Caseating lymphadenopathy at imaging: When ethnicity is deceptive

Dario Fabbri\textsuperscript{1}, Chiara Baldovini\textsuperscript{2}, Raffaele Pezzilli*\textsuperscript{1}

\textsuperscript{1}Department of Digestive System, Sant’Orsola-Malpighi Hospital, Bologna University, Bologna, Italy
\textsuperscript{2}Department of Experimental, Diagnostic and Specialty Medicine, Sant’Orsola-Malpighi Hospital, Bologna University, Bologna, Italy

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ABSTRACT

Background: Lymph node enlargement represents a clinical challenge in clinical practice and the underlying diagnosis represents the cornerstone of adequate treatment.

Case report: A caseating-like mediastinal lymph node investigated using computer tomography (CT) was found in an adult male patient coming from Pakistan, and a diagnosis of sarcoidosis was made only on a pathological specimen obtained by transbronchial needle aspiration.

Conclusion: To the best of our knowledge, caseating lymph-nodes have never been reported in sarcoidosis. It is important to note that only the presence of the typical aspect of sarcoidosis in the pathological specimen of an apparent caseating lymph node seen at imaging permits the real diagnosis of sarcoidosis especially in those patients in whom infectious disease is prevalent.

Key Words: Sarcoidosis, Tuberculosis, Computed Tomography, Pathology

1. INTRODUCTION

Lymph node enlargement represents a challenge in clinical practice and the underlying diagnosis represents the cornerstone of adequate treatment. Characterized by migration from developing countries to Western countries, tuberculosis has affected poor and vulnerable populations, especially in recent years; migrants are a key affected population, and migration as a social determinant of health increases tuberculosis-related morbidity and mortality for migrants and their communities along all migration pathways.\textsuperscript{[1]} Sometimes, other diagnoses of lymph node enlargement may go unrecognized in this group of patients, and sarcoidosis is a good example of this misdiagnosis. Sarcoidosis is a chronic systemic disease and its etiology is unknown and prognosis varies greatly; usually its affects young adults, and the most common presentation is the presence of bilateral hilar lymphadenopathy associated with pulmonary infiltrates.\textsuperscript{[2]} Ocular involvement, represented mainly by uveitis and skin lesions, may also be present.\textsuperscript{[2]} The diagnosis is based on characteristic clinical-radiological features confirmed by the presence of epithelioid cell granulomas at histology and when other causes of granulomatous inflammation are excluded.\textsuperscript{[2]} The case of an adult male patient coming from Pakistan in whom the caseating-like mediastinal lymph node investigated using computer tomography (CT) was found, and a diagnosis of sarcoidosis made is herein reported. To the best of our knowledge, caseating lymph nodes have never been reported in sarcoidosis, and our group believes that this case is worthy of being
2. Case Report

A 54-year-old Pakistan man was admitted to our Internal Medicine Unit in March 2015 for a persistent cough, sore throat, chest pain exacerbated by attacks of coughing and profuse sweating. He had migrated to Italy in 1989, working as a waiter, and he reported having an uncle, in Pakistan, with a previous diagnosis of tuberculosis. On admission, clinical examination of the abdomen, and the cardiac and pulmonary systems was unremarkable, and his vital signs were normal. Laboratory tests showed a slight leukocytosis (white cell count: 12,000 /mmc, neutrophils 77%) and an increase in the inflammatory indices (C-reactive Protein: 7.09 mg/dl, n.v. < 0.80; erythrocyte sedimentation rate: 26 mm, n.v. < 20); blood cultures were negative. Beta-2 microglobulin was slightly increased (3.5 mg/L, n.v. < 2.0), as was total IgE (125 UI/ml, reference value < 100) and serum CD4+/CD8+ ratio (3.06%, reference range 1.00-2.70); the antinuclear antibodies were border-line (1:80) having a speckled pattern. Rheumatoid factor, C3, C4, IgA, IgM, IgG and lactate dehydrogenase serum concentrations were normal, and serologic tests for toxoplasma infection, cytomegalovirus and Epstein-Barr virus were also negative. As shown in Figure 1, a chest X-ray showed a diffuse thickening of the interstitial plot, associated with an increase in size of the hilar shadows and mediastinal profile due to lymphadenopathy. A thoracic and abdominal CT showed multiple enlarged lymph nodes at the mediastinum, the majority being confluent, some being colliquate (see Figure 2), a thickening of the septa, and centrilobular micro-nodules and multiple subcentimeter lymph nodes in the retroperitoneal area and in the mesentery. In addition, as shown in Figure 3, a nodule of the lingula of the lung was also detected. Thus, the differential diagnosis was between lymphoma, tuberculosis and sarcoidosis. The patient underwent 18F-fluorodeoxyglucose (FDG) positron emission tomography which confirmed the presence of multiple and diffuse hypermetabolic lymphadenopathy in the mediastinum, in the hilum, in the carenal and paratracheal region, and in the celiac and crural area. All these lesions had a maximum standardized uptake value (SU-Vmax) of 29 (see Figure 4). Interferon-gamma release assays (IGRAs; QuantiFERON-TB Gold, QIAGEN GmbH, Hilden, Germany) and a tuberculin skin test (TST) were negative while the serum angiotensin converting enzyme (ACE) levels were lower (4 U/L, n.v. 66-114). For these reasons, a flexible bronchoscopy with bronchoalveolar lavage (BAL) for microbiologic testing and transbronchial needle aspiration (TBNA) of the mediastinal lymph nodes for cytology and mycobacterial research was carried out. The microbiologic test did not show acid-fast bacilli (AFB), and both the polymerase chain reaction (PCR) and the culture were negative for Mycobacterium tuberculosis infection. Cytological examination showed the presence of lymphocytes and macro and macro noncaseating granulomas with focal necrosis. The patient then underwent a video-assisted mediastinoscopy with multiple lymph node biopsies in the precarenal and right paratracheal regions. The pathological analysis confirmed the absence of neoplastic cells, fungine cells and acid-fast bacilli, and showed the presence of chronic granulomatous lymph nodes with epithelioid cells and focal necrosis (see Figure 5). A diagnosis of sarcoidosis was made, and the patient started steroid therapy with prednisone (40 mg per day for three months which is tapered to every-other-day six weeks) and healed rapidly (see Figure 6).

Figure 1. Chest X-ray showing a diffuse thickening of the interstitial plot, associated with an increase in size of hilar shadows and mediastinal profile due to lymphadenopathy

Figure 2. Thoracic computer tomography showing multiple enlarged lymph nodes at the mediastinum, the majority being confluent and some being colliquate
Figure 3. Thoracic computer tomography showing a nodule of the lingula.

Figure 4. FDG-PET which confirmed the presence of multiple and diffuse hypermetabolic lymphadenopathy in the mediastinum, in the hilum, and in the carenal and paratracheal regions.

Figure 5. Panel a: (4 ×; H&E): numerous confluent granulomas, mainly composed of epithelioid cells in a lymphoid background. Panels b and c: (20×; H&E, PAS-D): granulomas showing an area of necrosis consisting of a central fibrinoid focus.
Figure 6. Thoracic computer tomography showing complete healing of the sarcoidosis with the disapperarance of the multiple enlarged lymph nodes at the mediastinum

3. DISCUSSION

Sarcoidosis is a systemic disease manifestation pathologically characterized by a chronic noncaseating granulomatous inflammation, usually involving the lung in more than 90% of the cases[33] and affected patients may be asymptomatic.[4]

Sarcoidosis is progressive in 30% of cases, whereas may have a spontaneous regression in 40%-90% of patients. The mortality range from 1% to 5% of the cases mainly due to cardiorespiratory complications; an early diagnosis may be difficult when an elusive and non-specific onset is present.[5–9]

From a clinical point of view, the differential diagnosis was between tuberculosis, lymphoma or sarcoidosis. The fact that the patient came to Italy from a developing country and there was a familial history of tuberculosis, a suspicion of infective disease was compatible. In addition, the CT findings supported the diagnosis of infectious disease due to the presence of a suspected caseating lymph node. However, the absence of serology and isolation of Mycobacterium tuberculosis did not support the diagnosis of infectious disease. It is well known that CT is the standard technique for the diagnosis as well as the follow-up of sarcoidosis but it should be underlined that CT is often used for regional imaging of the chest and it also explain the low number of extrathoracic localizations detected. As in our case, abdominal lymphadenopathy is frequently detected in more than 70% of cases followed by lymph nodes located near the portal vein (86%), the para-aortic region (77%) and the coeliac axis (59%). 18FDG-PET/CT has recently been proposed for differentiating the solid lesions of the chest found at CT examination from malignant and benign lesions based on the 18FDG metabolism.[11] 18FDG accumulating within the sarcoid granuloma show the classical presence of a rich infiltrate of lymphocytes and macrophages[12,13] even if 18FDG-PET/CT is not specific for sarcoidosis, and other pathological benign thoracic lesions showing 18FDG uptake include infection, inflammation, granulomatosis and sarcoidosis.[14,15]

The appearance of lymph nodes at thoracic computer tomography is quite characteristic of sarcoidosis and in our case, multiple enlarged lymph nodes at the mediastinum were found, the majority being confluent which was compatible with sarcoidosis, but some lymph nodes were colliquate and this was not typical of the disease. Thus, the findings of the 18FDG-PET/CT carried out were not conclusive, and only pathological examination of the lymph nodes involved permitted us to reach a diagnosis. Even if our patient had a suspicion of other diseases involving the lung, such as tuberculosis or lymphoma, only pathology of the specimens of the mediastinal lymph nodes obtained permitted us to reach a diagnosis of sarcoidosis. In conclusion, it is important to note that only the presence of the typical aspects of sarcoidosis in the pathological specimen of an apparent caseating lymph node seen at imaging permits the real diagnosis of sarcoidosis, especially in those patients in whom infectious disease is prevalent.

CONFLICTS OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

REFERENCES


