A rare association of Primary Biliary Cholangitis and pericarditis - A case series and review

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Case report

A 38-year-old female, a known case of PBC (Ludwig’s stage III-IV; diagnosed 1 year ago) with anti-phospholipid antibody syndrome (APLA), Sjogren’s syndrome, and a history of deep vein thrombosis on a vitamin-K antagonist, was referred to us by a primary care physician for progressively increasing dyspnoea with hypotension. She gave a history of right-upper-quadrant abdominal pain, anorexia, fever, atypical non-radiating chest-pain, and associated orthopnoea for 2 weeks. She had generalized malaise and was restricted to her bed. She had a recent history of gum bleeding.

Introduction

Primary Biliary Cholangitis (PBC), earlier known as Primary Biliary Cirrhosis, is a debilitating autoimmune disorder involving intrahepatic biliary ducts. It is characterized by chronic inflammation followed by fibrous obliteration of biliary ducts. The PBC is sometimes associated with other autoimmune disorders (32%) like Sjogren’s syndrome (10%), CREST syndrome (5%), systemic lupus erythematosus (3%), Raynaud syndrome (3%), and mixed connective tissue disease.1,2 PBC complications include cirrhosis of the liver, portal hypertension, and extrahepatic complications like sicca syndrome.3 Pericarditis in the backdrop of PBC is an extremely rare complication and is sparsely reported as compared to pleural effusion and ascites caused by portal hypertension. This case report presents a patient with a rare combination of PBC with APLA syndrome, complicating into pericarditis followed by large pericardial effusion (PE) leading to tamponade. We have summarized all the cases of PBC with PE reported to date. All the cases which met the criteria mentioned below reported to date were included in the study.

- The PE being diagnosed either on trans-thoracic-echocardiography or computed tomography (CT) imaging in PBS patient,
- Patients of all age groups, genders, and races were included.

The findings were interpreted using descriptive statistics, including mean, median, ranges, standard deviation, and percentages. A total of 5 cases corresponding to the criteria for the diagnosis of PE in proven PBC patients.
Figure 1. A, B: The trans-thoracic echocardiography of heart in parasternal long axis showing large pericardial effusion with the epicardial-pericardial distance of 2.68 cm at Cardiac Apex and 2.37 cm at Posterior wall (A). The image shows a parasternal short-axis view of the heart at the level of the mitral valve with large pericardial effusion and partial collapse of the right ventricle (B).

Figure 2. A, B: The non-contrast plain computed tomography (CT) of chest and abdomen showing heart with large pericardial effusion (yellow arrow) and calcified portal and splenic veins (white arrow) (A). The abdominal CT shows ‘shrunken and nodular’ liver, splenomegaly, and portal hypertension with congested inferior vena-cava (B). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1

<table>
<thead>
<tr>
<th>SL no</th>
<th>Year</th>
<th>Country</th>
<th>Author</th>
<th>Case report details</th>
<th>Clinical Features</th>
<th>Primary Disease</th>
<th>Associated Disease</th>
<th>Co-morbidities</th>
<th>Effusion</th>
<th>Antibodies</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>1998</td>
<td>France</td>
<td>B Agraou</td>
<td>No details</td>
<td>No details</td>
<td>Primary Biliary Cirrhosis</td>
<td>Anti-Phospholipid syndrome</td>
<td>No details</td>
<td>Moderate</td>
<td>No details</td>
<td>Colchicine and Ursodesoxycholic acid</td>
<td>Improvement</td>
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<tr>
<td>2</td>
<td>2000</td>
<td>Korea</td>
<td>Jun-Ki Min</td>
<td>46-year, Female</td>
<td>Abdominal pain; dyspnea; sicca symptoms; cognitive dysfunction</td>
<td>Primary Biliary Cirrhosis</td>
<td>Sjogren’s syndrome; Systemic mononuclear inflammatory vasculopathy</td>
<td>None</td>
<td>Moderate</td>
<td>AMA ARA</td>
<td>Prednisolone</td>
<td>Improvement</td>
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<td>3</td>
<td>2004</td>
<td>Greece</td>
<td>E. Cholongitas</td>
<td>68-year, Female</td>
<td>Cough; back pain;</td>
<td>Primary Biliary Cirrhosis</td>
<td>Anti-Phospholipid syndrome</td>
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<td>Large</td>
<td>AMA ANA ACA</td>
<td>Improvement</td>
<td></td>
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<tr>
<td>4</td>
<td>2011</td>
<td>USA</td>
<td>Z. Taimeh</td>
<td>49-year, Female</td>
<td>Fatigue; Dyspnoea</td>
<td>Primary Biliary Cirrhosis</td>
<td>None</td>
<td>Large</td>
<td>AMA</td>
<td>Prednisolone</td>
<td>Improvement</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2018</td>
<td>USA</td>
<td>Asha Jamal</td>
<td>63-year, Female</td>
<td>Abdominal pain; cough; fever; anorexia; chest pain; dyspnoea</td>
<td>Primary Biliary Cirrhosis</td>
<td>Sjogren’s syndrome</td>
<td>None</td>
<td>Moderate</td>
<td>AMA</td>
<td>Pericardiectomy with Pericardial window</td>
<td>Improvement</td>
</tr>
<tr>
<td>6</td>
<td>2020</td>
<td>India</td>
<td>Present Case</td>
<td>38-year, Female</td>
<td>Abdominal pain; cachexia at rest; Hypotension; abdominal pain; anorexia; fever, chest pain</td>
<td>Primary Biliary Cirrhosis</td>
<td>Anti-Phospholipid syndrome</td>
<td>None</td>
<td>Large</td>
<td>AMA ACA Anti-SSA</td>
<td>Pericardiectomy Mortality</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AMA = anti-mitochondrial antibody; ANA = anti-nuclear antibody; ACA = anti-cardiolipin antibody; Anti-SSA = Anti-SS antibody; VKA = vitamin-K antagonist.
Smith antibodies. She has low hemoglobin of 7.3 gm/dL, total leukocytes are borderline positive for anti-nuclear antibodies (ANA) and negative for anti-mitochondrial antibodies, anti-SSA/Anti-Ro, and anti-cardiolipin antibodies. She was diagnosed with chronic inflammation of the liver, which is associated with the deposition of immune complexes and immunological normalization ratio (INR) of 5.1, alkaline-phosphatase of 680 U/L, and serum creatinine of 1.5 mg/dL and C-reactive protein of 33.7 mg/dL. All routine viral markers (HIV/HBV/HCV) were negative, and her physical examination revealed a low volume pulse rate of 120/min, physical examination revealed a low volume pulse rate of 120/min, and she had cold extremities. She was moderately built, dyspnoeic, and alert. Her general physical examination revealed a low volume pulse rate of 120/min, blood pressure 80/56 mmHg, oxygen saturation of 78%, distended jugulars (6 cm), and dry oral cavity with multiple aphthous ulcers. Her left upper limb was less mobile, and she had bilateral pedal edema. Auscultation revealed bilateral crepitations in basal lung areas. Also, there were muffled heart sounds noted.

Her electrocardiogram showed a generalized low amplitude QRS pattern in all leads. Echocardiography revealed large PE with good left ventricular (LV) and right ventricular (RV) function with partial collapse of right atrium (RA) and RV (Fig.-1A and B). The pericardial thickening was also visible on transthoracic-echocardiography. Her high-resolution CT-scan of the chest showed large PE and pleural effusion (Fig.-2A and B).

Previously she tested positive for anti-mitochondrial antibodies (AMA), anti-SSA/Anti-Ro, and anti-cardiolipin antibodies. She was borderline positive for anti-nuclear antibodies (ANA) and negative for anti-dsDNA antibodies, anti-SSB/Anti-La antibodies, and anti-Sm/anti-RNP antibodies. She has low hemoglobin of 7.3 gm/dL, total leukocytes of 16,7 thousand/mm³, platelets of 110 thousand/mm³, serum albumin of 2.0 g/dL, total bilirubin of 10.2 mg/dL, international normalized ratio (INR) of 5.1, alkaline-phosphatase of 680 U/L, and serum creatinine of 1.5 mg/dL and C-reactive protein of 33.7 mg/dL. All routine viral markers (HIV/HBV/HCV) were negative, and her ultra-sonography of the abdomen showed cirrhosis of the liver with small nodules in the parenchyma.

Because of the high INR, coagulopathy was treated with multiple fresh frozen plasmas (FFP). The patient was also started on multiple inotropes along with BiPAP support for hypotension and low urine output. Five hours after admission her saturation with blood pressure dropped further, she was intubated and under the cover of FFP bedside pericardiocentesis was performed. Almost 1360ml of blood-stained pericardial fluid was tapped and the pigtail was kept in-situ for further tapping if required. Meanwhile, crystalloids were transfused along with 1 unit of packed red blood cells (PRBC). The patient continued to deteriorate and had bradycardia followed by cardiac arrest, she failed to respond to the resuscitation attempt.

**Discussion**

Pericarditis with large PE and its association with PBC is extremely rare. It is a diagnosis of exclusion. In our case, pericardial fluid tested negative for tuberculosis (Adenosine deaminase) or malignancy and fluid cytology showed plenty of RBCs, with very few lymphocytes. After tapping of fluid, there was no recollection of PE, also there were signs of pericardial thickening on echocardiography and CT-scan imaging. These findings point towards the possibility of pericarditis as extra-hepatic manifestations of PBC. Previously reported cases of PBC had possible auto-immune pericarditis as they were associated with auto-immune diseases.1-3 As mentioned in table -1, the previous studies on the pathophysiology of PBC involve chronic inflammation of the liver with extra-hepatic chronic inflammation of fibrosing alveolitis and nephritis.3,7,9 Therefore, it can be assumed that the pericarditis associated with PBC is inflammatory.4

Although typically hemorrhagic pericardial effusion is seen in multiple systemic disorders such as tuberculosis, neoplasms involving pericardium, collagen vascular disorders of 7.3rs – autoimmune etiology. The cause of pericardial disease in autoimmune disorders is associated with the deposition of immune complexes and inflammatory cells. It is fibrinous pericarditis, often recognized as "bread and butter" pericarditis due to its presence in which the pericardium appears opaque and granular, and macroscopically mimics two pieces of buttered bread compressed together but then set apart.10

When various online databases were searched, a total of 5 patients with PBC and PE were found. There was no detail about 1 patient's age and gender, whereas the remaining 5 patient's mean age was 52.8 ± 11.0 years. Medical management was preferred in 3 cases and all the 3 (100%) improved whereas the remaining 3 cases including our case pericardiocentesis with or without pericardial window formation were performed, out of which 2 (66.67%) improved and 1 patient (33.33%) had mortality. None of the cases provided the PBC staging information. There were 3 patients including our patient where PBC was associated with APLA syndrome and 2 of them had ACA positive.

Our patient was the youngest among the series and in advanced PBC. She was a transplant candidate and was being listed. Our case (a) was the youngest, (b) with advanced PBC, (c) had coagulopathy with high INR, and (d) was in early tamponade at presentation. As a result, our patient's overall outcome was detrimental.

**Conclusion**

The association of pericarditis and PBC needs careful consideration as our case series emphasizes the importance of early diagnosis and treatment of PBC patients with cardiac complications to reduce patient morbidity and mortality.

**Consent from patient/Patient’s attender**

Yes.

**Financial and non-financial relations**

None.

**Icmje criteria for authorship**

Kartik Pandurang Jadhav: Design of the work, acquisition, analysis, interpretation of data, drafting of work, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy.

Pankaj V. Jariwala: Conception of the work, revising it critically for important intellectual content, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Hari Kishan Boorugu: Conception of the work, revising it critically for important intellectual content, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Srijan Kumar Dasym: Conception of the work, revising it critically for important intellectual content, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Avinash Bai: Conception of the work, revising it critically for important intellectual content, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Declaration of competing interest

None.

References


