Mediastinal lymphadenopathies and skin lesions in a 49-year-old Sinhalese man

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Abstract

Leprosy is a neglected disease sporadically reported in high-income countries. Skin lesions and peripheral nerve involvement represent the most common manifestations. Mediastinal lymphadenopathy in the absence of superficial lymph node involvement is very rare. Atypical or rare clinical presentations of the disease may delay diagnosis and therapy and cause potential life-threatening manifestations and disabilities. We describe the case of a 49-year-old Sinhalese man who was admitted to our hospital with a one-month history of peripheral neurological symptoms and skin lesions on lower limbs. A computed tomography scan showed the presence of mediastinal lymphadenopathies without lung parenchymal and superficial lymph node involvement. Endobronchial ultrasound-guided transbronchial needle aspiration showed the presence of granulomas, while skin biopsy revealed dermo-hypodermic granulomas with perineural lympho-histiocytic inflammatory reaction. Fite-Faraco staining demonstrated the presence of acid-fast bacilli in both lymph nodal and skin biopsy, and the polymerase chain reaction was positive for *Mycobacterium leprae*. Multibacillary leprosy was then diagnosed.

Case Report

A 49-year-old, never-smoker Sinhalese man, living in Italy for 20 years and with a medical history of type 2 diabetes mellitus and alcoholism, was admitted to the emergency department. He referred a one-month history of asthenia, diffuse chest and abdominal hyperesthesia, and weight loss (12 kg). Because of a rapid worsening of peripheral neurological symptoms and the occurrence of skin lesions on the lower limbs, the patient sought medical attention.

He was afebrile, with a blood pressure of 115/70 mmHg, a heart rate of 74 beats/minute, and an oxygen saturation of 97% on room air. Abdominal, pulmonary, and cardiac examinations were unremarkable. No superficial lymphadenopathies were detected. A maculopapular rash and erythematous nodules and plaques were detected on the lower limbs (Figure 1). Blood tests showed elevated lipase (1021 U/L; normal values (nv): 23-300 U/L) and alanine aminotransferase (68 U/L; nv: < 50). Other liver and renal function tests, blood count, and C-reactive protein were within normal limits. Chest X-ray showed an enlarged right hilum, whereas contrast-enhanced chest computed tomography (CT) scan showed bilateral paratracheal, para-aortic, right hilar, and subcarinal medi-

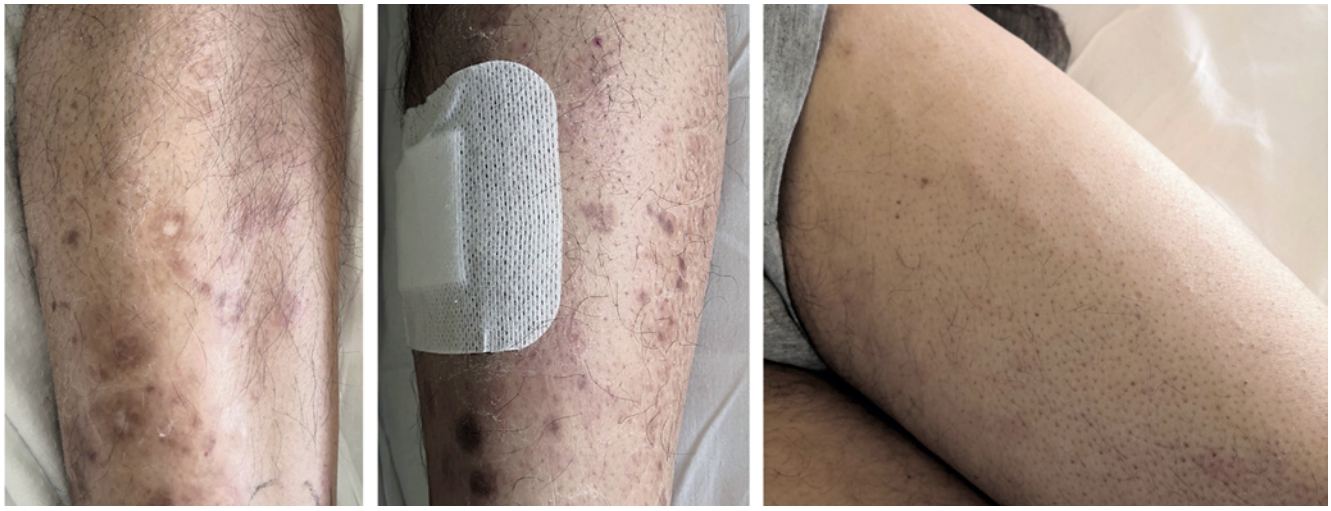

Figure 1. Maculopapular rash and erythematous nodules and plaques on the lower limbs.

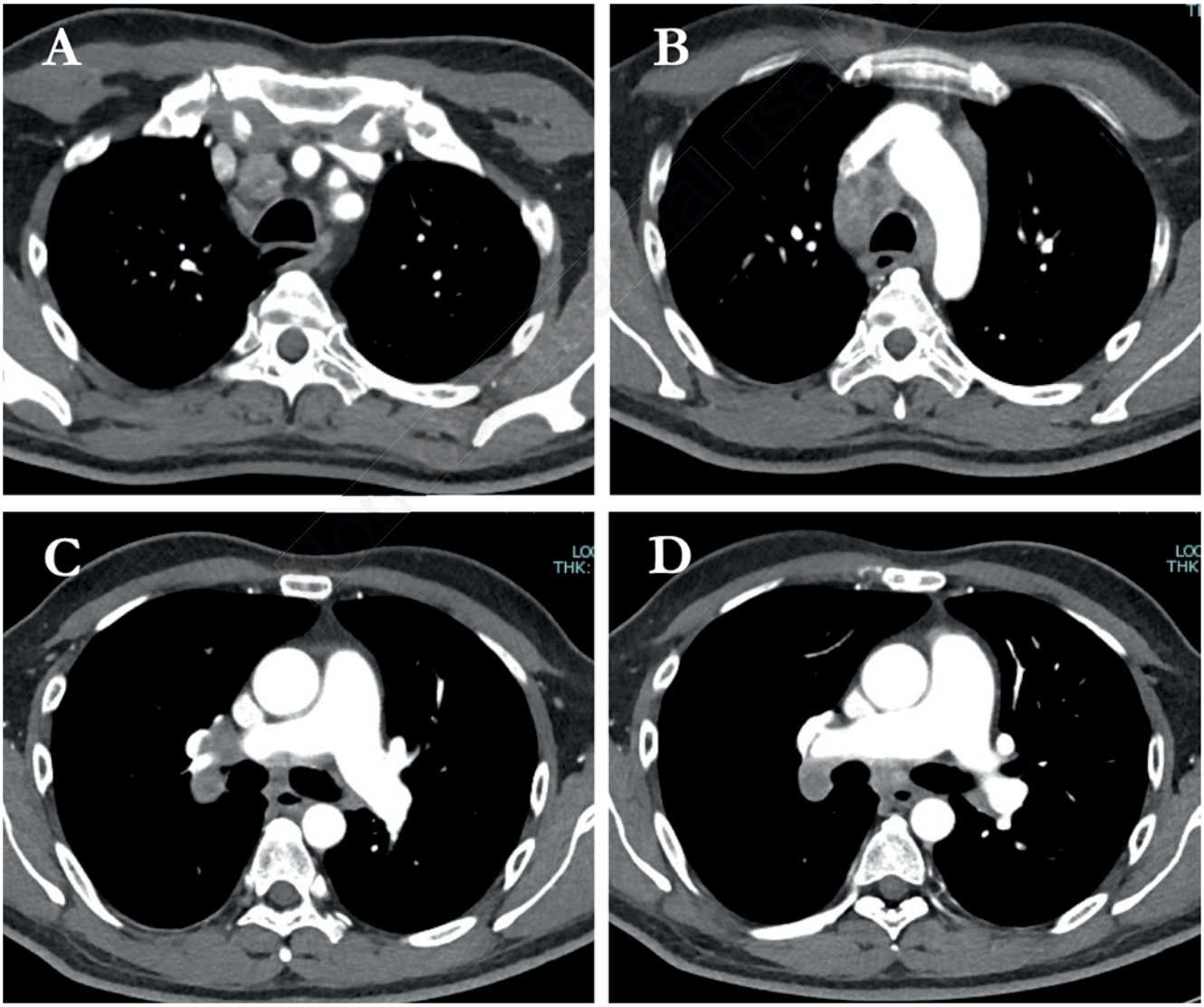

Figure 2. Chest computed tomography scan showing right paratracheal (A, B), paraaortic (B), right hilar (C, D) and subcarinal (D) lymph adenopathies.

astinal lymphadenopathies (Figure 2). No lung parenchymal or pleural abnormalities were detected. Abdominal CT resulted negative. Then, he underwent bronchoscopy with bronchial washing and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) of the lower paratracheal lymph node; a paralysis of the right vocal cord was found. Rapid on-site evaluation of the needle aspirate showed granulomas. A skin biopsy was also performed. HIV antibodies 1 and 2, antinuclear antibodies, extractable nuclear antigen antibodies, anti-neutrophil cytoplasmic antibodies, anti-citrulline antibodies, rheumatoid factor, and viral markers of hepatitis B and C were negative. Brain magnetic resonance imaging was normal; the spinal tap showed a slight increase of proteins and leukocytes with negative microbiological tests, whereas serial electromyography revealed small fiber sensory neuropathy of the lower limbs and brainstem dysfunction.

Skin biopsy was characterized by dermo-hypodermic granulomas with perineural lymphohistiocytic inflammatory reaction, and lymph nodal biopsy by large non-necrotizing granulomas (Figure 3). Smear microscopy, Xpert MTB/RIF, and culture failed to detect *Mycobacterium tuberculosis,* while Fite-Faraco staining demonstrated the presence of acid-fast bacilli in both lymph nodal and skin biopsy. Polymerase chain reaction (PCR) for *Mycobacterium leprae* resulted in positive.

During the hospital stay, he experienced progressive dysphagia, dysmetria, and worsening of paresthesia. He started the 12-month World Health Organization (WHO)-recommended treatment with clofazimine 300 mg monthly plus 50 mg/day, dapsone 100 mg/day, and rifampicin 600 mg monthly. Skin lesions and neurological symptoms slowly improved, while mediastinal lymphadenopathies showed a mild volume reduction. After 8 months of treatment, following acute hepatitis, rifampicin was replaced with minocycline 100 mg daily and moxifloxacin 400 mg daily, which were better tolerated.

Discussion

Leprosy, also known as Hansen's disease, is a multisystemic, communicable, chronic infectious disease caused by *Mycobacterium leprae*, which mainly affects the skin, peripheral

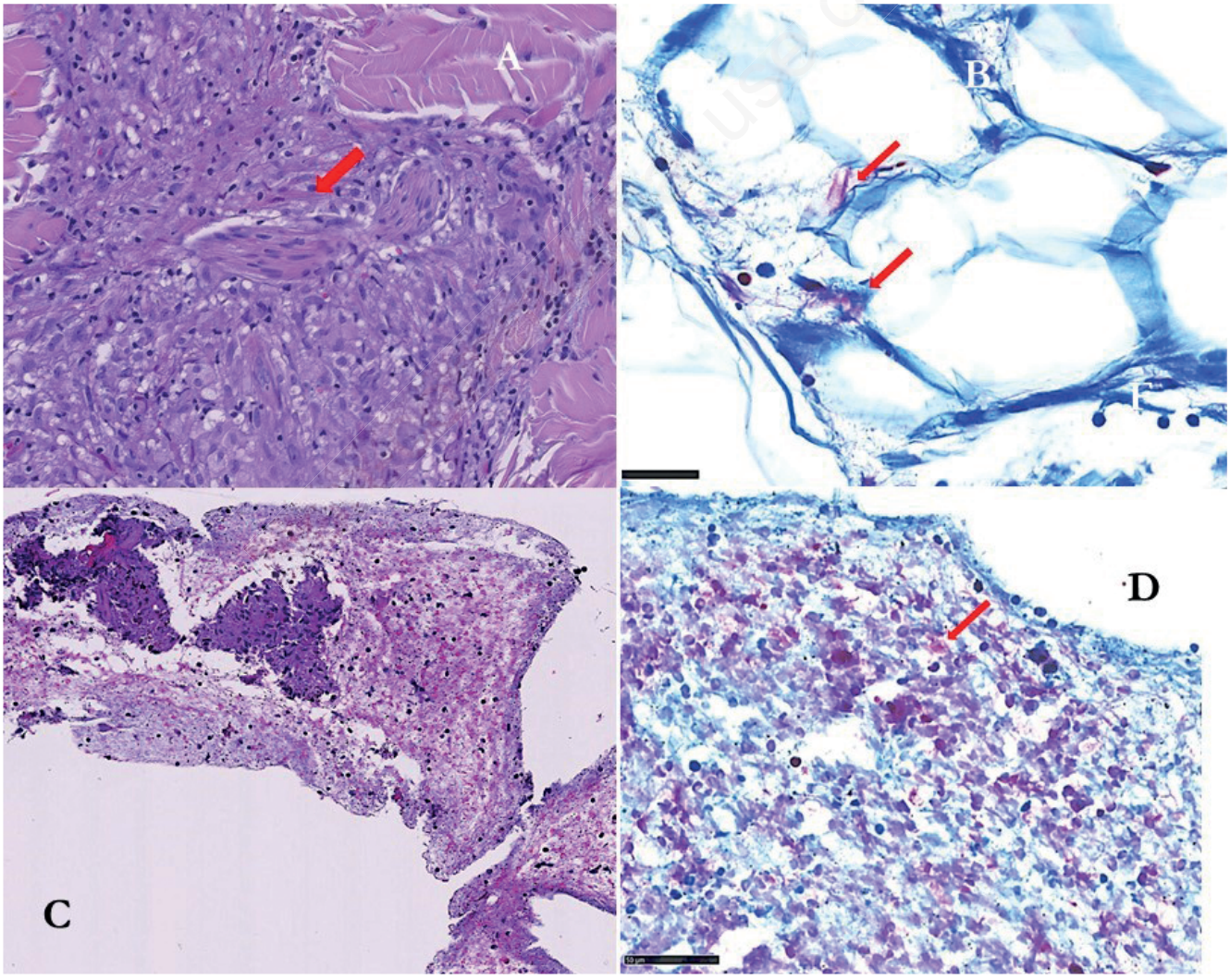

Figure 3. Skin biopsy: hematoxylin & eosin staining showing the presence of dermo-hypodermic granulomas (A) with perineural (red arrow) lymphohistiocytic inflammatory reaction (B). Endobronchial ultrasound-guided transbronchial needle aspiration: hematoxylin and eosin staining showing large non-necrotizing granuloma (C). Fite-Faraco staining demonstrating the presence of acid-fast bacilli (B, D).

nerves, mucosal surfaces of the upper respiratory tract, and eyes. It could be pauci- or multi-bacillary, depending on the number of skin lesions, nerve involvement, and detection of bacilli on skin smear microscopy [1,2].

Leprosy may occur at all ages. Early diagnosis and therapy in the early stages of the disease are key to preventing disability [1-3]. Despite the elimination of leprosy as a public health problem, defined by the WHO as a point prevalence of <1 per 10.000 population, new cases occurred with >200.000 incident cases in 2019 [1].

In Italy, leprosy is sporadically reported, with 25 cases diagnosed from 2009 to 2019, mostly in migrants from Asia and Africa. The incubation period is long: the patient described in this article might have probably been infected up to 2 years before the symptoms' onset during a long stay in the country of origin [4].

The diagnosis of leprosy may be based on clinical signs, with or without slit-skin smears or pathological examination of biopsies. PCR may be associated with a higher diagnostic accuracy, but it is not available in primary health-care settings [1].

The etiology of mediastinal lymphadenopathy is challenging: thoracic and extra-thoracic malignancies, lymphoproliferative disorders, and benign diseases (*i.e.*, sarcoidosis and tuberculosis) may affect the mediastinum without any pulmonary clinical involvement and specific radiological features. Lymph nodes are frequently affected during the course of Hansen's disease, with inguinal, cervical, and axillary being the most frequent [5,6]. Mediastinal lymphadenopathy without any superficial involvement is unusual [7]. To our knowledge, this is the first case of leprosy diagnosed by EBUS-TBNA.

Endosonography is the gold standard for mediastinal staging of lung cancer, with a good sensitivity in the diagnosis of granulomatous lymphadenitis (*i.e.*, sarcoidosis and tuberculosis) [8-10].

Keeping into account its low Italian incidence and the clinical presentation with skin, neurological, and mediastinal lymph nodes, sarcoidosis, tuberculosis, and malignancy were considered the most probable diagnoses.

Low epidemiological burden, atypical or rare clinical presentations, as well as poor knowledge of healthcare workers in high-income countries, may result in a delayed diagnosis and treatment, with potential life-threatening clinical manifestations and/or disabilities [1].

Conclusions

Mediastinal lymphadenitis is an uncommon presentation of leprosy that may resemble sarcoidosis, tuberculosis, or malignancies. EBUS-TBNA may be accurate and safe in its diagnostic work-up.

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