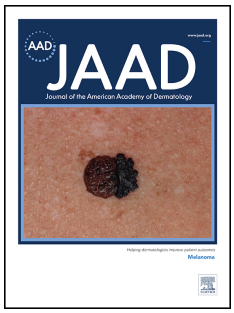

Cutaneous tuberculosis. Part I: Pathogenesis, classification, and clinical features

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Abbreviations:

BCG: bacilli Calmette-Guerin

CTB: Cutaneous TB

HIV/AIDS: Human immunodeficiency virus/Acquired immune deficiency syndrome

LV: Lupus vulgaris

MTB: *Mycobacterium tuberculosis*

PCR: Polymerase chain reaction

TB: Tuberculosis

TBVC: Tuberculous verrucosa cutis

US: United States

Abstract

Tuberculosis is an ancient disease that continues to affect an estimated 10 million people per year and is responsible for 1.4 million deaths per year. Additionally, the HIV epidemic and multi-drug resistance present challenges to disease control. Cutaneous tuberculosis is an uncommon, often indolent, manifestation of Mycobacterial infection that has a varied presentation. Diagnosis is challenging as lesions mimic other more common conditions and microbiological confirmation is often not possible. Cutaneous tuberculosis can be broadly categorized into multibacillary and paucibacillary forms. About one-third of skin tuberculosis is associated with systemic involvement. By early recognition of cutaneous tuberculosis, dermatologists can play an important role in disease control. The first article in this 2-part continuing medical education series describes the latest epidemiology, microbiology, and pathogenesis of tuberculosis. Furthermore, we review the classification, clinical manifestations, common clinical differentials, and systemic involvement that occurs in cutaneous tuberculosis.

Introduction

Tuberculosis (TB) is a chronic granulomatous infection caused by *Mycobacterium tuberculosis* (MTB), and rarely by *M. bovis* or *bacille Calmette-Guérin* (BCG) strains, that can possibly affect any organ. Although the bacterium has been in existence for over 70,000 years, and effective treatment is available, it continues to be a major public health concern in developing nations.[1] Moreover, with globalization and the movement of populations across nations, TB can spread to areas of low prevalence.[2] Infection can present either as latent infection (asymptomatic and detected by screening), or progress to active disease (symptomatic) in those with low immunity. Globally, over 1.5 million deaths were from TB in the year 2020.[3] Apart from its infectious nature, chronic course, and the need for prolonged treatment, the worldwide spread of Human immunodeficiency virus/Acquired immune deficiency syndrome (HIV/AIDS) and the emergence of multi-drug resistant strains represent additional challenges to disease control.[1,4] Lungs are the most common site of infection and extra-pulmonary TB constitutes between 8 – 24% of cases.[3] Cutaneous TB (CTB) accounts for about 1.5 – 3% of extra-pulmonary cases.[5,6] As infection of the skin is an uncommon, often insidious manifestation that has myriad possible morphologies, it can be overlooked. CTB frequently has systemic involvement and dermatologists can play a role in early identification and management. The first part of this continuing medical education series elucidates the epidemiology, pathogenesis, and the spectrum of CTB.

Epidemiology of Tuberculosis

Key points

- Tuberculosis remains a global public health concern with an incidence of 10 million cases annually
- In endemic areas, cutaneous tuberculosis is more common in children than adults
- HIV co-infection promotes disseminated disease, drug resistance, and mortality from tuberculosis

Worldwide distribution

Globally, TB has long been the most common cause of death from a single infectious agent, surpassing HIV since 2007. According to the World Health Organization Global tuberculosis report, in 2020, the incidence of new infections was about 9.9 million worldwide.[2,3] The majority of the burden is in a few geographical areas: 43% in South-East Asia, 25% in Africa, and 18% in Western Pacific.[3] Notably, five countries account for over half of the global disease burden: India, China, Indonesia, the Philippines, and Pakistan.[3] By comparison, in 2019 the United States (US) recorded a total of 8,916 cases of TB that represents an incidence rate of 2.7 per 100,000 persons. About 71% of these infections occurred in persons born outside of the US.[5,7] In areas of low prevalence, such as Japan and Hong Kong, CTB accounts for 0.03 – 0.06% of dermatology patients, whereas data from endemic areas, such as India and Brazil, showed that CTB comprises about 0.1 – 2% of dermatology patients [5,6,8-13] Over time, there has been a trend towards change in the distribution of CTB types – decrease in true CTB (especially, scrofuloderma and tuberculous verrucosa cutis (TBVC)) and increase in tuberculids (particularly, erythema induratum of Bazin and papulonecrotic tuberculid).[9,10]

Age and Gender

TB can affect people of any age or sex; worldwide, infections are more prevalent in men (56%), followed by women (32%), and children (12%).[3] Similarly, most CTB studies have reported a male preponderance, except for studies from Brazil, Spain, and Ethiopia.[5,10,12–18] Compared with developed nations, studies from India, China, and Morocco reported more children and young adults affected with CTB, comprising 48 – 63% of all cases.[8,11,12,18-21]

Effect of HIV co-infection

Worldwide, about 8% of all TB infections occur in those with HIV.[3] HIV/AIDS is the strongest predisposing factor to TB disease.[2] Additionally, HIV co-infection predisposes to severe disease, multi-drug resistant TB disease, and mortality.[2,4] The depletion of CD4 cells in HIV/AIDS is a proposed explanation for poor granuloma formation and high bacillary load.[7, 22] Both primary drug resistance, due to transmission of resistant Mycobacterial strains, and acquired resistance, due to de novo mutations can occur.

Malabsorption, difficulty adhering to complex medication regimens, and a possible higher mutation rate in dual infected persons contribute to acquired resistance.[4]

Pathogenesis of Cutaneous Tuberculosis

Key points

- The most common causative agent is *Mycobacterium tuberculosis*
- The *M. tuberculosis* genome facilitates evasion of innate immunity
- Disease manifestation is a result of a complex interplay between bacterial virulence, host immune status, and route of infection

Microbiology

MTB is the predominant causative agent of tuberculosis. Rarely, CTB can be caused by *M. bovis* or BCG bacillus (an attenuated *M. bovis* strain used for vaccination).[23,24] MTB is an acid-fast non-spore forming aerobic bacillus that is a facultative intracellular pathogen.[25] It has a prominent lipid-containing cell envelope that assists in immune evasion. Additionally, it replicates slowly and has a duplication time of 20 hours.[26] MTB is neither gram positive nor negative but can be identified by Ziehl-Neelsen staining as it retains the red fuchsin stain and resists decolorization with acid or alcohol.[25,27]

Immunopathogenesis

Clinical presentation and disease progression are a result of a complex interplay between bacterial virulence, host immune status, and route of infection.[23]

The tubercle bacillus has several properties that allow it to survive intracellularly. One tenth of the *M. tuberculosis* genome is made up of genes that encode antigens for evasion of innate immunity.[25] The inhaled bacilli infect alveolar macrophages and dendritic cells, invade the phagosomes, and arrest phagosome maturation by secretion of serine/threonine kinases. The bacilli can survive in the hostile phagosome environment by expression of stress-adaptive genes, production of enzymes (KatG) to inactivate phagosomal reactive oxygen species (ROS), and prevention of phago-lysosome fusion. The bacilli that

survive replicate in the phagosomes, and their complex envelope lipids facilitate escape from the phagosomes.[26]

Both innate and adaptive immunity play a role in the control of mycobacterial infection.[28] Toll-like receptors (TLRs), especially, TLR2, TLR4 and TLR9, present on alveolar macrophages and dendritic cells help recognize mycobacteria via pathogen associated molecular patterns present on the bacilli.[28] This interaction triggers the innate immune response. TLR activation also upregulates the vitamin D pathway to promote production of antimicrobial peptides that inhibit *M. tuberculosis* growth.[26] The initial anti-mycobacterial activity is via production of reactive nitrogen and oxygen in the macrophages. Then cytokines and chemokines (IL-6, IL-12, IL-1*α*, IL-1*β,* TNF-*α*) released by activated dendritic cells recruit other inflammatory cells, such as monocytes, neutrophils, lymphocytes, and Natural Killer (NK) cells.[26,28] Activated CD8+ and NK cells release interferon-γ (IFN- γ) in response to IL-12 and IL-18 produced by dendritic cells.[26,28] IFN-γ promotes phagosomal maturation and induces autophagy of macrophage phagosomes, thereby promoting mycobacterial killing. Furthermore, NK cells facilitate direct lysis of infected macrophages and secrete IL-22, which hampers bacterial replication.[26] Further control of infection is mediated by TNF-α, which is produced by several inflammatory cells, through the formation of granulomas.[28] Associated caseation necrosis is characteristic.[29] Recent evidence points to an important role of Th17 cells in the development and maintenance of granulomas.[26] An exuberant immune response can lead to neutrophil mediated tissue destruction, as in cavitary pulmonary TB.[26,28]

Host and environmental factors

Host factors

About one-fourth of the world's population is estimated to have latent TB.[3,30] An estimated 5 – 10% of the population exposed to MTB develops active TB.[26] The fact that exposure to the tubercle bacillus is much more common than clinical infection highlights the importance of host factors in infection and disease progression. Genetic alterations that interfere with components of the immune pathway required to contain mycobacteria can lead to more severe disease; polymorphisms in Mannose binding protein and mutations in the genes for IFN-γR and IL-12 receptor β1 promote the development of disseminated TB.[31]

Presence of comorbid conditions, such as HIV, diabetes, and malnutrition can dampen the immune system's ability to contain TB.[29] HIV/AIDS increases the risk of disseminated infection and mortality from TB by depleting the CD4 pool, which decreases available IFN- γ, which is an essential mediator in defense against TB.[26,31] Children are more likely to develop active TB infection after exposure with a 60 – 80% infection rate postexposure. [31] If the first exposure to TB leads to a disease manifestation, it is termed a "primary" infection. If initially contained without symptoms, there is potential for reactivation ("secondary" CTB).[31] In those with a history of BCG vaccination (only approved TB vaccine used in endemic areas), there may be partial immunity to MTB. Although vaccination prevents disseminated and meningeal involvement in children, efficacy in adults is lower and varies from 0 – 80%.[32]

Route of infection

The route of infection, in conjunction with immune status, determines the presentation. Inoculation TB presents as a chancre in those without prior exposure to tubercle bacilli, lupus vulgaris (LV) in those with partial immunity, and TBVC in those with a robust immune response.[23,33] By hematogenous spread, an immunosuppressed host can develop acute miliary CTB or TB abscess, whereas in a host with some immunity to TB, hematogenous spread can present as LV.[34,35] In those with suppressed immunity, autoinoculation from the gastrointestinal or respiratory tract presents as erosive disease characteristic of orificial TB. Contiguous spread from lymph nodes or bones gives rise to scrofuloderma.[23]

Geographical variation

Much of the TB burden is concentrated in resource poor nations. The WHO global TB report reported the countries with the highest caseload: India accounts for 26%, Indonesia 8.5%, China 8.4%, the Philippines 6%, Pakistan 5.7%, and Nigeria 4.4%.[3] This distribution is due to downstream effects of socioeconomic differences.

Socio-economic considerations

Poverty and lack of education are associated with overcrowding, poor sanitation, insufficient nutrition, and inadequate access to healthcare.[36, 37] These factors contribute to spread of TB, inadequate treatment, and severe disease supported by evidence from endemic areas. The prevalence of tuberculosis in

those below the poverty line in India was reported to be 1.5 times higher than those above it.[36] Similarly, in China, illiteracy is a risk factor for TB, whereas a higher income is protective.[37] Furthermore, malnutrition is a risk factor for severe disease. [31]

Classification

Key points

- The classification of cutaneous TB is complex and depends on several factors, including route of infection, immune status, prior tuberculosis exposure
- Based on bacillary load, it can be multibacillary or paucibacillary
- Based on the route of infection, it is categorized as endogenous or exogenous

Because of the many factors that determine disease presentation, including route of infection, prior exposure, bacterial load and immunity, the classification of cutaneous tuberculosis is complex and variable. In general, CTB is divided into true TB and tuberculids. True CTB have demonstrable MTB in the lesions, by conventional (microscopy and culture) or molecular diagnostic methods (PCR). Tuberculids are hypersensitivity reactions ("id" reaction) to mycobacterial antigens, indicate a strong immune response, and do not have any detectable lesional mycobacteria.[38-40] However, rarely PCR may be positive.[39,40]
True CTB can be further classified based on bacillary load and route of infection. The classification is outlined in Table 1.[23,41]

Based on mycobacterial load and host immunity

Multibacillary forms of CTB have a high bacilli load, which facilitates detection of mycobacteria on microscopy or isolation in culture. These forms include tuberculous chancre, TB gumma, acute miliary TB, scrofuloderma, and orificial TB.[20,42]

Paucibacillary types have sparse mycobacteria, thus, microscopy and culture are usually negative: LV, TBVC and all the tuberculids.[20,42]

Based on route of infection

Endogenous TB encompasses all the forms spread by hematogenous or contiguous routes. Acute miliary TB and TB gumma occur by hematogenous spread. Scrofuloderma spreads from underlying structures, while self-inoculation from the gastrointestinal tract can result in orificial TB.[38]

Exogenous TB refers to those acquired by inoculation, and classically includes tuberculous chancre and TB verrucosa cutis. LV can also occur after inoculation, such as after tattooing or injections, in a host with some immunity due to prior BCG vaccination or TB exposure.[33,38,43]

Clinical features of Cutaneous Tuberculosis

Key points

- Cutaneous TB has a wide range of morphological presentations and may mimic several infectious and non-infectious dermatoses
- Clinical diagnosis is often delayed and requires a high index of suspicion
- All cases should be evaluated for regional lymphadenopathy and a systemic focus of TB

Symptoms and physical exam findings

True cutaneous tuberculosis

Tuberculous chancre

Also called primary inoculation TB, it is a rare form (0 – 1% of all CTB) and occurs after mycobacterial entry via an injury that is often unnoticed.(Figure 1) About 2 – 4 weeks later, a brown-red asymptomatic papule develops at the site of entry, which can form a friable painless ulcer with undermined edges.[12,27,44] Regional lymphadenopathy may or may not be present.[44,45] If left untreated, it can progress to scrofuloderma, LV, disseminated TB, or exceptionally resolve with scarring.[27]

Tuberculosis verrucosa cutis

Earlier terminologies including prosector's or butcher's wart allude to the appearance and route of infection of TBVC (inoculation from infected cadavers). It accounts for about 3 – 19% of all CTB.[8,11,18,19,35] It presents as a verrucous, asymptomatic, slow-growing plaque at the site of inoculation, most commonly

on the lower extremities and buttocks.[46] (Figure 2) Feet and buttocks are common sites due to the practice of spitting outdoors combined with the habit of walking barefoot and squatting outside.[9,46] With education and improved sanitation, the incidence of TBVC has decreased in some nations.[9,10] Due to its insidious growth, patients often present years after onset.[35] Dermoscopy can aid in diagnosis and is characterized by papillated surfaces with a yellow-red background, and dirty white thick scales. Dilated papillary vessels with multiple yellow to orange structureless and globular areas are observed at 40x magnification.[47]

Lupus vulgaris

LV is one of the most common types of CTB (4 – 63%).[5,9,15,18,48] Classically described as a slow-growing asymptomatic red-brown infiltrated plaque with one advancing border with overlying scale-crust, and other scarred or fibrosed border, with a central atrophic area.[9,49,50] (Figure 3) Multiple lesions may occur in a "sporotrichoid" fashion.[51-53] Diascopy may reveal "apple-jelly" nodules. The most common locations are head, neck and legs.[5,10,49] LV can present on the upper extremities from inoculation by acupuncture, tattooing or injection.[33,43,54-56] Diagnosis is often delayed by years or decades due to its gradual growth, asymptomatic nature, and similarity to myriad dermatoses.[51, 57–62] Dermoscopic features have been studied in Indian skin and include scattered yellow-white globules, white scales, white structureless areas and a pink-red background in all cases, followed by telangiectasias in 84%. On facial lesions, four-dot clods, white rossettes, and patulous follicles were observed.[63]

Acute miliary cutaneous tuberculosis

Patients are usually ill appearing, and have multiple subcentimetric, polymorphic, erythematous papules and pustules, with or without central necrosis or umbilication, predominantly on the limbs and trunk. A large proportion of patients are coinfected with HIV/AIDS and have disseminated systemic TB.[64] It is uncommon (0 – 11%) and associated with increased mortality.[15,18,19,27,48]

Metastatic tuberculous abscess

Also termed TB gumma, it is an uncommon presentation (0 – 13%) and manifests as fluctuating subcutaneous nodules in immunocompromised patients.[5,12,15] (Figure 4) It indicates a hematogenous spread and poor prognosis.[18,27]

Orificial tuberculosis

This rare CTB form accounts for up to 2.7% of cases.[9,12,15,19] Painful or painless non-healing punched out ulcers are characteristic of orificial TB.[65–67] These occur in immunosuppressed individuals due to autoinoculation from pulmonary, gastrointestinal or genitourinary TB. The most common site is the oral cavity (including hard palate, tongue and lips), and can also affect the anogenital areas.[62–65]

Scrofuloderma

Also called tuberculosis colliquativa cutis, scrofuloderma is common in endemic areas (rates range from 2.8 – 72%).[8,12,13,15,19,48,69,70] It is characterized by painless, solitary, or multiple subcutaneous swellings, undermined ulcers with violaceous edges or indurated plaques with fistulae draining purulent or caseous material.[27,45] (Figure5) Depending on the contiguous TB focus, the lesions usually overlie enlarged lymph nodes, sometimes bones or joints, and rarely testes.[6,45,71] The most common site is the neck – hypothesized to be from consumption of unpasteurized milk contaminated with *M. bovis* that may infect the tonsils and draining cervical nodes. This is followed by groin, trunk, mandible, axilla, and hands.[11,35,45,49,72] If present in bilateral axillae, scrofuloderma can mimic hidradenitis suppurativa.[73]

Tuberculids

Diagnostic criteria

Certain features assist in the diagnosis of a tuberculid: a past or present history of TB, presence of a positive tuberculin test (Figure 6), and a complete response to antitubercular treatment. Several dermatoses were hypothesized to be associated with TB and termed “tuberculids”, however, now only a few conditions are recognized as true tuberculids.[38] Some studies suggest rare variants such as nodular granulomatous phlebitis, but the conventional ones are discussed here.[74]

True tuberculids

(i) Lichen scrofulosorum: It is characterized by asymptomatic, innumerable grouped erythematous perifollicular papules, often with a scale crust, that have a predilection for the trunk and proximal extremities.[69,75,76] (Figure 7) Prevalence varies, and it accounts for 0.1% CTB in Japan and 33% in India. On dermoscopy, pale monomorphic perifollicular round dots with central black plugs and peripheral scaling

and hyperpigmentation can be visualized.[77] These dermoscopic details can help assist in diagnosis. About 72% of cases have an underlying systemic focus of TB.[75]

(ii) Papulonecrotic tuberculid (PNT): Recurring crops of painless polymorphic erythematous to violaceous papular, pustular and nodular lesions, on extremities and trunk, that resolve with varioliform scarring are characteristic. (Figure 8) It accounts for 3 – 12.8% of CTB.[8,69]

(iii) Erythema induratum of Bazin: It is characterized by tender, erythematous nodules, commonly present on bilateral posterior calves, that ulcerate. It predominantly affects young women and is more common in Japan and China, accounting for 35 – 40% of CTB.[9,10,78] Morphologically, it resembles erythema nodosum and nodular vasculitis which have several etiologies unrelated to TB.[38,79]

Pseudo tuberculids

Lupus miliaris disseminatus faciei and rosaceiform tuberculid are chronic granulomatous dermatoses that present with multiple monomorphic infiltrated erythematous papules on the face. These were earlier considered tuberculids but are not accepted as such due to limited evidence.[80,81]

Differential diagnoses

CTB can mimic several infectious and non-infectious dermatoses. Apart from histopathology, culture, and PCR, a high index of suspicion is required for diagnosis. . If there is a strong clinical suspicion for TB and inconclusive laboratory results, a trial of antitubercular treatment can be used. Drug sensitive CTB responds in about 6 weeks; thus, symptom relief confirms the diagnosis.[20] The classical clinical features and differential diagnoses for CTB are detailed in Table 2 and 3, respectively.

Systemic involvement

Simultaneous systemic involvement in CTB varies widely and ranges from 2 – 53%.[5,6,9–13,15,18,20,69,71] Possible explanations are that lymphadenopathy is not considered systemic involvement by all, rates are higher in endemic areas, and some studies included only children (higher rates of organ involvement).[10,20,43,69] The frequency varies with the type of CTB; in general, it is higher for multibacillary types.[5,6,9,15,71] Although tuberculids are paucibacillary, high rates of systemic involvement are noted.[69,71]

Lymphadenopathy is a marker of disseminated disease (72% versus 32% in localized disease) and is more common in children.[5,48] Overall rates vary from 8% to 92%.[12,18,33,48] It is reported in 26 - 81%, 35%, 45%, of scrofuloderma, LV, and lichen scrofulosorum respectively.[6,69] The lungs are the most common extra-cutaneous systemic organs involved in CTB.[9,10,12] Up to 100% of orificial TB, 64% of lichen scrofulosorum, 7 - 45% of cases scrofuloderma have pulmonary TB.[6,9,11,71] Underlying bone (osteomyelitis) or joint (TB arthritis) is common in scrofuloderma; 10 – 35% are reported to have contiguous spread from bone whereas 8% have associated arthritis. [6,11,69,71] Central nervous system involvement is reported in up to 9% of LV and 13% of scrofuloderma cases. Abdominal TB (hepatic or splenic involvement, ascites, mesenteric lymphadenopathy) occurs in 53%, 5 – 13%, 9% of TB gumma, scrofuloderma, and LV cases, respectively.[5,69] Rarely, breast involvement in the form of granulomatous mastitis and epididymal involvement in scrofuloderma can occur.[6,18,69,71]

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534 **Table 1: Classification of cutaneous tuberculosis based on route of infection and host immunity.**

Classification	Route of infection	Form	Immune status
True cutaneous TB	Inoculation	Tuberculous chancre*	No prior TB exposure
		TB verrucosa cutis	Good immunity
		Lupus vulgaris	
	Hematogenous	Acute military TB*	Low immunity
		TB gumma*	
	Contiguous/autoinoculation	Orificial TB*	
	Contiguous	Scrofuloderma*	
Tuberculids	Endogenous	Lichen scrofulosorum	Strongest immune response (hypersensitivity)
		Papulonecrotic tuberculid	
		Erythema induratum of Bazin	

535 *Multibacillary type

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548 **Table 2: Clinical features of cutaneous tuberculosis variants with the expected tuberculin skin test.**

Tuberculosis type	Characteristic clinical features	Tuberculin skin test
Tuberculous chancre/Primary inoculation tuberculosis	A slow growing painless papule or nodule that later develops into an ulcer with undermined margins	Negative; may become positive in later stages
Tuberculous verrucosa cutis	Verrucous plaque with or without fissuring. May also have perilesional erythema or atrophy Advanced lesions may show peripheral irregular extension with central involution.	Strongly positive
Lupus vulgaris	Classic Plaque: painless reddish-brown papules or plaques with peripheral extension and central atrophy. Apple jelly nodules on diascopy. Variants include hypertrophic, ulcerated, atrophic lupus vulgaris.	Commonly positive
Acute miliary TB	Multiple pustules or erythematous papules with central vesiculation or necrosis	Negative
Gumma/Metastatic tuberculous abscess	Painless fluctuating subcutaneous nodules	Negative or positive
Orificial TB	Painful ulcers, nodules, or papules with undermined margins. Usually located in the oral cavity, genital, or anal areas.	Negative or positive

Scrofuloderma	Shallow ulcerated plaques with bluish margins and fistula/sinus formation. Caseous discharge may be present. Puckered scarring is often present.	Usually, positive. May be negative in some cases
Lichen scrofulosorum	Multiple grouped perifollicular papules with an overlying scale-crust. Other variants are psoriasiform and lichenoid forms	Strongly positive
Papulonecrotic tuberculid	Inflammatory papulo-pustules with necrosis. Associated with hepatosplenomegaly and phlyctenular conjunctivitis.	Strongly positive
Erythema induratum of Bazin	Inflammatory subcutaneous nodules, most commonly on calves, that later form deep ulcers.	Strongly positive

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560 **Table 3: Clinical differential diagnoses for each type of cutaneous tuberculosis.**

Cutaneous TB	Differential diagnoses	
	Non-infectious conditions	**Infections**
Tuberculous chancre	• Traumatic ulcer	• Syphilitic chancre • Bacterial ulcer
Tuberculosis verrucosa cutis	• Plantar keratoderma • Hypertrophic lichen planus	• Verruca vulgaris • Chromoblastomycosis
Lupus vulgaris	• Sarcoidosis • Psoriasis • Granuloma annulare • Discoid lupus • Lichen simplex chronicus • Granulomatous rosacea • Squamous cell carcinoma	• Tinea corporis • Tuberculoid leprosy • Sporotrichosis • Chromoblastomycosis • Blastomycosis • Atypical mycobacterial infection • Secondary syphilis • Leishmaniasis
Acute miliary cutaneous tuberculosis	• Drug eruption • Pityriasis lichenoides varioliformis et acuta	• Varicella
Tuberculous abscess	• Panniculitis	• Bacterial abscess • Nocardiosis • Sporotrichosis
Orificial tuberculosis	• Chron's disease	• Mucosal leishmaniasis
Scrofuloderma	• Hidradenitis suppurativa	• Dental sinus tract • Actinomycosis • Bacterial ulcers • Sporotrichosis
Tuberculids		
Lichen scrofulosorum	• Lichen planus • Lichen spinulosus • Lichen nitidus • Psoriasis	• Secondary syphilis
Papulonecrotic tuberculid	• Pityriasis lichenoides varioliformis et acuta • Lymphomatoid papulosis	• Varicella
Nodular tuberculid	• Erythema nodosum • Polyarteritis nodosa	• Bacterial ulcers

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Figure legends:

Figure 1: An ulcer caused after BCG vaccine in an infant characteristic of primary inoculation tuberculosis

Figure 2: Characteristic verrucous plaque of tuberculosis verrucosa cutis on the dorsum of the finger in a healthcare worker (A) with similar plaques present linearly on the sole of right foot in another patient (B)

Figure 3: Lupus vulgaris as a large well-defined plaque with advancing verrucous lateral borders and an atrophic center present on the gluteal fold and upper thigh (A). A similar plaque present on the upper limb (B) with a magnified image of an early red-brown lupus vulgaris plaque on the elbow in (C). D demonstrates Inoculation lupus vulgaris in a tattoo where the disease activity is most evident within the borders of the tattooed ink.

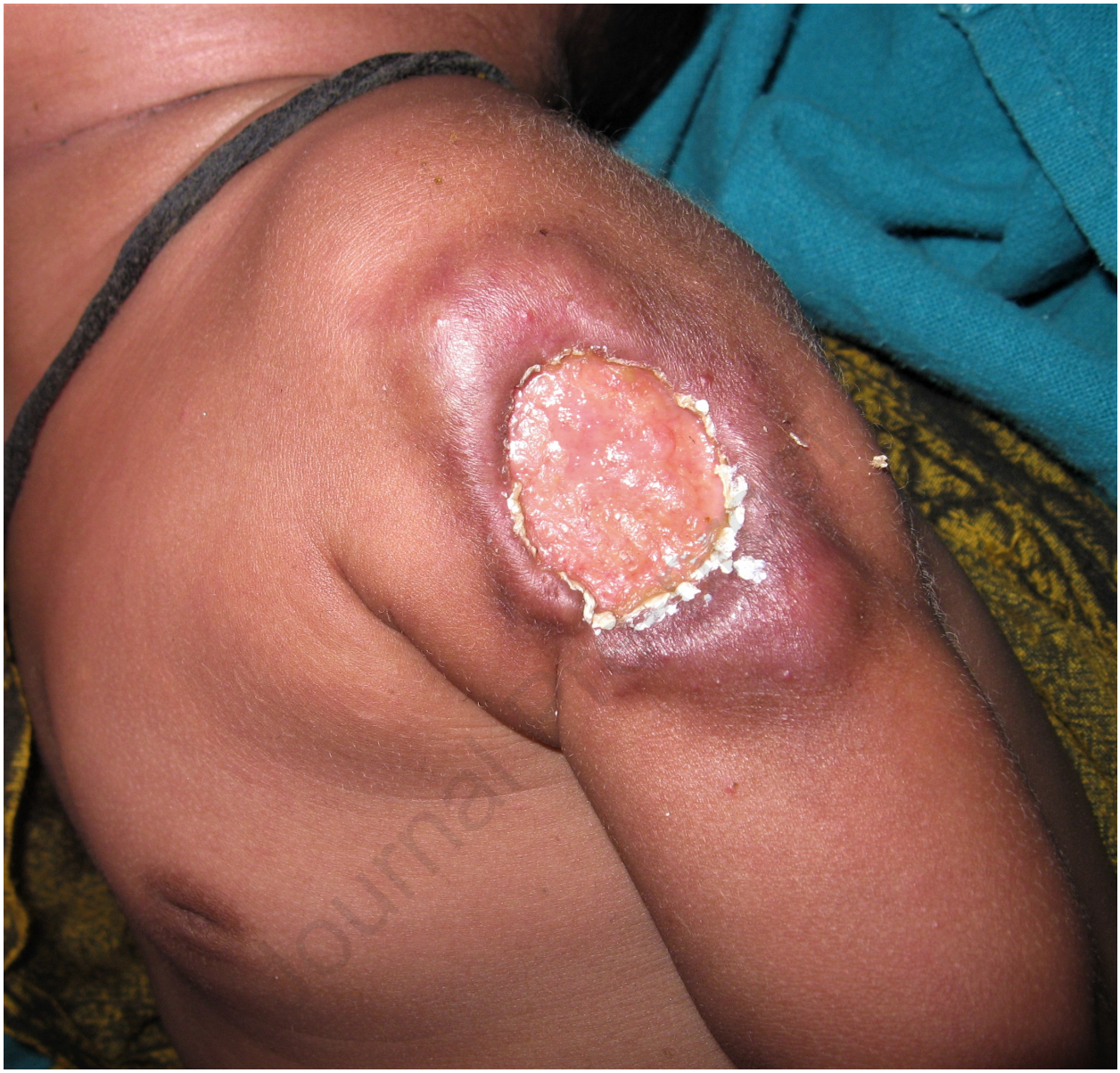
Figure 4: Metastatic tubercular abscess present on the left upper eyelid

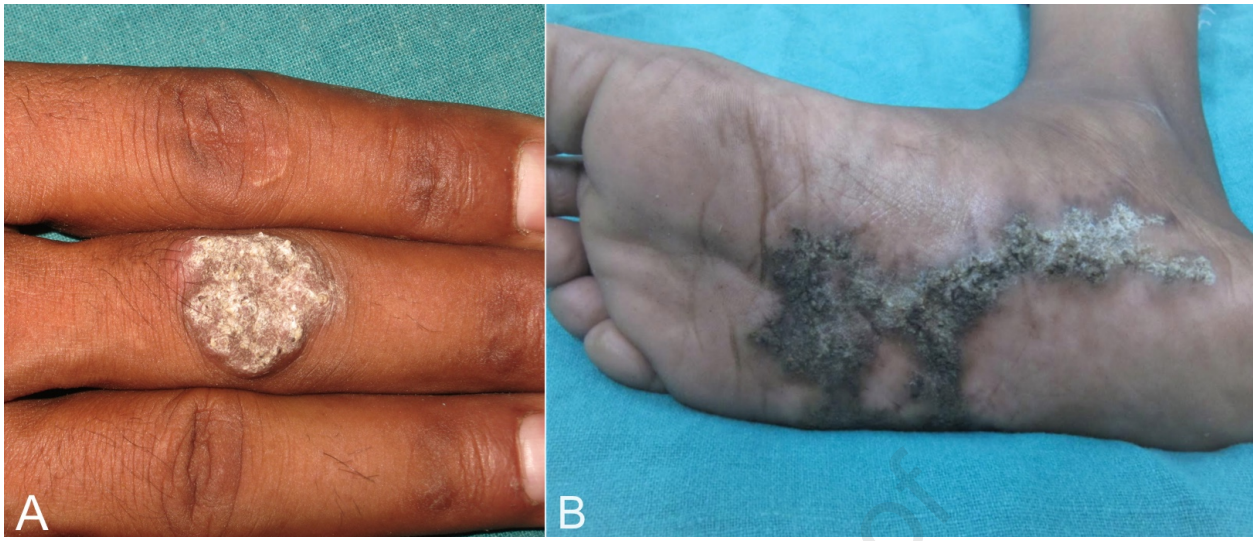
Figure 5: A. An ulcer with violaceous edges in a child with scrofuloderma with radiographic evidence of underlying tuberculous osteomyelitis in the same patient (B). Tuberculous dactylitis of the index finger with an overlying ulcer (C). Scrofuloderma as an atrophic scar with a hyperkeratotic plaque in the proximal and distal ends signifying ongoing activity, overlying the involved mandible (D) Multiple ulcers with undermined edges and violaceous borders overlying the hip bones (E).

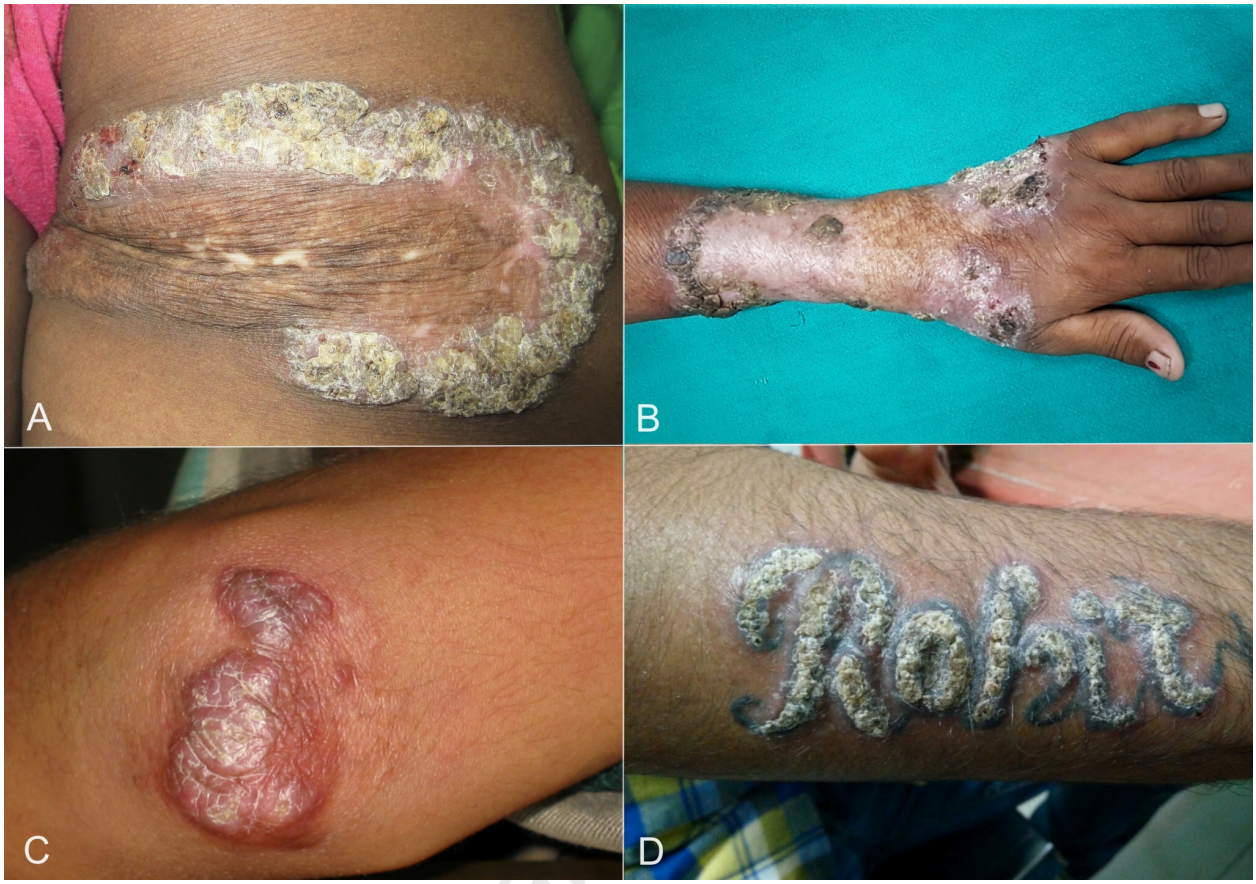
Figure 6: Strongly positive tuberculin skin (Mantoux) test that has blistered in (A) and another patient with lichen scrofulosorum with an ulcerated Mantoux site, the volar aspect of the forearm, indicative of good immunity

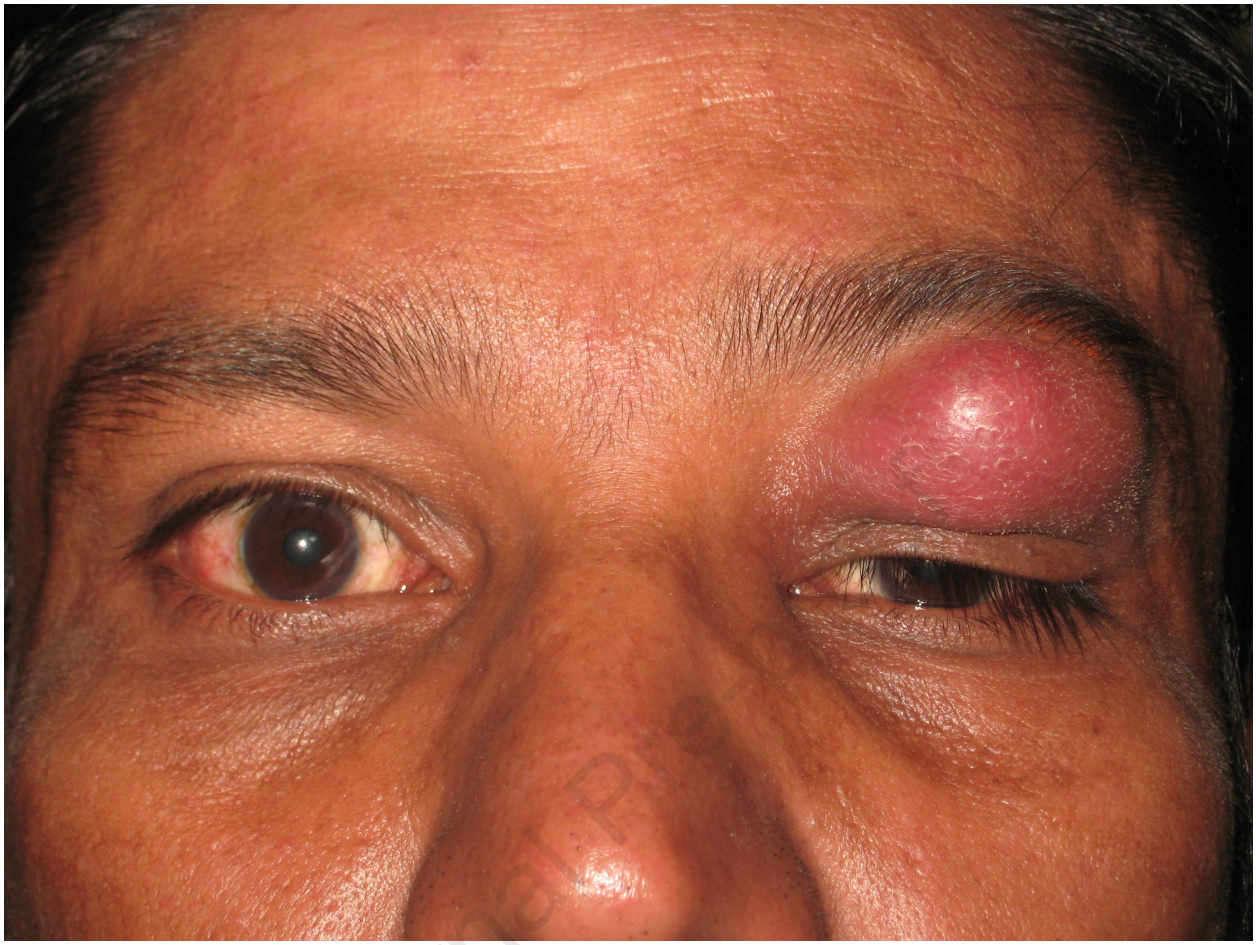
Figure 7: Innumerable grouped monomorphic erythematous perifollicular papules with a scale crust present on the trunk of a young boy typical for lichen scrofulosorum

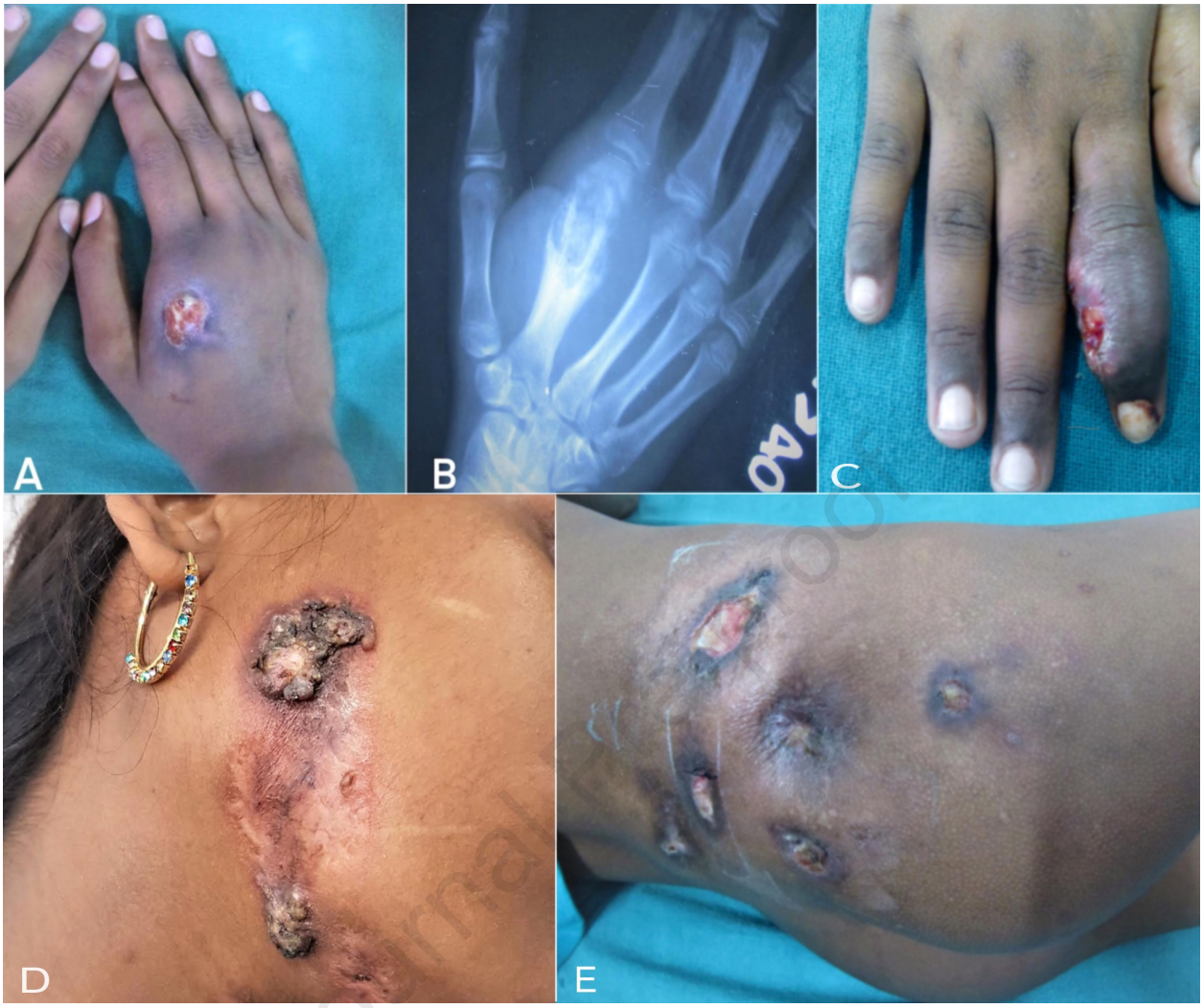
Figure 8: Papulonecrotic tuberculid lesions on trunk and buttock (A) and characteristic red brown to violaceous papules, in various stages of evolution, with round atrophic scares involving bilateral legs (B)

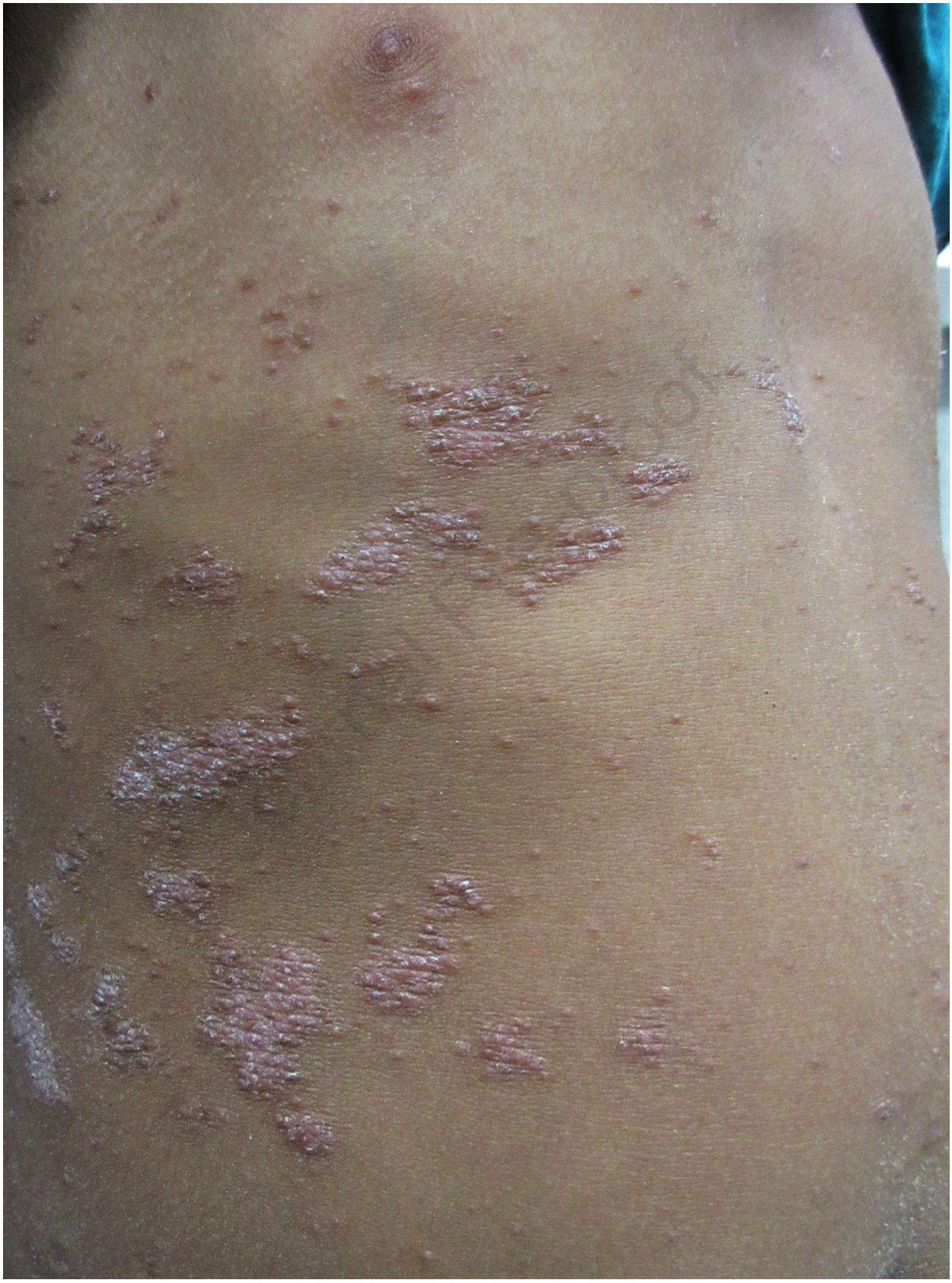


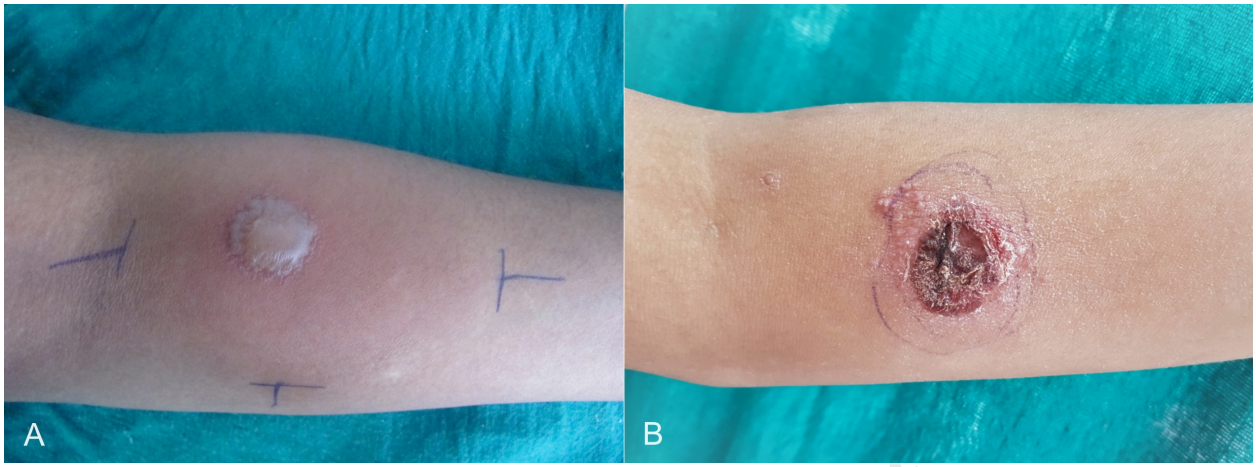


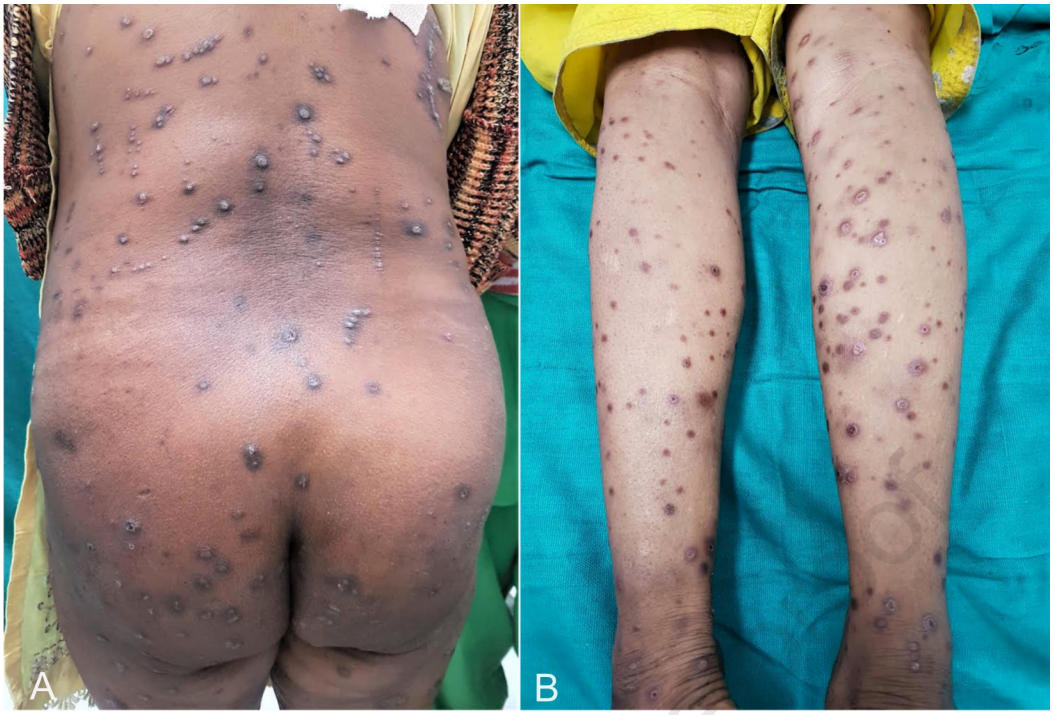












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