Chapter 13
Cutaneous Tuberculosis

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Tuberculosis, an infection caused by *Mycobacterium tuberculosis* bacilli, has existed for millennia, and till today it continues to be a major global public health concern. WHO estimates that 20–40% of the world population is affected and that in 2015 alone there were 10.4 million new TB cases (including 1.2 million among HIV-positive people), of which 5.9 million were among men, 3.5 million among women, and 1.0 million among children. Overall, 90% of cases were adults and 10% children, and the male/female ratio was 1.6:1. The bulk of the disease globally is pulmonary TB, but the bacilli can affect any other body organ including the skin in the form of extrapulmonary TB in about 8.4–13.7%. This makes tuberculosis of the skin a relatively uncommon infectious disease comprising only 1–2% of the extra-pulmonary tuberculosis cases and approximately 0.1–1% of all cutaneous disorders [1]. Only 5–10% of infections with *M. tuberculosis* lead to disease, highlighting the low virulence of the organism. Cutaneous tuberculosis increases with concomitant infection with HIV, an increase in multidrug-resistant TB and the recent rise in the therapeutic use of biologics specifically antitumor necrosis factor (Anti-TNF) [2].

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13.1 Classification

The clinical presentation depends mainly on the route of infection, cellular immunity, and virulence of the infecting organism. A variety of local factors play a role as well such as interrupted skin barrier, vascularity, lymphatic drainage, and the proximity to the regional lymph glands [3]. There are numerous presentations and morphologies that are classified based on the mode of infection and immunologic status of the host. Cutaneous TB is classified into three main categories:

1. Exogenous inoculation
2. Endogenous infection
3. Hematogenous spread

13.1.1 Exogenous Inoculation

Tuberculous chancre is the resulting lesion from autoinoculation into the skin or mucous membrane of a patient with no prior exposure or immunity to *Mycobacterium tuberculosis*. Introduction of the bacteria into the skin may result from interruption of the skin barrier resulting from skin or mucous membrane injury such as wounds, tattoos, piercings, tooth extraction, ritual circumcision, and mouth-to-mouth resuscitation [4]. It commonly appears on the face and limbs of children. The tuberculous chancre presents with a painless non-healing papule or ulcer that may enlarge to a size of 5 cm [5], typically 2–4 weeks after inoculation. The ulcer is shallow with undermined edges and granular or hemorrhagic base. Regional lymphadenopathy develops in 3–8 weeks. The development of a cold abscess may occur weeks to months later that may perforate resulting in sinus formation. If untreated, the lesion may last up to a year and eventually heal leaving a scar. The regional lymph nodes slowly subside and may calcify in 50% of the cases [5].

Reactivation of the disease or hematogenous spread may occur if the immune response was inadequate.

Mucous membrane lesions may present as conjunctival edema or ulceration with regional lymphadenitis [6]. Oral lesions, although rare, have been reported [7].

In the early phase, the histopathology of the lesion shows a mixed dermal inflammatory infiltrate and an abundance of acid-fast bacilli. After a 3–6-week period, a tuberculoid granuloma develops in the lesion and regional lymph node and may be accompanied by caseation necrosis [8].

Tuberculosis verrucosa cutis (warty tuberculosis) occurs in individuals with a moderate to high immunity on re-exposure or inoculation. It commonly presents on the hands in adults or lower extremities in children. It usually starts as a painful firm papule with a purple inflammatory halo. The lesion, usually solitary, grows slowly into an asymptomatic hyperkeratotic verrucous plaque. Irregular extension of the edges leads to a serpiginous appearance [9]. If untreated the lesion grows very slowly for many years. Occasionally, spontaneous resolution occurs leaving an atrophic scar.

Histopathology of such lesions shows marked hyperkeratosis and hyperplasia of pseudoepitheliomatous proportions of the epidermis accompanied by caseating granulomas in the dermis. Acid-fast bacilli can be seen if the specimen is carefully examined [5, 8].

13.1.2 Endogenous Infection

This results from involvement of the skin as direct extension from an underlying focus of infection such as subcutaneous tissue, lymph gland, lacrimal gland or duct, or bones and joints.

Scrofuloderma is reported as the commonest form of cutaneous tuberculosis in children under the age of 10 years [10]. Overlying the infected focus, a red-blue, mobile, firm, asymptomatic nodule develops. Subsequent liquefaction and breakdown may take months and form ulcers and sinuses. Ulcers may follow a linear or serpiginous pattern with bluish undermined edges and granulation tissue at the base [9]. Scarring and granulation tissue may give rise to irregular fungating tumors.

Histopathology shows caseation necrosis at the center with tuberculous granulomas at the periphery of the lesion. Acid-fast bacilli can usually be isolated from the necrotic debris.

Orificial tuberculosis (tuberculosis cutis orificialis) autoinoculation of the mucous membranes or skin adjacent to orifices with large number of viable tubercle bacilli in patients with advanced infection of pulmonary, intestinal, genital, or urinary systems. These patients are severely ill and have low immunity. The lesions, commonly in the oral mucosa, are red painful nodules that quickly form shallow ulcers with bluish edges that fail to heal [9].

13.1.3 Hematogenous Tuberculosis

Infection of the skin through hematogenous dissemination or lymphatic seeding is referred to as hematogenous tuberculosis. Lupus vulgaris is the commonest form of hematogenous spread and occurs in individuals with moderate to high degree of immunity [4]. It may also occur as a result of inoculation, BCG vaccination, direct extension, or lymphatic spread. Over 80% of the lesions are located on the head and neck, especially around the nose [9]. A reddish-brown plaque is the initial presentation with the characteristic apple-jelly appearance on diascopy. The lesion slowly increases in size and becomes firm, elevated, and brown in color. There are five main clinical presentations. The plaque form, most common, is red-brown in color and may have a smooth or psoriasiform surface with irregular edges that become hyperkeratotic. Variable scarring occurs in these lesions. Ulcerating and mutilating form is destructive and invades deep tissue and cartilage leaving necrosis

crusts and scars. The vegetative form is characterized again with ulceration and necrosis but with minimal scarring. It is disfiguring especially when nasal or auricular cartilage is invaded. Tumorlike forms, either smooth or hyperkeratotic, commonly involve the earlobe and may cause lymphedema and vascular dilatation. Papular and nodular form present as multiple lesions after temporary immunosuppression.

A skin biopsy shows tuberculoid granulomas with lymphocytes at the periphery in the upper and mid dermis. Occasional central caseation is demonstrated. Lesions are paucibacillary, but acid-fast bacilli can be seen in some sections [8].

Tuberculous gumma also known as metastatic tuberculous abscess is a rare form of hematogenous dissemination in hosts with low immunity and results in single or multiple cutaneous or subcutaneous lesions. Abscesses are generally non-tender and may present as a fluctuant abscess nodule or firm subcutaneous nodule [9]. The overlying skin will eventually breakdown and result in ulcers and sinuses. Tubercle bacilli can be isolated from the discharge [5, 9].

Miliary tuberculosis (tuberculosis cutis miliaris disseminata) is a rare life-threatening form and commonly affects young children and patients with immunosuppression. Multiple bluish to red-brown papules, vesicles, and hemorrhagic lesions initially appear. The vesicles later become necrotic and ulcerate. Histopathology shows a chronic non-specific inflammatory infiltrate in the dermis surrounding a necrosis and abscess formation with abundance of acid-fast bacilli.

Tuberculids, initially described by Darier in 1896, result from a hypersensitivity to tuberculous organisms or its products in individuals with high immunity. They characteristically have a positive tuberculin test, a positive response to anti-tuberculous therapy and difficulty in isolating the organism.

True tuberculids can be classified into three main categories:

1. Micropapular: lichen scrofulosorum
2. Papular: papulonecrotic tuberculid
3. Nodular: erythema induratum of basin, nodular tuberculid

Lichen scrofulosorum is an uncommon lichenoid eruption presenting in children and young adults. A crop of asymptomatic skin-colored, yellowish, or reddish-brown lichenoid papules commonly appear on the trunk and proximal extremities. Histopathology of the involved skin shows perifollicular noncaseating tuberculoid granulomas. AFB are not demonstrable [8].

Papulonecrotic tuberculids present as dusky red necrotic papules mainly on the extremities of young adults. The lesions heal with a varioliform scar. Histopathology of the lesion shows ulceration involving the epidermis and variable thickness of the dermis with area of necrosis. A palisade of histiocytes can be seen surrounding the lesion. Vasculitis, fibrinoid necrosis, or thrombosis can be seen in adjacent vessels.

The lesions of erythema induratum of Bazin are localized to the subcutaneous fat and present with ill-defined nodules commonly located on the posterior aspect of the lower legs. The lesions may ulcerate and yield shallow ulcers with irregular bluish edges. It is a lobular panniculitis with neutrophilic vasculitis.

13.2 Non-tuberculous Mycobacteria

Infections with atypical mycobacteria, as they were previously named, occur predominantly in immunocompromised hosts. In immunocompetent hosts, infection follows skin penetration and is usually localized, while there is a tendency for dissemination in immunocompromised patients. There are many species in this category, but the commonest organisms causing cutaneous disease are members of the *M. fortuitum* complex (*M. fortuitum*, *M. chelonae*, and *M. abscessus*), *M. marinum*, *M. haemophilum*, and *M. ulcerans*. These organisms are widely distributed in the environment and can be found in soil, water, flora, commensal organisms of the skin, and some fauna [4, 5].

M. fortuitum complex species are fast-growing mycobacteria capable of causing disease in both immunocompetent and immunocompromised hosts. In the former, there is a history of trauma resulting in a localized disease, while in the latter it causes disseminated disease with no history of penetrating injury. Localized disease may present as nodules, abscesses, ulcers, cellulitis, and sinuses. Disseminated cutaneous disease presents with multiple nodules with no specific pattern.

Fish tank granuloma or swimming pool granuloma is the cutaneous disease caused by inoculation with *M. marinum*. It is isolated from both salt water and freshwater. Incubation period can be as early as 2–3 weeks or as late as 9 months. Lesions start as nodule or pustule that may later form an ulcer or abscess and eventually a verrucous plaque. Lesions are usually multiple and may extend in a sporotrichoid pattern along lymphatic drainage.

Buruli ulcer is the local name given to the cutaneous disease caused by *M. ulcerans* when it was first described in 1897 in Uganda [9]. It has since been reported mainly in tropical and subtropical riverine areas. Mode of transmission is not known yet. Most patients are children under the age of 15 years. They present with a firm mobile subcutaneous nodule that breakdown into a painless shallow necrotic ulcer with undermined necrotic edges. Ulcers are usually single but grow over weeks to several centimeters in size.

The natural habitat and mode of transmission of *Mycobacterium haemophilum* is not known. It affects immunocompromised individuals especially organ transplant recipients and patients on long-term immunosuppression. Patients present with multiple painful, violaceous nodules on the extremities that develop into ulcers or abscesses. Systemic symptoms may accompany cutaneous disease such as weight loss, tenosynovitis, osteomyelitis, joint effusions, or respiratory tract symptoms [9].

13.3 Treatment

The current therapeutic options for cutaneous TB are limited to the conventional anti-tuberculous drugs in addition to some surgical interventions in certain indications (surgical excision of lesions and correction of deformities). The standard

therapeutic agents used include the combination of isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin. It is important to note that most of the reported cases of cutaneous TB are sensitive to the commonly used agents and resistant cutaneous TB is very unusual. The treatment of cutaneous tuberculosis is similar to that of pulmonary TB, where a combination of anti-tuberculous agents are used in two phases: intensive or bactericidal phase using the combination of isoniazid, rifampicin, ethambutol, and pyrazinamide for 8 weeks and the maintenance or sterilizing phase for 16 weeks with isoniazid and rifampicin. In cutaneous TB cases in HIV-positive patients, the maintenance phase of the treatment is extended from 16 to 28 weeks. If the cutaneous TB lesions are close to natural orifices, we can use lactic acid 2% and local anesthetic agent.

For cutaneous infections with atypical mycobacterium, the anti-TB drugs are less effective, and hence a variety of antibiotics could be used to treat such infections depending on sensitivity profile. The therapy in such cases is usually difficult and requires prolonged duration. To date there are no topical anti-TB drugs that are available for use in cutaneous tuberculosis [4].

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