Nodular Lesion of the Skin as Primary Cutaneous Tuberculosis
Caterina Casalini, Alberto Matteelli, Nuccia Saleri, Silvio Caligaris, Severo Graifemberghi, Cecilia Pizzocolo, Francesco Castelli and Giampiero Carosi

Tuberculosis, one of the oldest diseases known to humankind, continues to be a significant problem in the third millennium. Worldwide, it remains the leading cause of death by a single infectious disease. Factors responsible for the resurgence of tuberculosis in the low-endemicity countries of Europe and the US include the presence of HIV infection, immigration from areas of high prevalence of the disease, adverse social conditions, development of multiresistant Mycobacterium tuberculosis and, mostly, ineffective control programs for high-risk groups.

Extrapulmonary tuberculosis is of secondary importance from the public health perspective, because it is not contagious; nevertheless, it constitutes up to 40% of all cases. Cutaneous tuberculosis is a rare condition in countries with low endemicity of the disease, and thus represents a serious diagnostic challenge to clinicians. We describe a case of primary cutaneous tuberculosis following inapparent infection with M. tuberculosis acquired through the skin.

Case Report

C.B. is a 30-year-old male, born in Senegal, who moved to Italy in July 2000 as a migrant laborer. On 11 January 2002 he consulted the emergency department of the Spedali Civili, Brescia, for abdominal and thoracic pain, fever and vomiting of 10-days’ duration, and was admitted for a complete diagnostic procedure.

At clinical examination, there were no signs of thoracic and abdominal diseases. A single ulcerative nodular lesion of diameter 0.5 cm was present on the left hand, between the fingers (Fig.). The lesion was painful and produced a serohematic discharge. The patient could not say when the lesion had first appeared. One single lymph node of diameter 2 cm was present at the epitrochlear site on the same arm. The chest x-ray demonstrated minimal signs of reduced ventilation at the bases bilaterally; the abdomen ultrasound scan revealed mild splenomegaly (spleen of 13.6 cm) and ecographic signs of medical nephropathy. Blood hematochemistry results were unremarkable, except for an increased erythrosedimentation rate (47 mm/h) and increased C-reactive protein (102 mg/dL). Malaria hemoscopy was negative. As cat-scratch disease was suspected, antibacterial therapy was started with azithromycin 500 mg daily for 5 days, followed by amoxicillin and clavulanic acid 2 g three times daily for 1 week. Bronchoscopy, a tuberculin skin test, microbiological cultures and serologic investigations were requested. Results of serology for HIV, hepatitis C virus, hepatitis B virus, Bartonella, Brucella, Legionella, Mycoplasma, Chlamydia, Epstein–Barr virus, and cytomegalovirus were negative. Microbiological cultures for bacteria and fungi from blood urine and sputum samples

Figure  Nodular lesion, 0.5 cm in diameter, on the left hand, with progression to ulcer, in a patient with primary skin tuberculosis due to exogenous inoculation.
all gave negative results. Bronchoalveolar lavage fluid was negative for bacteria, fungi, and mycobacteria. The Mantoux test (purified protein derivative 5 IU) was negative. Two weeks after admission, the patient was still febrile (continuous fever with daily peaks at 38°C) with diffuse muscular pain, although vomiting had disappeared spontaneously; skin and brachial lymph node biopsies were then performed. The histologic examination of both showed granulomatous lesions with the presence of acid-fast bacilli. Eventually, *M. tuberculosis* sensitive to major antituberculosis drugs was cultured from the lymph node specimen. A chest x-ray repeated 2 weeks after admission was normal. Standard antituberculosis therapy consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol was started. The fever resolved after 3 weeks; during the monthly follow-up, there was gradual regression of the skin lesion and the regional lymphadenopathy. The complete regression of both lesions occurred 5 months after the start of antituberculosis treatment.

**Discussion**

The increased risk of tuberculosis in immigrants in countries with low TB endemicity is due to reactivation of latent tuberculosis infection or spread of new infections by the respiratory route in conditions of overcrowding. There may sometimes be alternative routes of infection, and the skin is potentially one of these. We describe a case of primary extrapulmonary tuberculosis originating from skin inoculation of *M. tuberculosis*. The single skin lesion with regional lymphadenitis is characteristic of the primary complex, without signs of lung involvement or patent hematogenous dissemination of *M. tuberculosis*. The negativity of the skin tuberculin reaction in a patient with no immune abnormalities presenting with systemic constitutional signs of the disease supports this hypothesis. Despite all our efforts to collect a detailed history, we were unable to identify the source of infection. There was no history of trauma. Language and cultural barriers are unlikely to have prevented adequate data collection in this case, as cultural mediators are routinely used in the department. Cutaneous tuberculosis may have very diverse clinical presentations. Cases of exogenous inoculation should be differentiated from secondary localization observed as a consequence of the spread from a subjacent focus (scrofuloderma from adenitis, osteomyelitis, or epididymitis) and by hematogenous dissemination during acute miliary disease (lupus vulgaris and acute miliary tuberculosis of the skin) or reactivated disease (tuberculotic gummas). A fourth category in the classification of cutaneous tuberculosis has recently been proposed, to include cases with a paradoxical reaction to antituberculous treatment, appearing as an expansion of the skin lesions.

Cutaneous tuberculosis poses a serious challenge to the clinician, who must differentiate this condition from several other diseases of the skin presenting as papules, nodules, or ulcers. The initial presentation may resemble that of common bacterial infection (usually related to small trauma), but antibiotics targeting Gram-positive cocci exert no effect on the lesion. Other mycobacteria have a specific tropism to the skin: *M. ulcerans* and *M. marinum* produce painless ulcers with deep necrotic bases and satellite lesions communicating with the original one. Diagnosis is made by histology, and typing of the mycobacteria requires culture isolation. Plague should be suspected in febrile patients with adenitis returning from endemic areas, whenever exposure to rodents cannot be ruled out. Since plague has not been reported from either Italy or Senegal, plague was not included in the differential diagnosis of this case. Cutaneous anthrax can rarely occur in tropical countries or even in Western countries in professionals exposed to skin products. It presents as a small, painless papule which progresses to a vesicle with an erythematous and edematous base, becomes hemorrhagic, ulcerates and reveals a necrotic area. We ruled out this diagnosis on the basis of the history and the lack of edema at the site of the ulcer. The typical lesion of cutaneous leishmaniasis begins as a papule at the site of the sandfly bite and slowly progresses to a nodule, and a painless ulcer, 3 to 12 cm in diameter, with violaceous borders. The diagnosis is made on histologic grounds, although culture can also be attempted. The disease has not been reported from Italy; it is endemic in the tropical belt, but the incubation period is much shorter than the 2 years that had elapsed since the last stay in Senegal of our patient. Sporotrichosis, an unusual fungal infection, starts as a small papule which develops into a nodule, may ulcerate and has a chronic evolution; diagnosis is made by histology and culture. In the case of cat scratch disease, due to *Bartonella henselae*, the initial skin lesion is often inapparent and the picture is dominated by the regional lymphadenitis. The diagnosis is suspected on histologic grounds, and confirmed by serology.

In contrast to other diseases which remain confined to the skin, primary tuberculosis has the potential to evolve as a systemic disease, and the prognosis is serious in the absence of accurate diagnosis and specific therapy. The clinical history may not help at all. The patient we describe had given little attention to the nodule and was unaware of the lymph node. He would not have sought medical aid for either condition, and the reason for consultation was indeed the occurrence of the constitutional signs of tuberculosis.

The resurgence of tuberculosis in low-endemicity countries is associated with the occurrence of unusual clinical pictures of the disease. Tuberculosis should be included in the differential diagnosis of single, nodular
lesions with regional lymphadenitis in people at increased risk of acquiring the disease.

References