CHEST

Original Research

PULMONARY VASCULAR DISEASE

Frequency of Mediastinal Lymphadenopathy in Patients With Idiopathic Pulmonary Arterial Hypertension

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Objective: **The objective of this study was to assess the frequency of mediastinal lymphadenopathy in patients with idiopathic pulmonary arterial hypertension (IPAH) and describe the correlative clinical features.**

Methods: **We conducted a retrospective review of patients with IPAH who underwent right-sided heart catheterization (RHC) and chest CT scan within 3 months of each other. Patients were from a single tertiary institution. CT scans were reviewed for the presence of mediastinal lymphadenopathy (MLAD) with correlating demographic and clinical data, including lymph node size and location, right atrial pressure (RAP), mean pulmonary arterial pressure (mPAP), and the presence of pleural and pericardial effusion.**

Results: **The study population included 85 patients with a mean age of 48 ± 17.3 years; 70 (82%) were women. Fifteen patients (18%) had MLAD on chest CT scan. The mean short-axis diameter of the largest lymph node in these patients was 13.6 mm (range, 11-20 mm). The enlarged lymph nodes were located predominantly in the lower paratracheal and subcarinal stations. There was no association of MLAD with age, sex, RAP, or mPAP. MLAD was associated with presence of pleural effusion ($P < .02$) but not pericardial effusion. Mean left ventricular ejection fraction for those with lymphadenopathy was 63% (range, 45%-76%).**

Conclusions: **MLAD without other identifiable causes is seen in approximately one in five patients with IPAH and is associated with pleural effusion but not mPAP, RAP, or left ventricular function.**

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Abbreviations: CHF = congestive heart failure; IPAH = idiopathic pulmonary arterial hypertension; LV = left ventricular; LVEF = left ventricular ejection fraction; MLAD = mediastinal lymphadenopathy; mPAP = mean pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; PH = pulmonary hypertension; RAP = right atrial pressure; RHC = right-sided heart catheterization

Mediastinal lymphadenopathy (MLAD) is a commonly encountered radiologic finding. Diagnostic considerations generally include lymphoma, metastatic disease, sarcoidosis, and infection. In addition, there are several benign causes of MLAD that may be overlooked and lead to unnecessary invasive diagnostic procedures. For example, enlarged mediastinal lymph nodes (short axis > 1 cm) have been described in 35% to 66% of patients with systolic congestive heart failure (CHF) who undergo chest CT scan.[1-5] Some of these patients have undergone mediastinal lymph node biopsy to confirm congestive lymphadenopathy.[2,4]

MLAD has also been described in some forms of pulmonary hypertension (PH). Recently, Bergin et al[6] reported MLAD in 45% of patients with chronic thromboembolic PH. These authors also noted a frequent association of MLAD with pleural and pericardial effusions, suggesting right-sided heart failure

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with increased lymphatic flow as a possible underlying pathophysiologic mechanism. It is not known whether a similar mechanism may induce MLAD in patients with idiopathic pulmonary arterial hypertension (IPAH). In this study, we sought to identify the frequency of MLAD in patients with IPAH and any associated clinical features.

Materials and Methods

A computer-assisted search of medical records was conducted to identify patients diagnosed with IPAH at Mayo Clinic, Rochester, Minnesota, over a 10-year period between January 1, 1999, and December 31, 2008. Approval was obtained from the Mayo Clinic Institutional Review Board (IRB# 09-004811) before study initiation.

IPAH was defined as absence of identifiable causes for precapillary PH and a mean pulmonary arterial pressure (mPAP) ≥25 mm Hg and pulmonary wedge pressure ≤ 15 mm Hg as assessed by right-sided heart catheterization (RHC).[7] Medical records were reviewed for abstraction of demographics, clinical presentation, underlying diagnoses, hemodynamic parameters, and imaging studies. For the purposes of this study, only those patients with chest CT scan performed within 3 months of RHC were included. Those patients who had underlying malignancy, infection, or other potential explanations for MLAD or other causes of PH during their initial evaluation or follow-up were excluded from this study cohort.

Collected RHC data included right atrial pressures (RAPs), mPAPs, pulmonary artery systolic and diastolic pressures, and pulmonary capillary wedge pressures (PCWPs). CT scans were reviewed by two of the authors (D. L. L. and J. H. R.) independently and without knowledge of the clinical context (ie, clinical presentation or hemodynamic data) to assess mediastinal lymph nodes. Enlarged nodes were defined as diameter > 1.0 cm on the short axis. The location of nodes was defined by conventional nodal station criteria.[8] Differences in interpretation were settled by consensus. Presence of pleural effusion was also assessed. Transthoracic or transesophageal echocardiogram data included assessment of right ventricular function, left ventricular ejection fraction (LVEF), and diastolic function (assessed by a combination of left atrial size, pulsed-wave mitral-inflow Doppler E and A wave velocities and E deceleration time, tissue Doppler of the medial mitral annulus, and pulmonary venous inflow[9]), the presence of left ventricular (LV) D-shaped anatomy, and the presence of pericardial effusion. Correlation with lymphadenopathy was performed for age, sex, RAP, mPAP, PCWP, and presence of pleural or pericardial effusion using Fisher exact test for categorical or binomial variables, and two-tailed, unequal variance *t* test for comparison of means with continuous variables (SAS Institute, Inc).

Results

Eighty-five patients with IPAH were included in this study. Their mean age (± SD) at diagnosis was 48.3 ± 17.3 years; 82% of the patients were women. Over the study interval 1999-2008 118 patients with IPAH who underwent RHC and high-resolution CT scan were identified. Original cardiac catheterization data were not retrievable for 15 patients, and an additional 18 patients had chest CT scan outside the 3-month interval. In these excluded patients, the interval between RHC and CT scan ranged from 5 to 70 months (median, 24 months).

Selected RHC and echocardiogram data are presented in Table 1 along with the frequency of pleural and pericardial effusion. There was no statistical difference in baseline demographic, cardiac catheterization, or echocardiogram findings.

Fifteen patients (18%) had MLAD with 27 enlarged nodes (Table 2). The mean short-axis diameter of enlarged nodes was 13.6 mm (range, 11-20 mm); none was > 20 mm. The most common nodal stations involved were lower paratracheal and subcarinal; no enlarged nodes were seen in the upper paratracheal station (Fig 1). Of the 15 individuals, nine underwent subsequent chest CT scan. One patient had resolution of lymphadenopathy at 61 months of follow-up. The remaining eight patients had unchanged lymph node size (median follow-up duration, 2.2 months [range, 5 days-63 months]) despite treatment of PH. None underwent invasive diagnostic workup of lymphadenopathy.

The mean LVEF was not statistically different between those with and without MLAD (62.5% vs 61.4%; $P = .63$), with eight of 15 (53%) patients with lymphadenopathy having D-shaped LV configuration on transthoracic echocardiogram. Review of echocardiogram data suggested eight patients overall had diastolic dysfunction, which was graded as "mild abnormal filling" in two patients and 1-2 out of 4 in severity in the remainder (where grade 1 = diastolic dysfunction [abnormal relaxation pattern]; grade 2 = diastolic dysfunction consistent with moderately increased filling pressures; grade 3 = diastolic dysfunction [reversible restrictive pattern] consistent with severely elevated filling pressures; and grade 4 = severe diastolic dysfunction [irreversible restrictive pattern] with severely elevated filling pressures). Only one patient with diastolic dysfunction had MLAD that was graded as 1 out of 4 ($P = .68$).

Five of the fifteen patients (33%) with MLAD had concomitant pleural effusions (two were unilateral [right-sided in both], three were bilateral), and three (20%) had concomitant pericardial effusions. Mean LVEF for all patients with pleural effusion (n = 11) was 65% (range, 45-76%). Elevated RAPs were increased in those with pleural effusion (mean RAP, 18.09 mm Hg vs 10.14 mm Hg; $P < .001$), but were not statistically different in those with or without lymphadenopathy (mean RAP, 12.71 mm Hg vs 10.98 mm Hg; $P = .44$).

When comparing the presence or absence of lymphadenopathy, there was no statistical association of MLAD with age, sex, RAP, mPAP, diastolic dysfunction, or presence of pericardial effusion. Frequency of pleural effusion was increased in those with MLAD (33% vs 9%, $P < .02$).