Acute cholecystitis - an isolated unusual presentation of thrombotic microangiopathy of gall bladder due to antiphospholipid syndrome with lupus positivity detected by [^{99m}Tc]Tc-mebrofenin scan

Case Report

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ABSTRACT

Occurrence of small-vessel occlusions (thrombotic microangiopathy, TMA) in association with antiphospholipid antibodies (aPL ab) has been documented. But isolated involvement of gall bladder due to TMA in secondary aPLS (antiphospholipid syndrome) in post-partum status has been unreported. aPL and systemic lupus erythematosus (SLE) are two closely related diseases that not only share lupus susceptibility genes but can also produce thrombosis. Here we present a young lady, recently delivered with SLE experiencing moderate to severe right abdominal pain and occasional vomiting. A hepatobiliary iminodiacetic acid (HIDA) scan revealed non visualization of gall bladder (GB) confirming the diagnosis of acute acalculous cholecystitis (AAC). Investigations revealed high titre of anti-β2 glycoprotein I (β2GPI) IgG and anti-Cardiolipin (aCL) IgG antibodies confirming aPL syndrome. Antinuclear antibody, double-strand dsDNA was found to be positive confirming SLE. Open cholecystectomy was performed and histology revealed AAC, vasculitis with small vessel ischemia of gallbladder. GB non visualization on HIDA scan (ACC) due to solitary thrombotic microangiopathy of GB is being highlighted in this case of active SLE and secondary aPLS. Early diagnosis is mandatory to avoid repetitive thrombotic occlusions in active cases of SLE with aPLS.

Key words: Thrombotic microangiopathy; Gall bladder; Mebrofenin scan; Acute cholecystitis; Antiphospholipid syndrome

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INTRODUCTION

Acute acalculous cholecystitis (AAC) is a well-recognized complication of many acute diseases [1] and gallbladder ischemia has major implication in its pathogenesis [2]. Antiphospholipid syndrome (aPLS) and SLE are entities that can produce single or multiple thrombotic events. aPLS is characterized clinically by recurrent venous and/or arterial thromboembolic events, or can occur in the background of pregnancy [3]. Presence of antibodies against β2-glycoprotein I (aβ2GPI) and cardiolipin (aCL), together with lupus anticoagulant (LAC) is a prerequisite [4]. For the definitive diagnosis of aPLS, at least one clinical criterion (thrombosis or pregnancy) is mandatory along with association of one laboratory criterion (LAC, aCL antibody or aβ2GPI antibody present on two or more occasions, at least 12 weeks apart, and thrombosis should be confirmed by objective validated criteria as per revised criteria) [5] [^{99m}Tc]Tc-mebrofenin imaging confirmed AAC.

CASE PRESENTATION

A 29-year-old lady non diabetic, primigravida, 65 days postpartum after completing full term pregnancy, presented with intermittent high grade fever for 1 week with upper abdominal pain, nausea with occasional vomiting. The patient had no history of jaundice, or melena. Patient was conscious, oriented and febrile (102 degree Fahrenheit). Pallor was present with no icterus or lymphadenopathy. Pulse rate 102 /min, blood pressure was 120/80mm Hg (right arm, sitting). Abdomen and other systemic examination was noncontributory.

Hemoglobin was 8.6 gm/dl with no thrombocytopenia, high Erythrocyte sedimentation rate (68 mmHg) and CRP levels (106 mg/L**)** was noted. Due to high clinical suspicion, HIDA scan was initially performed (Figure 1) and findings were consistent with diagnosis of AAC. USG (ultrasonogram) abdomen and CT (Computed Tomography) abdomen were also undertaken at a later date for reconfirmation prior to surgery (Figure 2). Due to the past history of SLE (fatigue, malaise, rash over neck and enlarged neck nodes) 5 years ago, antinuclear antibody (> 1:80 dilution by indirect immunofluorescence on HEp-2 cells with speckled pattern), double-strand ds DNA was also suggested and performed (> 35 IU/ml, more than 15 is abnormal). dsDNA, in high titer was also documented which is nearly specific to lupus as in this case. High titre of anti-β2 glycoprotein I (β2GPI), IgG (109 U/mL) and anti-Cardiolipin (aCL) IgG (> 60 U/mL) antibodies; low titre of anti-β2GPI and anti-aCL IgM (23 U/mL and 21 U/mL, respectively), confirmed the diagnosis of aPLS. Open cholecystectomy was performed and histology revealed AAC, vasculitis with small vessel ischemia of GB (Figure 3). Post-operative period was uneventful. Patient was started on steroids 15 mg once daily orally along with low dose aspirin 75mg daily as part of thromboprotective medications.

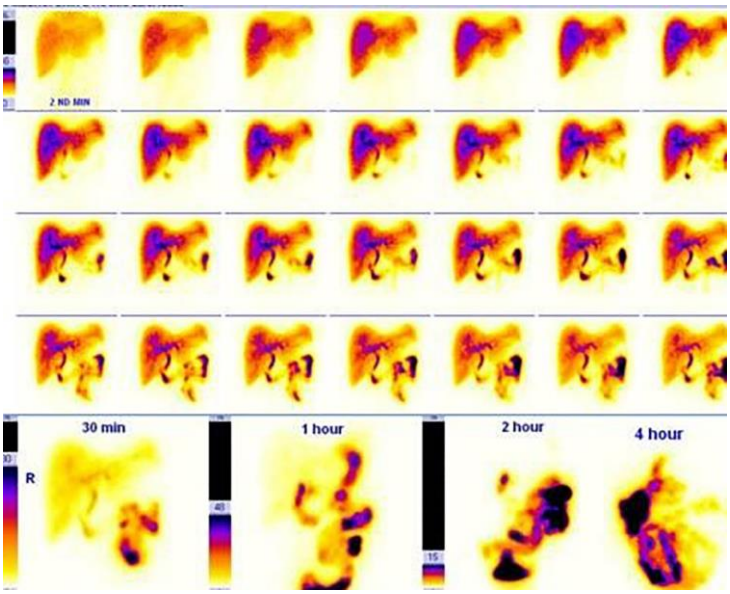

Fig 1. Above: 15 mCi of [^{99m}Tc]Tc-mebrofenin was injected intravenously. Dynamic images of anterior abdomen (1 min / frame for 30 min) were acquired. Prompt and good extraction of tracer seen by hepatocytes. Gall bladder is not visualized by end of dynamic study. Good progression of tracer noted into intestinal loops. Below: Serial static and delayed abdominal images show non visualization of gall bladder even at 4 hours. Findings suggest acute acalculous cholecystitis.

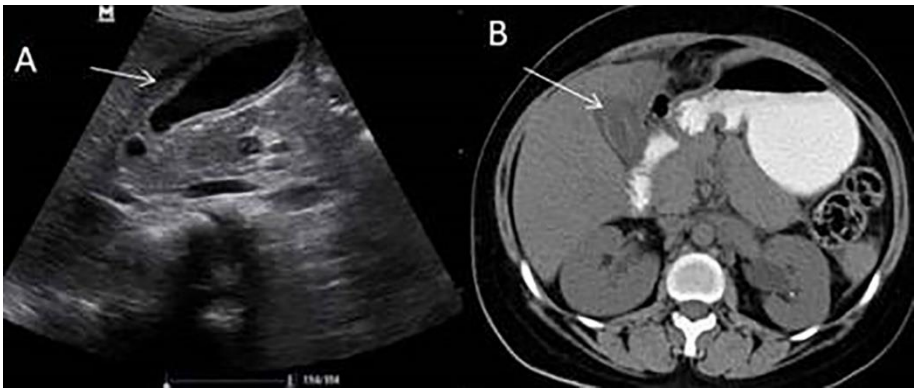

Fig 2. (A) Ultrasound imaging of the abdomen: shows diffuse wall thickening (9 mm) of gall bladder with septation. No calculi. Gall bladder (GB) is not abnormally distended. There is minimal pericholecystic collection. Features suggest acute acalculous cholecystitis. (B) Non contrast CT of liver support acute cholecystitis findings [no GB calculus, GB wall thickening of 9mm, subserosal halo sign (intramural lucency caused by edema) and pericholecystitic fluid collection, denoted by arrow.

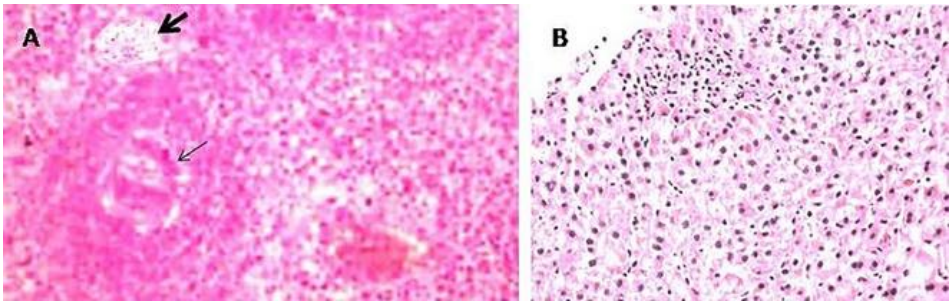

Fig 3. (A) Section showing vasculitis with perivascular inflammation (thin arrow) and thrombosis due to small vessel ischemia of gall bladder (GB) with fibrinoid necrosis (thick arrow), and neutrophil predominate infiltration. (B) Histological section of GB wall (slice thickness of 100 micrometers) reveals infiltration of all layers of the gallbladder wall with inflammatory cells.

DISCUSSION

HIDA scintigraphy is one of the commonly performed scans for the identification of acute cholecystitis. It provides both functional information of liver and bile ducts. It also provides insight on cystic duct obstruction status. [^{99m}Tc]Tc-mebrofenin is the ideal radiotracer which has better hepatic extraction, 98% and less renal excretion, 1%. The higher extraction of [^{99m}Tc]Tc-mebrofenin is also preferable in patients with hepatic insufficiency.

aPLS is an acquired autoimmune disorder that manifests clinically as recurrent venous or arterial thrombosis and/or fetal loss; if not managed early, mortality and morbidity can be high. aPLS can be primary when there is no evidence of autoimmune disease, or it can be secondary to autoimmune processes like SLE in 40% of the cases [6]. There is a strong association between the presence of aPL ab and multiorgan infarction, and ischemic stroke [7]. Although patients with SLE may possess coexisting aPL antibodies (ab), not all patients with aPL develop aPL syndrome [7]. Patients with coagulation factor mutations, HLA-DR7, DR4, infections (borrelia burgdorferi, treponema, HIV, and leptospira [2]), and drugs (chlorpromazine, procainamide, quinidine, and phenytoin), can induce APL ab production. Kidney, skin, cardiovascular and nervous systems are commonly affected. Solitary GB ischemia due to TMA producing AAC is extremely rare. Obstetrical complications in aPLS occur only in 9.7% patients [8]. Our patient with secondary aPLS [positive β2GPI – IgG, aCL - IgG antibodies], lupus positivity (dsDNA in high titer), small vessel ischemia of GB with no other known vascular occlusion demonstrated safe delivery and experienced no obstetrical complications. Difficulties in the diagnosis of aPLS in SLE patients are the overlapping of similar manifestations [9, 10].

CONCLUSION

Imaging and antibodies profile have helped in confirming the coexistence of various pathologies manifesting as small vessel ischemia of GB in this case, needing urgent surgical intervention. Early diagnosis is mandatory to avoid repetitive thrombotic occlusions in active cases of SLE with aPLS.

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