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Case Report

Amyloid Gallbladder as an Initial Presentation of Multiple Myeloma (MM): A Rare Presentation

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Abstract

We present a rare case of Amyloid (AL) deposition in the gallbladder as an initial presentation of MM. The patient was a 92-year-old female who was admitted to the hospital with right upper quadrant pain. Computed Tomography (CT) abdomen and pelvis showed stone in the distal common bile duct and mildly distended gallbladder with wall thickening, she underwent ERCP for stone extraction followed by cholecystectomy. A postoperative histological examination revealed congo red stain positive for amyloidosis, positive apple-green birefringence under polarized light, and was typed as AL. Further workup, showed a lytic bone lesion on the skeletal survey and bone marrow core biopsy showed hypercellular bone marrow with increased plasma cells confirming the diagnosis of MM.

Background

The amyloidosis are a rare and heterogeneous group of disorders that are characterized by the deposition of abnormally folded proteins in tissues. Amyloid deposits are formed from globular, soluble proteins, which undergo misfolding and, subsequently, aggregate into insoluble fibrils, leading to progressive organ damage [1]. There are several major forms of amyloidosis that may result in a wide range of clinical manifestation depending on the type, location, and amount of deposition. The current classification of amyloid in medical practice is based on the amyloid protein type. To date, there are about 36 proteins that have been identified as being amyloidogenic in humans. However, the major forms include light chain (AL or primary), Amyloid A (AA or secondary), ALECT2 (Leucocyte chemotactic factor 2), hereditary amyloidosis, amyloidosis of aging, and iatrogenic amyloidosis. Depending on the type of amyloidosis, amyloid deposits can be found in various organs such as kidneys, heart, the nervous system, the hepatosplenic, and the intestinal tract. Exclusively localized amyloid deposits may be associated with several endocrine organs or tumors, where they are derived from the respective hormones or local protein precursors. Localized deposits of amyloid may also involve the pulmonary and lower urinary tracts [2]. Deposits of amyloid are most frequently of the AL type, derived from Mucosa-Associated Lymphoid Tissue (MALT) lymphoma [3]. Localization to the gallbladder is uncommon [4]. AL amyloid is caused by plasma cell dyscrasia.

Although 10-15% of patients with Multiple Myeloma (MM) have coexisting primary amyloidosis, it is unusual for patients with primary amyloidosis to progress to MM later [5]. We describe a rare case of gallbladder amyloidosis as an initial presentation of MM.

Case presentation

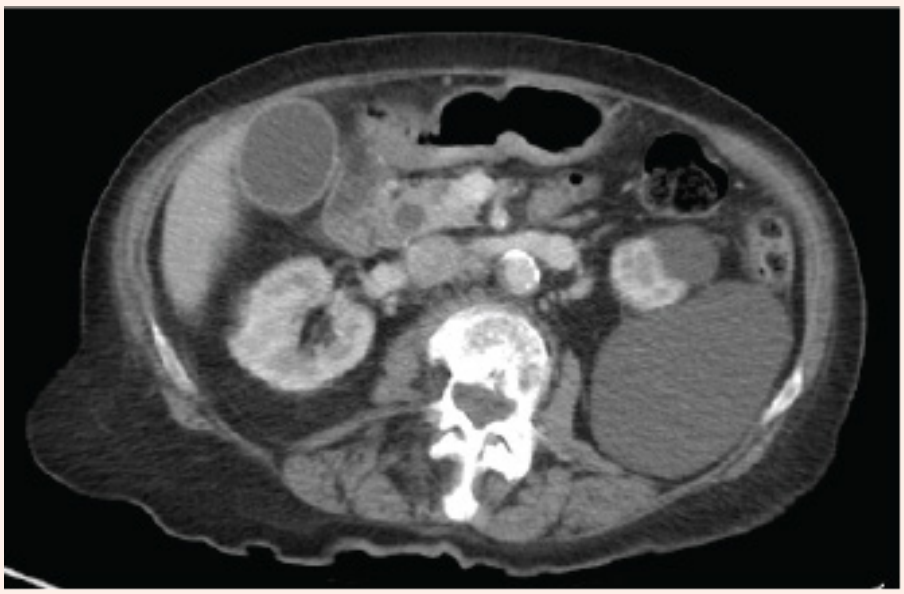

Image 1: CT abdomen and pelvis showing stone in distal common bile duct and mildly distended gallbladder with wall thickening.

A 92-year-old female patient with a medical history significant for coronary artery disease, hypertension, atrial fibrillation, and severe aortic stenosis presented to the emergency department for evaluation for Right Upper Quadrant (RUQ) pain and jaundice. The patient had ongoing intermittent non-radiating RUQ pain for the past two months before presentation, which worsened with eating and was associated with nausea and vomiting. She also noticed jaundice and dark-colored urine one week prior to the presentation. On physical examination, she had icteric sclera and RUQ pain with positive murphy's sign. Blood tests noted hemoglobin of 9.5 g/dL with normal MCV and low red blood cell count, creatinine of 1.4 with an estimated glomerular filtration rate of 34, elevated transaminases with Aspartate Amino Transferase (AST) of 256, Alanine Aminotransferase (ALT) of 217, alkaline phosphatase of 1179 and hyperbilirubinemia of 10.4 with direct bilirubin of 9.3. Lipase and serum calcium levels were within the normal range. Urinalysis showed no proteinuria, bacteriuria, or pyuria. Electrocardiogram showed Q waves in inferior leads but no ST-T wave changes. CT abdomen and pelvis showed stone in distal common bile duct and mildly distended gallbladder with wall thickening (Image 1).

She was evaluated by a gastroenterologist who performed ERCP with incomplete common bile duct stone extraction, papillotomy and stent placement. The surgery team evaluated the patient and performed laparoscopic cholecystectomy. Gross examination of the gallbladder showed intact gallbladder measuring 8.2 x 3 x 1.7 centimeter (cm), external aspect was pink tan, no gallstones identified, the mucosal surface was pink velvety and wall thickness ranged from 0.2 to 0.4 cm. Pathology results of the gallbladder were positive for acalculous acute on chronic cholecystitis and congo red stain positive for amyloidosis (Images 2, 3a, & 3b). The sample showed apple-green birefringence under polarized light and was typed as AL.

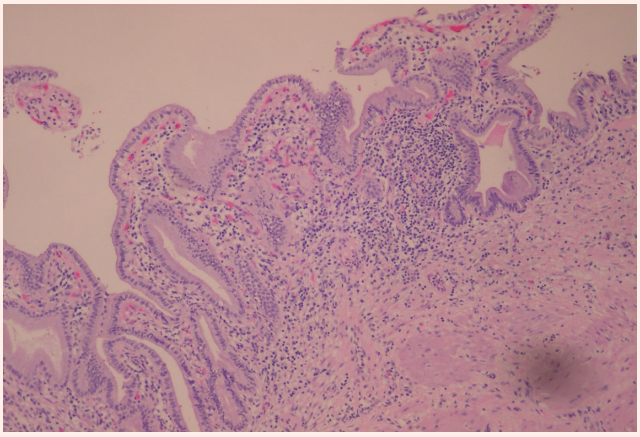

Image 2: Pathology results showing acalculous acute on chronic cholecystitis.

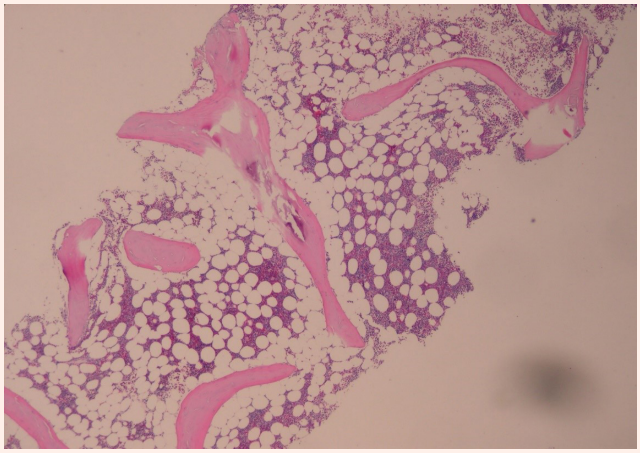

Image 3a: Core biopsy of bone marrow showing hypercellular bone marrow with increased plasma cells (40 X magnification).

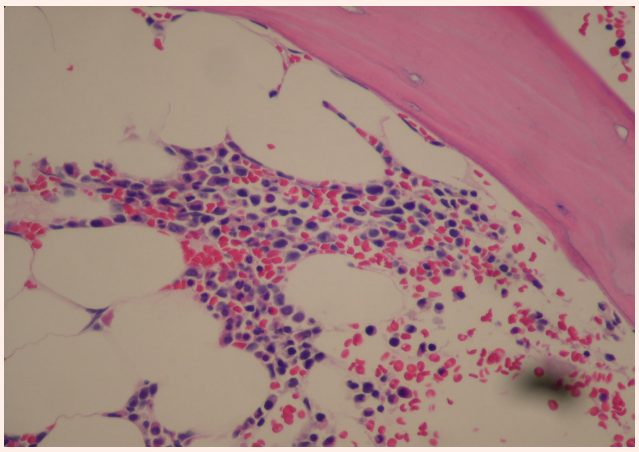

Image 3b: Core biopsy of bone marrow showing hypercellular bone marrow with increased plasma cells (400 X magnification).

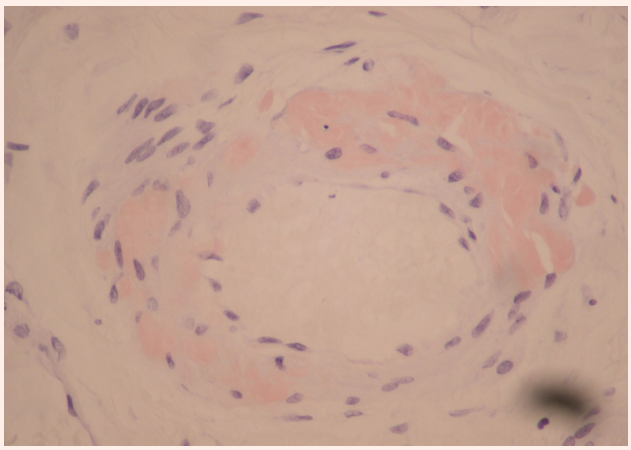

Image 4: Pathology results showing congo red stain positive for amyloidosis.

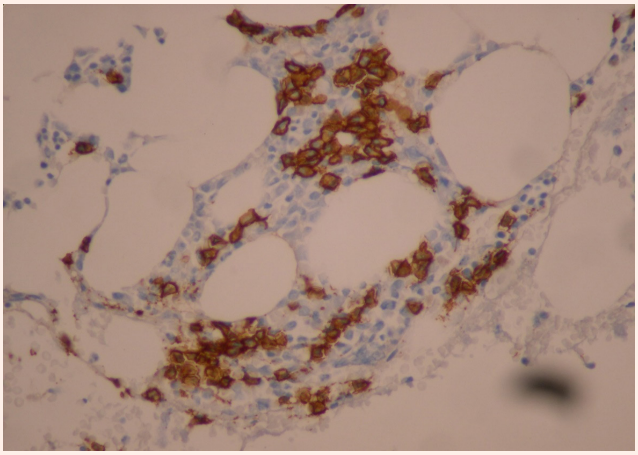

Image 5: Bone marrow immunohistochemical stain positive for CD 138.

She was referred to an outpatient oncologist for gallbladder amyloidosis workup. Her bone marrow biopsy showed hypercellular bone marrow with increased plasma cells (13%) (Image 4) and immunohistochemical stain positive for CD 138 (Image 5), suggestive of MM. The radiographic bone survey showed multiple lytic lesions within the

bony calvarium (Skull: Image 6).

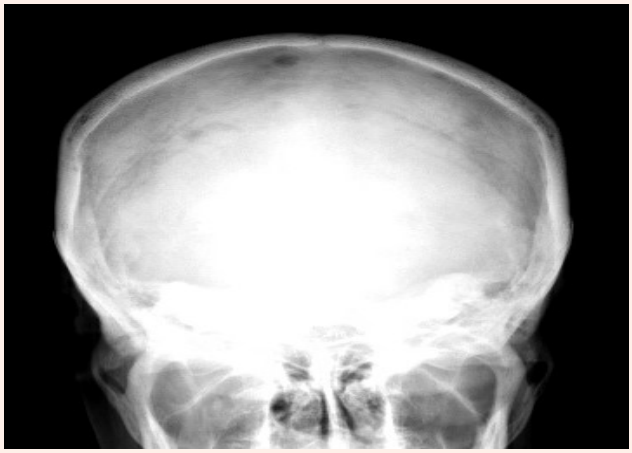

Image 6: Radiographic image of skull showing lytic lesions.

She met the diagnostic criteria for MM and her Eastern Cooperative Oncology Group (ECOG) performance score was 1. She is currently being treated with CyBORD (Bortezomib, cyclophosphamide, dexamethasone) regimen in an outpatient setting.

Discussion

Amyloidosis can either be systemic or localized. Localized amyloid deposition can be isolated to a single organ such as the kidney, heart, nervous system, liver, intestinal tract, or peripheral nerve involvement. Localization of amyloidosis confined to the gallbladder is extremely rare and appears to be present equally in both primary and secondary forms [3]. In our case, we did not see typical amyloid-related signs and symptoms of other organs. Gallbladder amyloidosis typically presents as either acute cholecystitis, chronic cholecystitis, anicteric cholestasis, jaundice, or incidental gallbladder finding as a part of investigation for chronic intermittent abdominal pain thought to be due to hepatobiliary origin. Most cases of amyloid gallbladder present as acalculous cholecystitis. Matsuda et al, hypothesized that the pathophysiology of acalculous cystitis patients includes the following: 1) amyloid deposition around the small vascular wall in patients with acalculous cholecystitis can rapidly lead to ischemic changes, leading to necrotizing cholecystitis; 2) amyloid deposition in the gallbladder wall that is blocking the normal contraction of the gallbladder can lead to bile stasis, leading to direct damage of the gallbladder wall epithelium. These pathophysiological conditions can occur concomitantly or separately and lead to the development of acalculous cholecystitis in cases with amyloid deposition on the gallbladder wall [6]. Our patient had a histopathological diagnosis of acalculous cholecystitis but presented with obstructive jaundice. It should be noted that there has been only one case report of gallstones associated with amyloidosis [7].

A concurrent diagnosis of AL amyloidosis is made at presentation or sometime during the myeloma in 10–15% of patients [5]. This diagnosis requires fulfilling diagnostic criteria for both conditions including histological confirmation of amyloid fibrils deposition and other myeloma-specific criteria such as hypercalcemia, lytic bone lesions, and anemia. The mere presence of bone marrow plasmocytosis is an insufficient criterion to establish the diagnosis of multiple myeloma as 18% of AL amyloidosis patients are reported to have more than 20% light chain restricted plasma cells in the bone marrow without any other myeloma-specific features [5]. In our case, we confirmed MM by the presence of increased plasma cells in the bone marrow (13%), CD 138 positivity, and lytic lesions noted in the skull.

Conclusion

This is a rare case of obstructive jaundice with acalculous cholecystitis due to gallbladder Amyloidosis (AL) as an initial presentation of MM. The rarity, variable spectrum of presentation, and its association with multiple myeloma can often result in missed or delayed diagnosis of MM [8].

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