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EXCELLENT OUTCOME OF AUTOIMMUNE HEPATITIS PRESENTING WITH AN ACUTE ACALCULOUS CHOLECYSTITIS

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Abstract:

Inflammation and dyskinesia of the gallbladder without evidence of calculi is known as acute acalculous cholecystitis (AAC) and can lead to high complications or death. AAC due to autoimmune hepatitis (AIH) is very rare. Options of therapy can be chosen according to the condition of the patient and the underlying cause of AAC. Early diagnosis and intervention have a positive effect on clinical outcome. Here, we presented an adult female patient diagnosed with AIH complicated with AAC. Her symptoms improved following the successful combination therapy of corticosteroids and immunosuppressive agents for AIH without any complications and may even be adequate for AAC by avoiding surgical interventions.

Keywords: *Acalculous cholecystitis, Autoimmune hepatitis, Corticosteroids, Immunosuppressive agents.*

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INTRODUCTION:

Acute acalculous cholecystitis (AAC) is defined as an acute inflammation of the gallbladder with no evidence of gallstones. [1] It accounts for 2-15% of acute cholecystitis. It has multifactorial pathogenesis and is indistinguishable from acute calculous cholecysitis. [2] AAC is observed in association with acute hepatitis. [3] During the course of acute hepatitis, gallbladder wall edema and slowing of bile clearance may lead to the formation of bile sludge and thickening of the gallbladder wall. [4] Wang et al. [5] stated that autoimmune diseases are identified as one of the trigger factors for AAC. Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease of unknown etiology that occurs at all ages and predominantly in young women with sex ratio of 3.6:1. Mostly, its prognosis is good and determined by response to corticosteroid therapy. [6] The diagnosis of AIH is based on symptoms and signs at clinical presentation, biochemical tests, and histology findings. However, the co-existence of AAC and autoimmune hepatitis has so far rarely been reported. Although surgical intervention for ACC including cholecystectomy remains as standard treatment, non-surgical management with high dose of corticosteroid therapy has successfully improved symptoms of AAC-associated in SLE patient with Sjogren's syndrome. [7] Here, our study reports the excellent outcome observed in a case of AIH presented with AAC as a complication.

CASE REPORT:

A 46-year old female was admitted at King Fahd Hospital of the University (KFHU), Dammam, Saudi Arabia due to sudden right upper quadrant pain associated with nausea, anorexia and generalized fatigue. Pain increased over the last 10 days with the radiation to right hypochondriac area and to the upper back. It was aggravated by meal. She had no history of similar previous attack, fever, itching, joint pain, erythema, or swelling. In addition, no past medical illness such as connective tissue diseases or surgical interventions; and no family history of gallbladder stones were noted. She also had a history of taking oral contraceptive pills for an unknown duration. On clinical examination at the time of admission, the patient was conscious, alert and oriented. Vital signs were recorded as body temperature (37°C), pulse rate (90/min), respiratory rate (18/min) and blood pressure (115/80 mmHg). At the time of admission, the patient presented with jaundice for the duration of one day and no medications were taken. On abdominal examination, the abdomen was soft and lax with mild right hypochondriac tenderness and negative murphy's sign. Rest of the physical examination were unremarkable.

Further, laboratory tests were done and viral hepatitis profile was found as negative. Results of laboratory evaluation are shown in Table 1. Liver and portal system Doppler ultrasound showed gallbladder wall thickness of 6 mm in absence of stone suggestive of AAC, otherwise unremarkable findings were found (Figure 1). Magnetic resonant imaging (MRI) showed diffuse peri-portal edema with no biliary dilatation or stone (Figure 2). Liver biopsy was done at 10^{th} day of her admission and specimens were sent for pathological examination. Further, it revealed that the portal tract was infiltrated by plasma cells associated with interface hepatitis which indicates grade three of AIH (Figure 3).

Table 1. Laboratory results

Tests	**At admission**	**4 weeks after therapy**
White blood cell (K\U)	5.7	7.2
Hemoglobin (g\dl)	8.4	10.7
Platelet (k\ui)	149	275
Total bilirubin (mg\dl)	6.5	0.5
Direct bilirubin (mg\dl)	5.8	0.3
Total protein (g\dl)	9.3	7.5
Albumin (g\dl)	2.4	2.8
GGTP (u\l)	161	50
SGPT	302	41
SGOT	340	25
Alkaline phosphatase u\l)	118	98
LDH (u\l)	254	291
Anti-smooth muscle antibody	Negative	Negative
DS DNA	Negative	Negative
ANA	Positive > 1280	Not applicable

GGTP –gamma-glutamyl transpeptidase; SGOT- serum glutamic-oxaloacetic transaminase. SGPT- Serum glutamic pyruvic transaminase; LDH – lactic acid dehydrogenase; DS DNA – double-stranded deoxyribo nucleic acid; ANA – antinuclear antibody

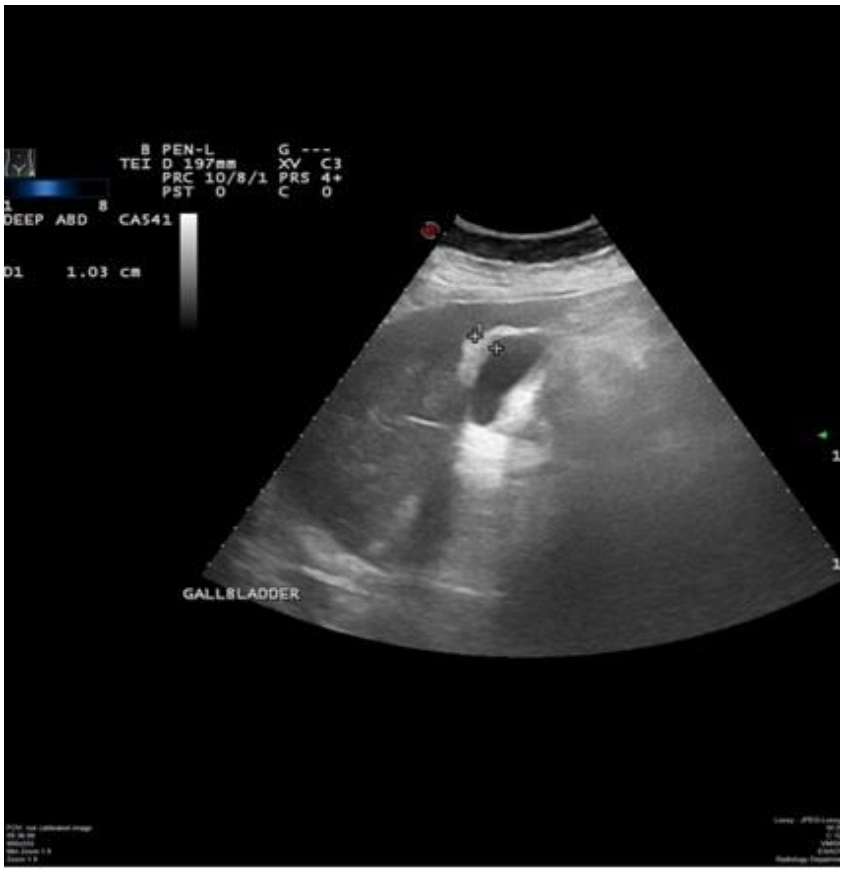

Figure 1. Abdominal ultrasound showing the thickened gall bladder of >4mm (6mm)

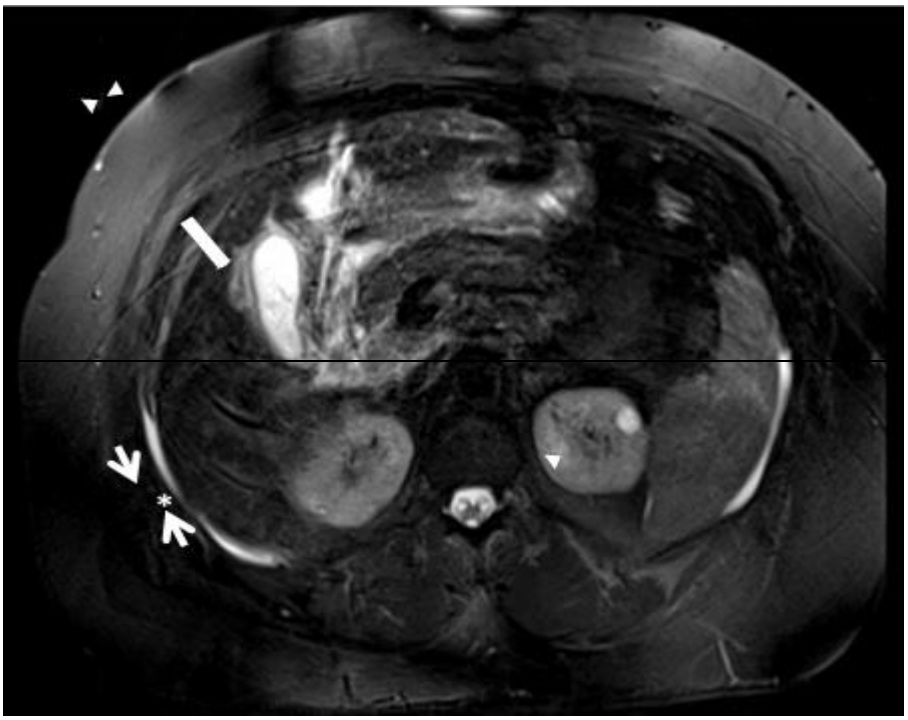

Figure 2. MRI SSFP image showing pericholecystic fluid collection

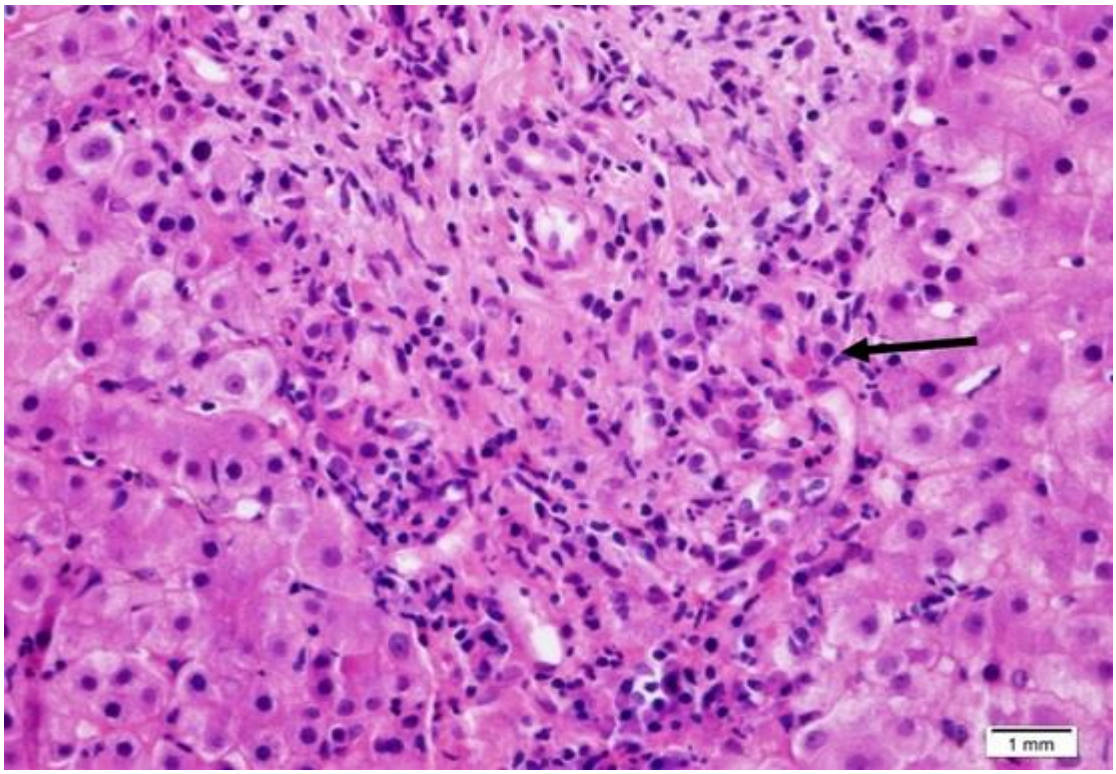

Figure 3. High power view of the portal tract showing moderate interface hepatitis and scattered plasma cells (Arrow) and severe focal lobular inflammation. Findings of this grade of chronic hepatitis and stage of fibrosis are compatible with autoimmune hepatitis (Hematoxylin and eosin, original magnificationx400)

From the date of admission, the patient was treated with supportive therapy of intravenous (IV) fluid and oral pantoprazole 40 mg once daily and continued till the patient discharge. Her response to supportive therapy was good. No jaundice was observed after 9 days of her admission. On 11th day of her admission, the diagnosis of AIH was confirmed and the patient was administered with methylprednisolone 40 mg (I.V.); and azathioprine 50 mg (oral) once daily for 3 days. During the follow up, her symptoms of abdominal pain, jaundice and nausea have improved gradually. Laboratory investigations showed normal results. On day 14th, the patient was discharged with good general condition. She was instructed to take prednisolone 40 mg once daily and azathioprine 100 mg (P.O) once daily for 4 weeks. Further, a medical clinic appointment for her follow up was given. After 4 weeks of therapy, the patients' symptoms improved, icterus disappeared, and liver function test normalized.

DISCUSSION:

AAC is defined as an acute inflammation of the gallbladder wall without evidence of stones and surgeons typically label it as a biliary dyskinesia.[1] The pathophysiology of AAC is multifactorial and likely results from bile stasis or ischemia. Bile stasis can result from fasting, obstruction, postsurgical irritation or ileus, which in turn lead to bile inspissation that is directly toxic to the gallbladder epithelium.[1,8,9] Here, our case presented with signs, symptoms, and radiological findings, which are consistent with AAC and AIH. Previous studies have revealed the association between AAC and autoimmune disease like SLE.[7,10] However, the co-existence of AAC and AIH is seldom reported.

The two major radiological diagnostic criteria of AAC include gallbladder wall thickness of >4 mm and pericholecystic edema.[1] These diagnostic criteria for ACC are well established in our case as the abdominal ultrasound revealed the thickened gallbladder wall of 6 mm, pericholecystic edema and the absence of ascites and no calculi or sludge. Clinically, the patient also had right hypochondriac pain radiating to the back and increased after meal.

AIH is an inflammation of the liver cells of unclear etiology. The diagnosis of AIH is based on clinical presentation, biochemical tests, and liver biopsy findings of prominent interface hepatitis and varying lobular cell damage associated with inflammation. In accord with clinical guidelines of the American

Association for the Study of Liver Diseases,[8] our case was diagnosed with AIH as laboratory results observed with negative serology for hepatitis, high level of ANA > 80 (>1280); and histopathological findings reported with interface hepatitis without biliary lesions. Finally, our case was confirmed with AIH complicated with AAC.

Shin et al.[7] had reported a successful medical treatment of high dose of corticosteroid therapy in patients with AAC associated with high SLE disease. However, our case was diagnosed as AIH associated with AAC. Here, the primary goal of treatment is to limit the destructive effects of the immune system on hepatocytes. For the last few decades, corticosteroids alone or combined with other immunosuppressive agents as azathioprine have been considered as the first line of therapy for AIH.[11,12] If AIH left alone without therapy, the outcome is fatal. Our patient was treated with combination therapy of corticosteroids and immunosuppressive agents in the form of prednisolone and azathioprine both during hospitalization and 4 weeks after discharge. The clinical outcome of this combination therapy is observed as excellent in our case without any complications and especially, surgical interventions for AAC was avoided.

CONCLUSIONS:

During the course of AIH, functional and structural changes can occur in gallbladder. As a result, our case presented with AAC as a benign complication of AIH. The combination therapy of corticosteroids and immunosuppressive agents for AIH may be adequate and effective for AAC by avoiding an invasive surgical intervention for AAC.

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