Cryptogenic Organizing Pneumonia and Mediastinal Lymphadenopathy

To the Editor: Cryptogenic organizing pneumonia (COP) is a clinicopathological syndrome characterized by the presence of organizing granulation tissue in the lumen of bronchioles and distal airways. Lange[1] first described this condition in 1901, using the term bronchitis or bronchiolitis obliterans. Other authors have subsequently described similar histological changes associated with different etiologies.[2] Organizing pneumonia has been attributed to many entities, but the cause remains unknown in most cases. We present a patient with alveolar infiltrates and respiratory insufficiency in conjunction with mediastinal lymphadenopathy.

A 37 year-old female smoker (20 pack-years) was initially admitted to hospital in May 2001 with cough, purulent expectoration, and fever. She had leukocytosis with neutrophilia, elevated erythrocyte sedimentation rate (99 mm/h), and partial respiratory insufficiency with hypocapnia (PaO_2, 44 mm Hg; $PaCO_2$, 29 mm Hg). Pneumonia of the left inferior lobe was apparent in the x-ray. Antibiotic therapy led to both clinical and radiographic improvement. In June of the same year, she was readmitted with another episode of fever, dry cough, and weight loss of 10 kg in the previous 2 months. Her physical examination was normal, but she had mild neutrophilia without leukocytosis, mild eosinophilia (12% of total leukocyte count), and moderate hypoxemia (PaO_2, 68 mm Hg) but $PaCO_2$ was normal. Biochemistry, ions, urine, and coagulation were all normal. An increased erythrocyte sedimentation rate was confirmed (96 mm/h). Immunoglobins lay within normal range, except for a slight increase in type A immunoglobin (269 mg/dL). The immunological study, which included determination of antinuclear antibodies and rheumatoid factor, was normal. Sputum samples were taken for microbiological analysis, but no acid-alcohol fast bacilli were found. A restrictive ventilatory pattern was observed (forced vital capacity [FVC], 72%; forced expiratory volume in 1 second [FEV_1] 63%; FEV_1/FVC, 75%). The carbon monoxide transfer factor lay within normal range (80%). A chest x-ray revealed parenchymal consolidation in the middle lobe with compression of the right costophrenic sinus. Computed tomography of the chest showed diseased superior and inferior right prevascular paratracheal lymph nodes. Pre and bilateral infracarinal nodes were also involved, and diseased hilar lymph nodes were observed in the aortopulmonary window. All these diseased lymph nodes were larger than 1.5 cm. Consolidation of the parenchyma with loss of volume of the middle lobe and presence of an air bronchogram were noted (Figure). Fiberoptic bronchoscopy showed no endobronchial lesions. The fluid collected from bronchoalveolar lavage contained 40% macrophages, 15% eosinophils, 12% lymphocytes, and 33% polymorphonuclear cells. The following lymphocyte subtypes were present in the bronchoalveolar lavage fluid: 75% CD4, 22% CD8, 4% CD19, and 88% CD3, with a CD4/CD8 ratio of 2.59. Cytology was negative for malignant tumor cells. Transbronchial biopsy showed the lung parenchyma had lesions indicative of COP (slightly thickened walls, cuboid metaplasia of alveolar cells, and desquamation of pneumocytes, in addition to frequent filling of alveolar lumens by slightly collagenized fibrillar or lamellar material). Mediastinoscopy showed minimal inflammation of mediastinal lymph nodes. After diagnosis of COP, corticosteroid treatment was started. The clinical improvement was evident, with resolution of hypoxemia. Likewise, subsequent x-ray monitoring showed a progressive reduction in the size of diseased mediastinal lymph nodes until no lymphadenopathy was apparent. Other radiographic examinations were normal.

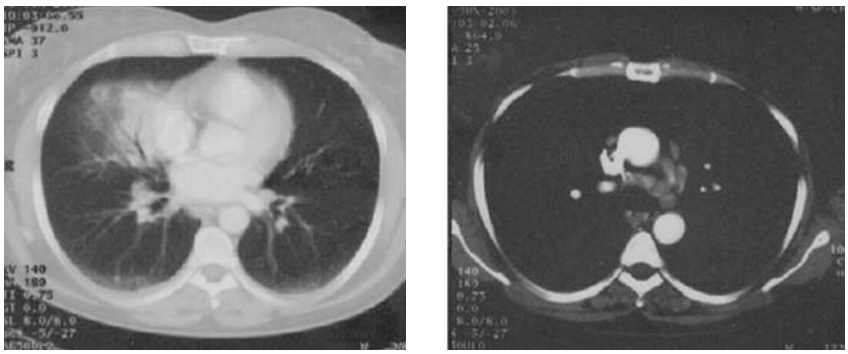

Figure. Computed tomography of the chest showing alveolar infiltration in the median lobe and mediastinal lymphadenopathy.

COP is a very well defined disease, but uncertainty or delay in its diagnosis can arise due to the wide range of clinical and radiographic signs. This patient presented with relapsing respiratory infection and bilateral infiltration. She did not respond fully to antibiotics and partial respiratory insufficiency was combined with a restrictive ventilatory defect, consistent with a clinical diagnosis of COP. This case is exceptional in that multiple diseased mediastinal lymph nodes were present, a finding which led us to consider other diagnoses such as lymphoma, sarcoidosis, or tuberculosis. To reach the correct diagnosis, fiberoptic bronchoscopy with transbronchial biopsy was necessary, thus providing other findings to corroborate diagnosis of COP.

Few cases of lymphadenopathy in conjunction with interstitial lung diseases have been described in the literature and when such cases are reported, the diseased lymph nodes are usually smaller than 1.5 cm.[3,4] To our knowledge, larger diseased lymph nodes or involvement of different lymph-node levels, as was the case in our patient, have not been described in such a context. Diseased mediastinal lymph nodes associated with interstitial lung disease usually indicate sarcoidosis, particularly when the lymph nodes are 2 cm or larger. However, the presence of diseased mediastinal lymph nodes in a patient with interstitial lung disease is not necessarily associated with another inflammatory or neoplastic process. Indeed, in this case, lymphadenopathy was linked to the general acute inflammatory process of COP because no other inflammatory or infectious processes could explain its presence.

We can conclude from this case that definitive diagnosis of COP can only be made by pathology, whether the tissue is obtained by transbronchial biopsy or open lung biopsy, because neither clinical signs and symptoms nor images are conclusive. This case suggests that COP should be considered in the differential diagnosis of bilateral infiltrates associated with lymphadenopathy because COP can present in a variety of forms.[5]

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