



Granulomatous-lymphocytic Interstitial Lung Disease in a Patient with Common Variable Immunodeficiency

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Each month we present highlights from the Ask the Expert section of the American Academy of Allergy, Asthma, & Immunology (AAAAI) Web site written by Phil Lieberman, MD. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Question:

My patient is a 37-year-old white man who presented to me for recurrent sinus infections. Immune workup results revealed IgG 69 mg/ml, IgA < 15 mg/ml, IgM 7 mg/ml, IgE 4 iu, 1% CD19, 1% CD20, 96% CD2, 93% CD3, 54% CD4, and 35% CD8. Pneumococcal titers were <0.3 to all 23 serotypes; tetanus titer was <0.05. Computed tomography (CT) of the sinuses showed pan-sinusitis. High-resolution CT of the chest showed nodular densities in right lower lobe and a ground-glass opacity in the right upper lobe, splenomegaly of 14.3 cm, and multiple enlarged axillary lymph nodes bilaterally. I diagnosed him with common variable immune deficiency (CVID) and started subcutaneous immunoglobulin replacement (Hizentra CSL Behring LLC, Bern, Switzerland, and Kankakee, Ill) at a dose of 4 g/kg. He has not improved, and I am concerned about the enlarged lymph nodes, splenomegaly, and granulomatous disease. Does he have granulomatous-lymphocytic interstitial lung disease (GLILD)? If so, how should he be managed?

Response:

Thank you for your inquiry. I am asking John Routes, MD, who is a nationally known expert of this disorder, to respond to your inquiry.

Response from John Routes, MD:

It is difficult to know how to proceed without seeing the high-resolution CT myself, but I would like to make some general comments. For all patients with newly diagnosed CVID, we get a high-resolution CT of the chest and abdomen, both with and without radiocontrast. These studies are very informative and provide information, not only about the presence or absence of lung parenchymal disease but also on the extent of liver or spleen enlargement and the presence of additional, undetected adenopathy. Having a baseline measurement of these variables also is important because patients with CVID are at increased risk of developing B-cell lymphomas, and it is important to detect the presence of GLILD because it can shorten the survival of patients with CVID.^{1,2}

The radiographic appearance of GLILD consists of scattered nodular disease (macronodular disease), areas of consolidation, and a “ground-glass” abnormality typically more prominent in the lower lung zones. Diffuse adenopathy and splenomegaly are almost always found as well because GLILD is a multisystem, lymphoproliferative disorder. Complete pulmonary function tests (PFTs), including plethysmography and diffusion of carbon monoxide (Dlco) as well as a 6-minute walk, are essential for the evaluation as well.

If patients have diffuse parenchymal lung disease, then the decision to biopsy is made by considering a number of factors. With patients with significant lung disease, in particular, if they are symptomatic, we perform a video-assisted thoracoscopic lung biopsy, with specimens taken from 3 to 5 sites to avoid sampling bias. The differential diagnosis of parenchymal lung disease is large and includes infection, cryptogenic organizing pneumonia, lymphoma, and GLILD, disorders that are treated quite differently. It is of utmost importance that the pulmonary pathologist who reads the lung biopsy has experience with the pulmonary pathology that occurs with CVID. We do not biopsy lymph nodes or perform a bone marrow biopsy unless there is strong suspicion for a high-grade lymphoma.

Decreased PFTs also would lead one to favor a lung biopsy. However, in our article on the treatment of GLILD, 4 of 7 patients had normal PFTs per the American Thoracic Society criteria.¹ We now have treated several patients with GLILD who had “normal” lung function by PFTs, with a significant improvement in PFTs after therapy. The issue is that we do not know what the PFTs were before the onset of disease, so a “normal” PFT does not mean normal for the patient.

I personally believe patients with CVID and diffuse parenchymal lung disease should be evaluated at a center with a clinical immunologist who routinely sees such patients. In the event that the diagnosis of GLILD is made, the immunologist can work with local physicians to administer systemic immunosuppression. We found that oncologists many times administer rituximab and azathioprine, and are quite familiar with the use of these drugs.

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