Pericarditis with massive pericardial effusion : an unusual complication of primary biliary cirrhosis

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Abstract

Primary Biliary Cirrhosis (PBC) is a debilitating autoimmune condition associated with a constellation of extrahepatic inflammatory manifestations accentuating its morbidity and mortality. Pericarditis and pericardial effusion had been rarely associated with and inadequately characterized in PBC. We present a challenging case of inflammatory pericarditis and life-threatening massive pericardial effusion in a 49 year old patient with PBC. This complication should be more recognized and appropriately treated to avoid progression to cardiac tamponade. (Acta gastroenterol. belg., **2012**, 75, **354-356**).

Key words : pericarditis, primary biliary cirrhosis, pericardial effusion.

Introduction

Primary Biliary Cirrhosis (PBC) is a progressive liver disease characterized by autoimmune destruction of intra-hepatic bile ducts, leading to fibrosis and liver failure. Although anti-mitochondrial antibodies (AMA) are most frequently associated with PBC, titers of more than 20 autoantibodies had been detected in their sera (1), emphasizing its autoimmune nature. The majority of the complications associated with PBC are either due to the resulting liver cirrhosis and portal hypertension, or the concomitant extrahepatic manifestations, such as uveitis, and sicca syndrome (2). Even though pleural effusion and ascites resulting from portal hypertension are commonly seen (3), cardiac complications are rarely reported and inadequately characterized manifestations of PBC. This rare case illustrates the importance of recognizing the occurrence of pericarditis in PBC, in light of the potential for chronicity and life-threatening complications such as pericardial tamponade, and treatment thereafter.

Presentation

A 49-year-old white female, with history of PBC diagnosed by biopsy and treated with ursodeoxycholic acid, presented with complaints of fatigue and shortness of breath. She denied any chest pain, fever, or night sweats. No joint pain, dry eyes or mouth, rash, abdominal pain, or diarrhea were reported. On physical examination, she was afebrile, moderately dyspneic, with blood pressure of 107/66 mmHg. Chest examination showed decreased breath sounds mainly on the left side, with distant heart sounds. No murmurs, gallops or friction rubs were audible. Jugular venous distention was absent and pulsus paradoxus was not elicited. Her abdomen was mildly distended and non-tender. Hemoglobin was 5.4 g/dL (normal 11.6-15.2), leukocyte count 11.6 thousand/mm^3 (normal 3.8-10), and platelets 235 thousand/mm^3 (normal 150-390). Alkaline phosphatase was 477 U/L (normal < 105), aspartate amino transferase 78 U/L (normal < 34), alanine amino transferase 43 U/L (normal < 37), total bilirubin 11.2 mg/dL (normal < 1.0), and albumin 2.1 g/dL (normal 3.3-4.5). Cardiac enzymes and thyroid function tests were within normal limits. She had positive AMA titers. Anti-nuclear, Anti-Ro, Anti-La, anti-ds and anti-sm antibodies were negative. The rheumatoid factor titers were marginally elevated, although the anti-cyclic cetrullinated peptide antibodies were negative. She also had negative titers for anticardiolipin, antiphospholipid and anti-b2-glycoprotein 1 antibodies. C3 and C4 complement levels were within normal range. The patient did have elevated erythrocyte sedimentation rate of 80 mm/H (normal 0-20). Rapid plasma reagent and quantiferon tuberculosis (Tb) tests were negative. Blood, sputum and urine cultures did not grow any bacteria, fungi or acid-fast bacilli (Tb). She had negative titers for recent mycoplasma, cytomegalovirus, hepatitis A, B, and C, human immunodeficiency virus 1 and 2, Epstein barr virus, coxsackie A and B, adenovirus, influenza A and B, mumps, varicella, and parvovirus B19 infections. She was transfused with packed red blood cells. Esophagogastroduodenoscopy (EGD) showed portal hypertensive gastropathy, however, no source of active bleeding was identified. A small bowel biopsy revealed benign intestinal mucosa with no granulomas, inflammation, or viral inclusions. Colonoscopy was normal. The electrocardiogram showed low voltage waves. Computed tomography (CT) of the chest revealed a massive pericardial effusion (Fig. 1). Transthoraric echocardiography (ECHO) demonstrated massive exudative pericardial effusion, with ejection fraction of 70%, and normal valvular function. No ECHO criteria for severe tamponade were observed (Fig. 2). ECHO records 2 months prior to this admission failed to show

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Submission date : 27/07/2011
Acceptance date : 12/08/2011

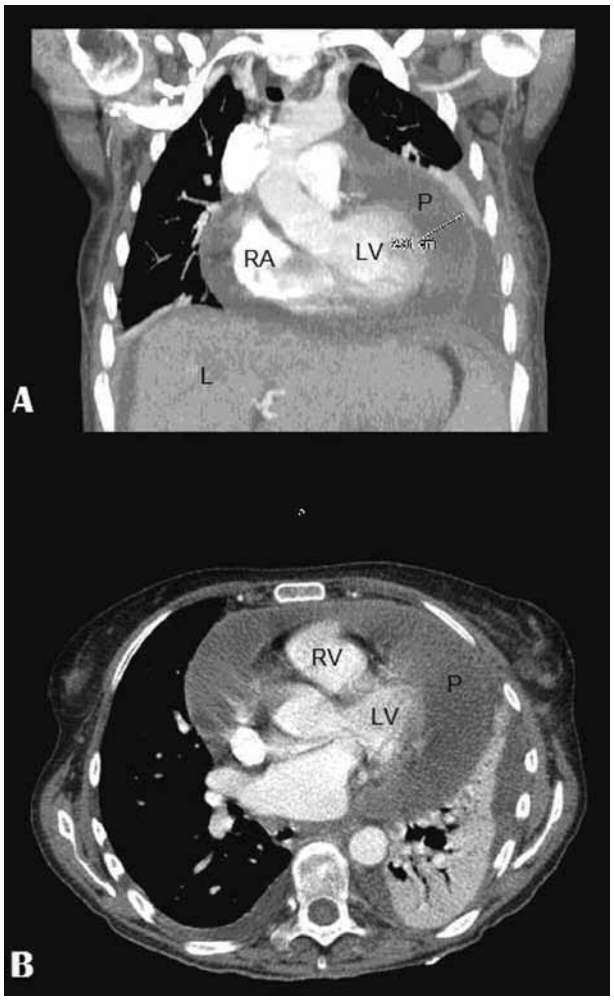

Fig. 1. — Computed tomography of the chest with contrast. A. Coronal section and B. Cross section demonstrating the massive pericardial effusion (P), occupying a significant space inside the thoracic cavity, with basal atelectasis of the left lung. LV, left ventricle ; RV, right ventricle ; P, pericardial effusion ; L, liver.

any evidence of pericardial effusion. Due to the massive size of the effusion, and to avoid recurrence, the patient underwent pericardiectomy with pericardial window. The pericardial fluid was exudative in nature upon further protein and albumin analysis. All fluid stains and cultures were negative for bacterial, fungal or Tb growth. No malignant cells were recognized. White blood cell counts were minimal, with no red blood cells. Pericardial biopsy revealed benign hyalinizing fibrous tissue with exuberant granulation tissue proliferation, and organizing fibrinoid pericarditis, without evidence of granulomatous disease or neoplasm. Tissue cultures were negative for any bacterial or fungal growth. Post-operative day one, the patient's respiratory status improved significantly. CT of the abdomen showed signs of liver cirrhosis. The patient had improved symptoms during two months of follow up. In preparation for pending liver transplantation, and in light of her worsening kidney function, we elected not to start any medical therapy, and proceed with the surgical approach described above.

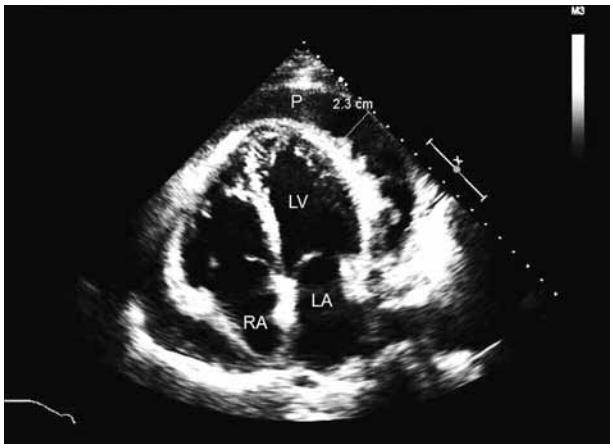

Fig. 2. — End-diastolic 4-chambers transthoracic echocardiogram. > 2 cm pericardial effusion (P) surrounding the heart chambers. LA, left atrium ; RA, right atrium ; LV, left ventricle.

Discussion

PBC is an autoimmune liver disease associated with increased incidence of other autoimmune disorders, such as inflammatory bowel disease (4), sicca syndrome (5), and systemic lupus erythematosus (6). Pericarditis can be infectious, malignant or autoimmune in nature (7). Development of pericarditis in PBC is rather rarely reported in the literature so far (8-11) ; most of them in association with other concomitant autoimmune diseases.

Pericarditis secondary to PBC is a diagnosis of exclusion. Other etiologies for pericarditis were excluded in this patient. For instance, she tested negative for other common autoimmune diseases well known to cause pericarditis, such as systemic lupus erythematosis, sjogrens syndrome, rheumatoid arthritis, polymyalgia rheumatica, and antiphospholipid syndrome. Other infectious causes were also excluded, such as tuberculosis, mycoplasma, coxsachie A and B, among others. The ursodeoxycholic acid was not previously associated with pericarditis or pericardial effusion.

This case clearly demonstrated the inflammatory nature of pericarditis in the setting of PBC. The exudative nature of the pericardial fluid in our patient, associated with the inflammatory microscopic findings on pericardial biopsy, further support the fact that pericarditis and pericardial effusion might represent an actual inflammatory extrahepatic manifestation of PBC, rather than fluid collection resulting from portal hypertension in advanced liver cirrhosis. The association of previously reported cases of pericardial effusion with other autoimmune diseases, in the setting of PBC (8-11), also supports, in part, the possible autoimmune nature of pericarditis.

The pericarditis with pericardial effusion had been well documented in this patient. CT scan imaging and echocardiography revealed massive collection of fluid

that failed to induce pericardial tamponade, emphasizing the chronicity of the process. The currently reported inflammation of the pericardium is consistent with the known pathophysiology of PBC as an inflammatory disease primarily affecting the liver, with well characterized extrahepatic inflammatory manifestations, such as fibrosing alveolitis (12) and tubulointerstitial nephritis (13).

This case report emphasizes important points regarding the association between PBC and pericarditis. First, the consideration, early detection of pericarditis and pericardial effusion, and the early intervention before progression to full blown life-threatening tamponade. Second, the therapeutic implications of such association in terms of NSAIDs and corticosteroids use ; whereas NSAIDs may be an optimal therapeutic option for pericarditis (14), it can be detrimental in cases of advanced liver failure usually seen in patients with PBC. On the other hand, the use of corticosteroids has been used as an adjuvant therapy in PBC (15), offering an advantage in pericardial inflammation.

Regardless of possible pathogenetic associations ; the recognition of pericarditis as a possible inflammatory complication of PBC, and the early detection and treatment would contribute in decreasing the patient's morbidity, and possible mortality, with a better outcome for those rare cases.

References

1. HU C., LI Y., ZHANG F., ZHANG X. Primary Biliary Cirrhosis : What do autoantibodies tell us. *World J. Gastroenterol*., 2010, **16** : 3616-3621.
2. GERSHWIN M., SELMI C., WORMAN H., GOLD E., WATNIK M., UTTS J., *et al*. Risk factors and comorbidities in primary biliary cirrhosis : a controlled interview-based study of 1032 patients. *Hepatology*, 2005, **42** : 1194-202.
3. WOJCIKIEWICZ T., GUPTA S. Primary biliary cirrhosis presenting with ascites and a hepatic hydrothorax : a case report. *J. Med. Case Reports*, 2009, **3** : 7371.
4. ARAI O., IKEDA H., MOURI H., NOTOHARA K., MATSUEDA K. Two cases of inflammatory bowel disease diagnosed in the course of primary biliary cirrhosis. *Nippon Shokakibyo Gakkai Zasshi*, 2010, **107** (6) : 900-8.
5. SKOPOULI F., BARBATIS C., MOUTSOPOULOS H. Liver involvement in primary Sjögren's syndrome. *Br. J. Rheumatol*., 1994, **33** (8) : 745-8.
6. CHOWDHARY V., CROWSON C., POTERUCHA J., MODER K. Liver involvement in systemic lupus erythematosus : case review of 40 patients. *J. Rheumatol*., 2008, **35** (11) : 2159-64.
7. IMAZIO M., BRUCATO A., TRINCHERO R., ADLER Y. Diagnosis and management of pericardial diseases. *Nat. Rev. Cardiol*., 2009, **6** (12) : 743-51.
8. CHOLONGITAS E., MAVROGIANNAKI A., PAPAIOANNOU C., KARAGIANNIS S., PAPATHEODORIDIS G. Pericarditis and possible antiphospholipid syndrome on primary biliary cirrhosis. *Ann. Hepatol*., 2004, **3** (4) : 167-8.
9. DUCLOUX G., LAURENT J., HICKMAN S., CARON C., RIVAT P. Pericarditis disclosing primary biliary cirrhosis. *Presse Med*., 1985, **14** (3) : 161-2.
10. DAY R., BENNETT J. Primary biliary cirrhosis with pericarditis. *Lancet*, 1981, **1** (8232) : 1266.
11. AGRAOU B., LE TOURNEAU T., AGRAOU H., LEROY F., ASSEMAN P., DUJARDIN J. Primary biliary cirrhosis associated with pericardial effusion. *Ann. Cardiol. Angeiol*., 1998, **47** (8) : 576-8.
12. SMITH J., SORENSEN P., PALLISGAARD G. Diffuse fibrosing alveolitis and primary biliary cirrhosis. *Ugeskr. Laeger*, 1990, **152** (25) : 1832-3.
13. KOMATSUDA A., WAKUI H., OHTANI H., MASAI R., OKUYAMA S., NIMURA T. *et al*. Tubulointerstitial nephritis and renal tubular acidosis of different types are rare but important complications of primary biliary cirrhosis. *Nephrol. Dial. Transplant*., 2010, **25** (11) : 3575-9.
14. PATWARDHAN R., HEILPERN R., BREWSTER A., DARRAH J. Pleuropericarditis : an extraintestinal complication of inflammatory bowel disease. Report of three cases and review of literature. *Arch. Intern. Med*., 1983, **143** (1) : 94-6.
15. LAZARIDIS K., TALWALKAR J. Clinical epidemiology of primary biliary cirrhosis : incidence, prevalence, and impact of therapy. *J. Clin. Gastroenterol*., 2007, **41** (5) : 494-500.