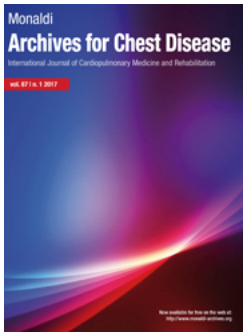

Monaldi Archives for Chest Disease

eISSN 2532-5264 https://www.monaldi-archives.org/

Monaldi Arch Chest Dis 2023 [Online ahead of print]

To cite this Article:
Cefalo J, Salerni C, Ferranti G, et al. **Mediastinal lymphadenopathies and skin lesions in a 49-year-old Sinhalese man.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2023.2736

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

Jacopo Cefalo,[1] Carmine Salerni,[1] Giulia Ferranti,[1] Manuela Bimbatti,[2] Laura Moneghini,[2] Paolo Carlucci,[1] Ottavia Viganò,[3] Giulia Marchetti,[3,4] Umberto Gianelli,[2,4] Stefano Centanni,[1] Giovanni Sotgiu,[5] Michele Mondoni[1]

[1]Respiratory Unit, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan
[2]Pathology Unit, ASST Santi Paolo e Carlo, Milan
[3]Infectious Diseases Unit, Department of Health Sciences, ASST Santi Paolo e Carlo, Milan
[4]Department Health Sciences, University of Milan
[5]Clinical Epidemiology and Medical Statistics Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, Italy

Corresponding author: Jacopo Cefalo, Respiratory Unit, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Via A. Di Rudinì 8, 20142 Milan, Italy. phone: 0039 0281843025; fax: 0039 0281843037 E-mail: jacopo.cefalo@unimi.it

Number of Figures: 3

Word count of the text: 836

Number of references: 10

Abbreviations list:

CT: chest computed tomography

EBUS-TBNA: endobronchial ultrasound-guided transbronchial needle aspiration

HIV: human immunodeficiency virus

ROSE: Rapid on-site evaluation

PCR: Polymerase chain reaction

WHO: World Health Organization

Abstract

Leprosy is a neglected disease sporadically reported in high-income countries. Skin lesion and peripheral nerve involvement represent most common manifestations. Mediastinal lymphadenopathy in the absence of superficial lymph nodes involvement is very rare. Atypical or rare clinical presentations of 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. CT scan showed the

presence of mediastinal lymphadenopathies without lung parenchymal and superficial lymph nodes involvement. Endobronchial ultrasound-guided transbronchial needle aspiration showed the presence of granulomas while skin biopsy revealed dermo-hypodermic granulomas with perineural lymphohistiocytic inflammatory reaction. Fite-Faraco staining demonstrated the presence of acid-fast bacilli in both lymph nodal and skin biopsy and polymerase chain reaction was positive for *Mycobacterium leprae*. Multibacillary leprosy was then diagnosed.

Keywords: leprosy, Hansen's disease; mediastinal lymph nodes; EBUS-TBNA; Fite-Faraco staining; bronchoscopy.

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 kilograms). Because of a rapid worsening of peripheral neurological symptoms and occurrence of skin lesions on the lower limbs, the patient sought medical attention.

He was afebrile, with a blood pressure of 115/70 mmHg, 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 bilateral paratracheal, para-aortic, right hilar, and subcarinal mediastinal lymphadenopathies (Figure 1). 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 lower paratracheal lymph node; a paralysis of the right vocal cord was found. Rapid on-site evaluation (ROSE) of the needle aspirate showed granulomas. Skin biopsy was also performed. Human immunodeficiency virus (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 1). 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 for *Mycobacterium leprae* resulted positive.

During the hospital stay he experienced progressive dysphagia, dysmetria, and worsening of paresthesia. He started the 12-month 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 lymph adenopathies showed a mild volume reduction. After 8 months of treatment, following an 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 skin, peripheral 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 prevent disability [1-3]. Despite the elimination of leprosy as a public health problem, defined by the World Health Organization (WHO) as a point prevalence of <1 per 10.000 population, new cases occur 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. Polymerase chain reaction (PCR) may be associated with a higher diagnostic accuracy, but it is not available in primary health-care settings [1].

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 which may resemble sarcoidosis, tuberculosis or malignancies. EBUS-TBNA may be accurate and safe in its diagnostic work-up.

Ethics approval and consent to participate: An ethics statement is not applicable because this study is based exclusively on published literature.
Consent for publication: Patient's informed consent was obtained for publication of the details of his medical case and any accompanying images.
Availability of data and material: All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.
Conflict of interest: none of the Authors has conflict of interest to disclose
Funding sources: This work did not receive any funding
Author contribution**:** Jacopo Cefalo, Carmine Salerni, Giulia Ferranti, Giovanni Sotgiu, Michele Mondoni**:** conception or design of the work; drafting of the work; final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Manuela Bimbatti, Laura Moneghini, Paolo Carlucci, Ottavia Viganò, Giulia Marchetti, Umberto Gianelli, Stefano Centanni: conception or design of the work; revising it critically for important intellectual content; Final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. World Health Organization. Regional Office for South-East Asia. Guidelines for the diagnosis, treatment and prevention of leprosy. 2018. Available from: https://apps.who.int/iris/handle/10665/274127
2. Chen KH, Lin CY, Su SB, Chen KT. Leprosy: a review of epidemiology, clinical diagnosis, and management. J Trop Med 2022;2022:8652062.
3. Britton WJ, Lockwood DN. Leprosy. Lancet 2004;363:1209-19.
4. Riccò M, Vezzosi L, Balzarini F, et al. Epidemiology of leprosy in Italy (1920 - 2019): a comprehensive review on existing data. Acta Biomed 2019;90:7-14.
5. Cavett JR 3rd, McAfee R, Ramzy I. Hansen's disease (leprosy). Diagnosis by aspiration biopsy of lymph nodes. Acta Cytol 1986;30:189-93.
6. Yang SYS, Leong WMS, Kasunuran CMT, et al. Extensive lepromatous lymphadenitis preceding lesions on the face and earlobes: an unusual presentation of leprosy in Singapore. Case Rep Dermatol 2018;10:35-40.
7. Kiran KU, Krishna Moorthy KV, Meher V, Narasimha Rao P. Relapse of leprosy presenting as nodular lymph node swelling. Indian J Dermatol Venereol Leprol 2009;75:177-9.
8. Mondoni M, D'Adda A, Terraneo S, et al. Choose the best route: ultrasound-guided transbronchial and transesophageal needle aspiration with echobronchoscope in the diagnosis of mediastinal and pulmonary lesions. Minerva Med 2015;106:S13-9.
9. Vilmann P, Clementsen PF, Colella S, et al. Combined endobronchial and oesophageal endosonography for the diagnosis and staging of lung cancer. European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). Eur Respir J 2015;46:40-60.
10. Mondoni M, Saderi L, Puci MV, et al. Xpert MTB/RIF in the diagnosis of mediastinal tuberculous lymphadenitis by endoscopic ultrasound-guided needle aspiration techniques: a systematic review and meta-analysis. Respiration 2023;102:237-46.

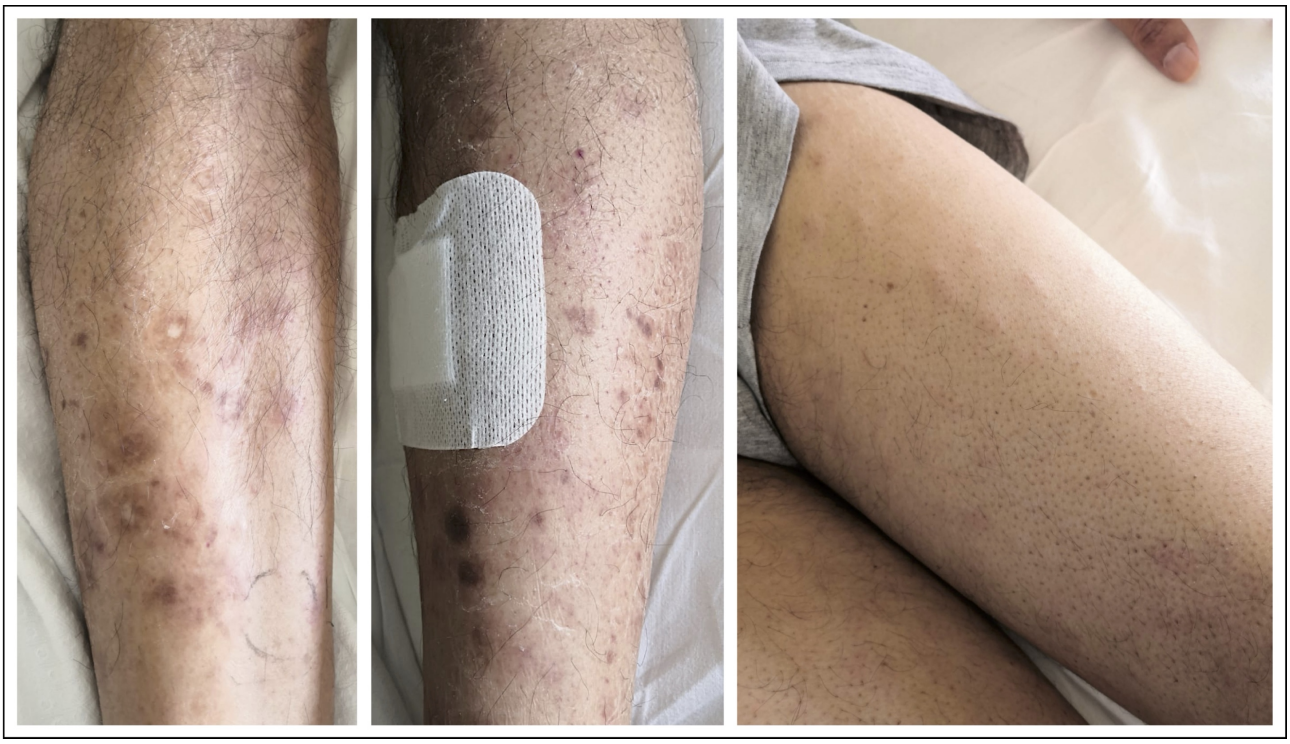

Figure 1. Maculopapular rash and erythematous nodules and plaques on the lower limbs.

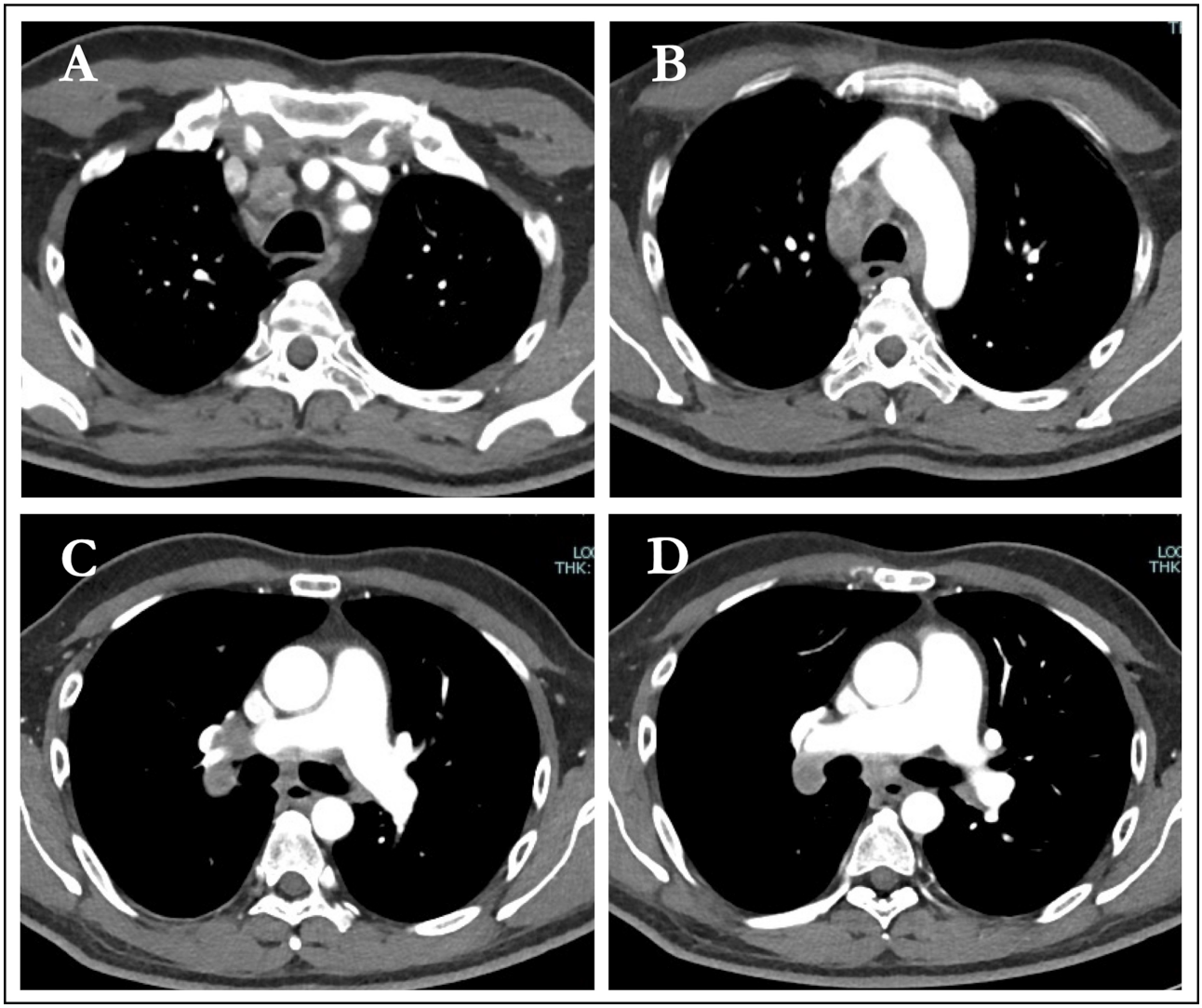

Figure 2. Chest CT scan showing right paratracheal (A, B), paraaortic (B), right hilar (C, D) and subcarinal (D) lymph adenopathies.

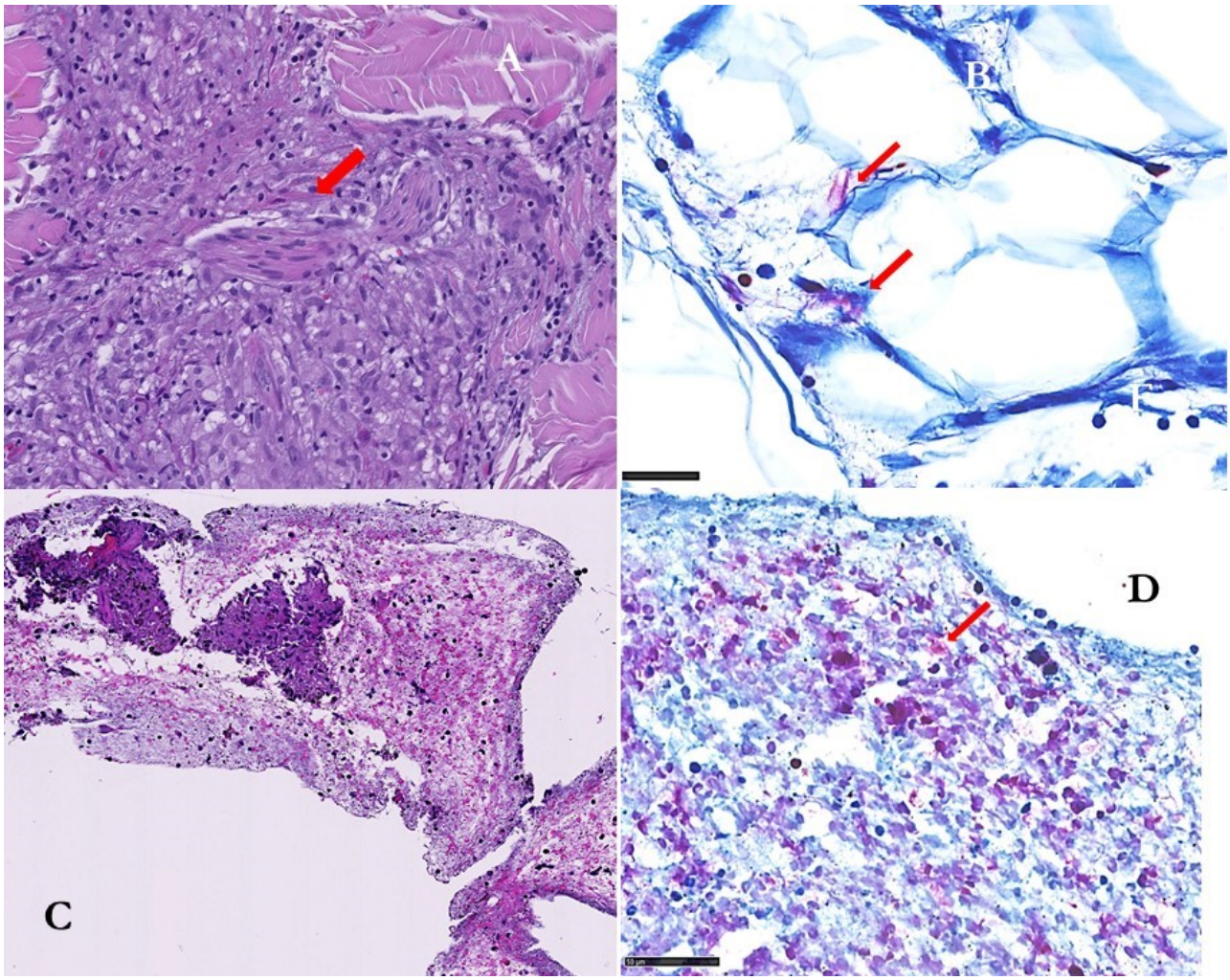

Figure 3. Skin biopsy: Hematoxylin & Eosin staining showing the presence of dermo-hypodermic granulomas (A) with perineural (red arrow) lymphohistiocytic inflammatory reaction (B). EBUS-TBNA: Hematoxylin and Eosin staining showing large non-necrotizing granuloma (C). Fite-Faraco staining demonstrating the presence of acid-fast bacilli (B, D).