Benign Mediastinal Lymphadenopathy in Congestive Heart Failure*

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We report three cases of benign mediastinal lymphadenopathy revealed by chest radiography in patients ranging in age from 61 to 75 years. All three patients had severe coronary heart disease and a history of several episodes of acute cardiac decompensation. Chest CT scanning contributed to the diagnosis by revealing the existence of multiple enlarged lymph nodes, mostly 10 to 17 mm in short-axis diameter. CT scanning also confirmed the disappearance of the mediastinal lymph nodes in one patient on follow-up after treatment with diuretics and digitalis. Histopathology investigations of biopsy samples obtained by mediastinoscopy consistently revealed noninflammatory, benign lesions that did not affect the node structure. Our report draws attention to the particular nosology of left heart disease represented by benign enlarged lymph nodes of the mediastinum and pulmonary edema.

The diagnostic approach to such lymphadenopathy should be guided by the radiologic regression seen on follow-up CT scanning while the patient was undergoing appropriate therapy for congestive heart failure, which constitutes a decisive argument for the congestive heart failure origin.

(CHEST 2001; 119:653–656)

Key words: left heart failure; mediastinal lymph nodes

Abbreviation: SaO₂ = arterial oxygen saturation

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Manuscript received December 16, 1999; revision accepted July 11, 2000.

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had primarily soft-tissue involvement. She did have two small brain lesions, but did not have evidence of extensive disseminated disease. Second, an aggressive chemotherapy regimen was combined with a reduction in the immunosuppressive regimen, which may have added to antifungal efficacy.

Obtaining itraconazole serum or plasma concentrations has been recommended to: (1) avoid potential drug interactions, (2) determine adequate clinical response, (3) assess compliance, and (4) determine GI absorption. Recommended concentrations of itraconazole based on high-performance liquid chromatography should be in a detectable concentration (reference ranges of 0.1 to 2.2 g/mL; Specialty Laboratories; Santa Monica, CA).

In summary, this case describes the successful treatment of _D. gallopava_ in a lung transplant patient without complete surgical excision of the fungal lesions. It is possible that the surgical incision and drainage of the right shoulder lesion were required for cure of this patient, but clearly multiple other lesions, including a lung abscess, were successfully treated with chemotherapy. We believe that successful treatment was related, in part, to combination chemotherapy, drug susceptibility testing, and reduction of immunosuppression. Itraconazole has been shown to penetrate the CNS poorly; therefore, obtaining itraconazole levels may be helpful in adjusting doses. The itraconazole solution in cyclodextrin (used in this case) has better absorption of agents that achieve higher serum and tissue concentrations, with presumably fewer side effects. The use of drug susceptibility testing definitely aided the clinician’s choice of antifungal agents in this case.

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Left-sided or complete congestive heart failure is a very common clinical situation. Although pulmonary or pleural edema is the most common radiologic and clinical finding, mediastinal edema and lymph node enlargement remain unrecognized in daily practice and have been little studied. However, according to Slanetz et al, at least 50% of patients with congestive heart failure are likely to develop enlarged mediastinal lymph nodes without evidence of an infectious, tumor-related, or specific inflammatory cause.

Three patients with advanced cardiac insufficiency and benign mediastinal lymphadenopathy fell into this etiologic category after routine examinations. Their clinical features are described.

CASE REPORTS

Case 1

A 73-year-old female nonsmoker was admitted in April 1994 for investigation of enlarged right mediastinal lymph nodes revealed by chest radiograph following a recent increase in exertional dyspnea. Her history included ischemic heart disease for which she had been treated for 5 years, with clear worsening of her condition in the previous 12 months.

On admission, the patient revealed she had had dyspnea with dry cough for 3 weeks. On physical examination, she was afebrile and orthopneic. Pulmonary auscultation revealed crackles, mainly at the bases of both lungs. Her arterial BP was 140/95 mm Hg. A mitral systolic murmur was noted along with irregular tachycardia. Hepatomegaly with hepatojugular reflux and malleolar edema were noted on palpation.

ECG showed sinus rhythm and left-axis deviation with auricular and ventricular extrasystoles. Measurements of arterial blood gas levels while the patient was breathing room air revealed the following: PaO₂, 54 mm Hg; PaCO₂, 35 mm Hg; pH, 7.35; and arterial oxygen saturation (SaO₂), 91%.

A chest radiograph showed cardiomegaly, bilateral alveolo-interstitial infiltrates predominating in lung bases and a right-sided homogenous suprahilar fullness with convex border, suggesting mediastinal lymphadenopathy (Fig 1). A CT scan of the chest subsequently revealed several lymph nodes of varying size, between 10 and 17 mm in short-axis diameter in the transverse plane (normal size, ≤10 mm), located in two mediastinal compartments, the left anterior mediastinal and the right lower paratracheal compartments. An abdominal CT scan demonstrated no lymphadenopathy. The WBC count was normal, and the C-reactive protein level was 3 mg/L. The results of tracheobronchial endoscopy were normal.

Mediastinoscopy was performed for biopsy sampling of the lymph nodes. Macroscopically, the lymph nodes appeared to be benign. The pathology examination reported sinus histiocytosis without inflammatory or tumoral features. RBCs and a few anthracotic pigments were visible on the sections. The results of microbiological studies (ie, for tuberculous bacilli, bacteria, parasites, and mycotic agents) were all negative on direct examination and on cultures of lymph node tissue.

The immediate outcome was favorable within 24 h after treatment with digitalis and diuretics, leading to improvement in the clinical picture and in blood gas levels while breathing room air (PaO₂, 72 mm Hg; PaCO₂, 41 mm Hg). A follow-up chest radiograph demonstrated the clearance of parenchymal and hilar infiltrates (Fig 2). The morphologic characteristics of the mediastinal lymph nodes remained unchanged on follow-up CT scans during 10 months of observation.

Case 2

This 75-year-old man was a smoker (18 pack-years) who had a history of chronic obstructive bronchitis, chronic arteritis obliterans of the lower limbs, and ischemic heart disease, which had necessitated a previous hospital admission for acute pulmonary edema.

In May 1997, the patient was admitted with dyspnea, exertion-related angina, and productive cough with hemoptysis. A clinical examination revealed a temperature of 38.4°C, an arterial BP of 100/60 mm Hg, a pulse of 80 beats/min, orthopnea, and diffuse bilateral crackles on pulmonary auscultation. A murmur due to mitral insufficiency and a grade 3 systolic murmur were noted. Sensitive hepatomegaly was palpable with hepatojugular reflux and edema of the lower limbs.

An ECG revealed sinus rhythm and ventricular extrasystoles. Arterial blood gas values, measured while the patient was breathing room air, were as follows: PaO₂, 75 mm Hg; PaCO₂, 38 mm Hg; pH, 7.35; and arterial oxygen saturation (SaO₂), 91%.

Figure 1. Chest radiograph taken at presentation (case 1), showing bibasilar alveolo-interstitial infiltrates with right-sided suprahilar fullness, suggesting mediastinal lymphadenopathy and cardiomegaly.

Figure 2. Chest radiograph taken after treatment (case 1). Improvement is marked by moderate clearance of parenchymal and perihilar infiltrates.
Hg; pH, 7.38; and SaO₂, 95%. A chest radiograph revealed right-sided pleural effusion with heterogeneous parenchymal infiltrates of the right hemithorax, hypertrophic hila, and cardiomegaly. Chest CT scan showed lymphadenopathy (lymph node size, 10 to 16 mm on short-axis diameter) in the right paratracheal compartment and hila. The WBC count was 15,000/µL with 76% neutrophils, and the C-reactive protein level was 123 mg/L. The pleural effusion was a transudate. The results of pleural cytology and biopsy specimen testing were both negative. Bronchial endoscopy demonstrated inflammatory features.

Mediastinoscopy was performed. The lymph nodes were macroscopically enlarged. Pathology investigations concluded that there were lesions of sinus histiocytosis, without changes in lymph node structure or surrounding tissues. The results of microbiological examinations were negative.

Treatment with antibiotics, digitalis, and diuretics was followed by resolution of the patient’s temperature 48 h later and by rapid improvement in blood gas values. Initial improvement in the pleural and parenchymal features was noted on follow-up radiograph, but the mediastinal features persisted after 8 months.

Case 3

This 61-year-old male smoker (20 pack-years) was admitted in August 1998 for cough with hemoptysis and dyspnea. He had a history of coronary artery disease that had necessitated hospital admission on three occasions for acute congestive heart failure.

On examination, auscultation indicated bilateral fine crepitant rales. Palpation revealed hepatomegaly, and there was edema of the lower limbs. Arterial blood gas values, measured while the patient was breathing room air, were as follows: PaO₂, 82 mm Hg; PaCO₂, 35 mm Hg; pH, 7.42; and SaO₂, 91%. An ECG showed signs of ventricular and auricular hypertrophy. Dilatation of the left ventricle with hypokinesis of the posterior wall and a systolic ejection fraction of 52% were noted on echocardiographic examination.

A chest radiograph revealed slight bilateral interstitial syndrome, predominating in the left base. A CT scan showed lymphadenopathy (lymph node size, 10 to 15 mm on short-axis diameter) located in paratracheal, pretracheal, and subcarinal compartments. A slight pleural effusion was visualized in the right hemithorax (Fig 3). Biochemistry study of the pleural effusion indicated a transudate. Cytologic studies failed to reveal malignant pleural cells. Bronchial endoscopy demonstrated no abnormality.

Mediastinoscopy showed enlarged lymph nodes that were macroscopically normal. Microscopic examination revealed lesions of sinus histiocytosis associated with follicular hyperplasia of the cortex, and no inflammatory lesions or capsular changes were seen (Fig 4). The results of microbiology studies were negative.

Treatment was started with digitalis and diuretics, resulting in immediate clinical and radiologic improvement. On follow-up 5 months after the acute phase, a radiograph and CT scan showed that most of the enlarged mediastinal lymph nodes and the right-sided pleural effusion had completely disappeared. The few remaining nodes measured < 6 mm in diameter (Fig 5).

Discussion

In contrast to alveolointerstitial edema, hypertrophy of mediastinal lymph nodes is not a usual sign of congestive heart failure. It is very probable that the frequency of lymphadenopathy in congestive heart failure is largely underestimated for various reasons, which can be explained mainly by the clinical presentation and the diagnostic circumstances.

Slanetz et al reported a study of 46 chest CT scan examinations in patients with heart failure, which were performed during periods of acute cardiac decompensation. Their retrospective analysis identified 55% of patients with enlarged lymph nodes that initially were undiagnosed. The enlarged lymph node localizations involved various mediastinal lymphatic chains but appeared to indicate higher frequency in the subcarinal, paratracheal, and hilar nodes. Follow-up of 17 patients with elevated levels of pulmonary capillary wedge pressure detected 14 patients with enlarged mediastinal lymph nodes (size, 10 to 20 mm on short-axis diameter).

The mechanisms underlying the pathogenesis of lymphadenopathy in cardiogenic pulmonary edema are unclear. Lymphadenopathy in such cases is the expression of
diffuse intrathoracic edema affecting the pulmonary parenchyma and neighboring structures, including the mediastinum and associated lymph nodes.

The lymphatic circulation has a primary role in the regulation of pulmonary fluids. It ensures continuous low-pressure drainage of excess fluids from the interstitial space to the collecting ducts via the lymph nodes. These nodes are distributed along the lymph vessels and filter the lymph during its circulation. The lymph flow rejoins the venous blood circulation, thus enhancing interactions between the two circulatory systems. Lymphadenopathy, therefore, might result from mediastinal edema, which itself is due to massive or repeated pulmonary edema that is able to extend above the limits of the lungs and the pleura at a very developed stage of congestive cardiac failure. Hypertrophy of the lymph nodes, thus, might be linked to edematous infiltration following lymphatic circulation overloading.

Drake et al. used an experimental approach in sheep to demonstrate that sudden induced cardiac insufficiency was associated with an increase in lymphatic flow measured in the efferent vessel of a previously cannulated mediastinal lymph node, when venous pressure was < 15 cm H₂O. This process was followed by a significant slowing of lymphatic flow for a venous pressure level > 15 cm H₂O. Leeds et al. showed that experimental congestive heart failure in dogs caused the dilatation of lymphatic vessels, which was provoked by excessive interstitial fluid. Slanetz et al. reported a particular hazy and heterogeneous appearance of mediastinal fat, which was consistently observed around enlarged lymph nodes that were visualized on CT scans. It was attributed to local effects of edema. These studies support the hypothesis of hemodynamic mechanisms in lymph node enlargement that are related to severe cardiac decompensation.

Our report draws attention to the particular nosology of late heart disease represented by benign enlarged lymph nodes of the mediastinum and pulmonary edema. The circumstances revealing the enlarged mediastinal nodes in the three patients reported were almost identical. All had known coronary heart disease and had experienced several episodes of acute congestive heart failure with recently worsened symptoms. A suspicion of lymphadenopathy was based on radiographs that were taken to investigate dyspnea and heart failure. The identification of suspicious features is theoretically easier on follow-up radiographic examinations, which provide better visibility of hilar and mediastinal areas, after treatment to reduce pulmonary edema. Although CT scanning is much more effective for the identification and follow-up of enlarged mediastinal lymph nodes, such examinations usually are not necessary in the clinical context of congestive heart failure. However, certain intrathoracic localizations of Hodgkin’s and non-Hodgkin’s lymphomas, involving the heart and attributable to metastatic infiltration, may cause congestive heart failure and, therefore, may present similar clinical pictures. The results of lymph node biopsies in all three patients showed similar histologic abnormalities (i.e., sinus histiocytosis with slight follicular hyperplasia of the cortex in one patient).

The spectacular regression or disappearance of the nodes in one of the three patients, who underwent therapy exclusively for heart disease, is evidence of the likelihood of cardiac origin. A similar outcome has been reported in the literature after an acute episode of congestive heart failure lasting for a month. The diagnostic approach to such lymphadenopathy should be guided by the radiologic regression seen on follow-up chest radiographs or CT scans performed while the patient is undergoing appropriate therapy for congestive heart failure, which constitutes a decisive argument for the congestive heart failure origin.

**References**