroma**
- Oral malignancy

Lupus vulgaris

- Deep fungal infection
- Leishmaniasis (**Old World** and **New World**)
- **Tertiary syphilis**
- **Discoid lupus erythematosus**
- **Lymphocytoma cutis**
- Tuberculoid **leprosy**
- **Pyodermatitis vegetans**
- **Sarcoidosis**
- **Rosacea**
- **Squamous cell cancer**

Papulonecrotic tuberculid

- **Pityriasis lichenoides et varioliformis acuta** (PLEVA)
- **Secondary syphilis**
- **Lymphomatoid papulosis**
- **Varicella**
- Perforating disorders
- **Vasculitis**
- **Prurigo nodularis**

Lichen scrofulosorum

- **Lichen nitidus**
- **Lichen planus**
- Papular **eczema**
- Papular **sarcoidosis**
- Lichenoid **secondary syphilis**

Erythema induratum

- **Erythema nodosum** and other panniculitides
- **Polyarteritis nodosa** and other medium vessel vasculitides
- **Tertiary syphilis**
- **Nodular vasculitis** – an eruption with a similar clinical and histopathologic appearance but not associated with TB

Best Tests

Tissue Diagnosis of CTB
Biopsy for histopathology, stain for acid-fast bacilli (AFB), culture, and nucleic acid amplification testing (NAAT) when available. It is best to combine histopathology with culture and NAAT for highest diagnostic yield.

Limitations:

- AFB stain: low sensitivity particularly in paucibacillary lesion, does not distinguish TB from non-tuberculous mycobacteria
- Culture: typically takes 4-6 weeks
- NAAT (MTD and Xpert MTB/Rif): higher sensitivity and specificity than AFB but can get false negatives in paucibacillary lesions and because of tissue processing

Histopathology Findings:
Common features:

- Acanthosis or atrophy of the overlying epidermis

- Tuberculoid granulomas (surrounded by a corona of lymphocytes) in the superficial and mid-dermis
- AFB located in the cytoplasm of histiocytes
- Scattered multinucleate giant cells
- Dermal fibrosis (late lesions)

Occasional features:

- Pseudoepitheliomatous hyperplasia
- Ulceration of the overlying epidermis
- Granulomas in a perifollicular distribution
- Caseation necrosis within tuberculoid granulomas
- Transepidermal elimination of granulomas

Immunologic Diagnosis of TB
Must evaluate in addition to tissue diagnosis as above, including tuberculin skin test (TST) and interferon gamma release assays (T-SPOT and Quantiferon gold):

Limitations:

- Does not distinguish between latent and active TB infection.
- TST: false negatives in HIV, miliary TB, and orificial TB, false positives in BCG vaccination
- Interferon gamma release assays: false negative in immunosuppressed patients

Systemic Workup:

- Chest x-ray (CXR), sputum for AFB / culture / NAAT
- Radiologic evaluation and/or biopsy of lymph node or other organs depending on clinical presentation

Management Pearls

Upon diagnosis of CTB, expedited referral to an infectious disease specialist is warranted to evaluate for systemic involvement, bacterial resistance, and treatment course.

Country of origin will dictate therapeutic ladder as polydrug and multidrug resistant strains are more prevalent in certain regions. Additional risk factors for resistance include medication nonadherence, TB reinfection, and contacts with drug-resistant TB.

In September 2006, there was an outbreak of highly lethal extensive / extreme drug-resistant TB (XDR-TB) in South Africa. This refers to strains resistant to first-line antimicrobials (isoniazid and rifampin) as well as 3 of the 6 second-line therapies (amikacin or kanamycin, capreomycin, ciprofloxacin or ofloxacin, ethionamide, cycloserine, and para-aminosalicylic acid). XDR-TB differs from multi-drug resistant TB (MDR-TB) in that MDR-TB is resistant to the first line of therapies, but not the second line.

Droplet precautions with N95 mask and negative pressure ventilation rooms are warranted until active pulmonary TB is excluded by CXR and sputum AFB / culture. In the United States, tuberculosis is reportable in every state and territory and the District of Columbia.

Childhood BCG vaccination for the prevention of TB is performed in much of the world, but practices vary by country and it is not routinely performed in the United States. CTB can occur despite BCG vaccination.

Therapy

The treatment of CTB is the same as for systemic TB. The following factors affect medication choice and treatment duration:

- Comorbidities and immune status (eg, HIV status)
- Degree of systemic involvement (ie, longer course in central nervous system, bone, joint disease)
- Drug resistance profile

First-line standard antituberculosis therapy includes:

Intensive phase (2 months)

- Isoniazid (5 mg/kg)
- Rifampin (10 mg/kg)
- Pyrazinamide (15-30 mg/kg daily)
- Ethambutol (25 mg/kg daily)

Continuation phase (4-7 months)

- Isoniazid (5 mg/kg)
- Rifampin (10 mg/kg)