Acalculous cholecystitis: A rare manifestation of acute abdomen in lupus

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Abstract

Lupus is an autoimmune disease of unknown aetiology with varied manifestations. There is a significant variation in the clinical presentation and severity of Gastro-intestinal (GI) disorders. The low index of suspicion often leads to delays in diagnosis and the wrong choice of management. Acute Acalculous Cholecystitis (AAC) is just one of the GI manifestations of lupus and is associated with high morbidity and mortality. There are few case reports of AAC in written literature. We introduce a 31-year-old black female who presented with abdominal pain that turned out to be ACC in a patient known to have lupus. She was successfully managed conservatively with steroids and antibiotics and did not require surgical intervention.

Key words: Systemic lupus erythematosus, Acute a calculous cholecystitis, corticosteroids, Kenya

Introduction

Acalculous cholecystitis is cholecystitis without evidence of gallstones or cystic duct obstruction[1]. It is usually associated with more severe morbidity and higher mortality rates than calculous cholecystitis[1]. There are several risk factors for developing AAC. Lupus accounts for 10% of cases of acute cholecystitis and is associated with high morbidity and mortality[2]. This partly may go unrecognized as a cause of abdominal pain. Abdominal pain in lupus can be a challenge due to the various possible aetiologies ranging from the disease to drugs used to treat the disease

Case report

A 30-year-old known lupus patient on hydroxychloroquine 200mg once a day and deflazacort 6mg referral from a peripheral facility with a three-day history of right upper quadrant pain, fever, and vomiting. This was associated with malaise, nausea, and poor appetite. She was diagnosed four years prior with lupus after presenting with fever, arthralgia, and symptoms of anaemia. At diagnosis, ANA and DsDNA were positive. On examination at admission, she had a body temperature of 38.5^{o}C, the pulse rate of 110/min, the respiration rate of 30/min, and the blood pressure of 130/90 mm Hg. She was pale and severely dehydrated. Physical examination revealed tenderness on the right upper quadrant of her abdomen and a positive Murphy's sign. Initial laboratory tests showed elevated ESR 50 mm/hr, CRP 222 mg/L, and WBC 13900mm^3. The haemoglobin and platelets were reduced by 8.5g/dL and 76,000/mm^3, respectively. The creatinine 109.2µmol/L and urea 7.7Mmol/l. the liver function tests had raised GGT and ALP at 355U/L and 150.3U/L, respectively, with a normal ALT and AST. The urinalysis had blood 1+, protein 1+. The complement levels were reduced with C3 at 70mg/dl and C4 at 5.22mg/dl. The chest X-ray was reported as normal. The CT scan abdomen demonstrated gallbladder wall thickening with pericholecystic edema without any evidence of stone or biliary sludge. Intravenous steroid pulse therapy (1g/day for three days) was done concurrently with ceftriaxone and metronidazole. The patient responded dramatically to treatment within 3-4 days. She did not undergo surgical intervention due to the excellent response to the steroids and antibiotics. She was discharged after ten days on steroid taper dose, hydroxychloroquine and azathioprine for review at the rheumatology and surgical clinic.

Discussion

The Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease of unknown cause that presents as a multisystemic disease characterized by the presence of immunological abnormalities antibodies to nuclear and cytoplasmic[3]. This elaborate heterogeneous clinical presentation and pathogenesis of lupus can pose a diagnostic challenge for the

clinician. Several diagnostic criteria have been proposed from ACR 1997, then Systemic Lupus International Collaborating Clinics 2012 criteria and now 2019 EULAR/ACR classification criteria for SLE[4]. A score of >10 is diagnostic for lupus based on the 2019 EULAR/ACR classification criteria for SLE. A validation study on the three criteria revealed new criteria had an improved sensitivity of 96.1% and specificity of 93.4%, compared with 82.8% sensitivity and 93.4% specificity of the ACR 1997 and 96.7% sensitivity and 83.7% specificity of the Systemic Lupus International Collaborating Clinics 2012 criteria[4]. The prevalence of SLE varies by gender, race, and region. Its predominantly found in women with rates highest in black ladies then Asian and white race. Despite the highest rates in blacks, the paucity of data on the disease in Africa[5]. The diagnosis of lupus in Africa is still a challenge, mainly due to underdiagnosis. Reasons include the high prevalence of tropical diseases, low numbers of rheumatologists, low index of suspicion, inadequate infrastructure, and access to health[5]. Symptoms of lupus range from mild skin and joint presentations to severe life-threatening conditions such as renal and haematologic[3]. A review of lupus literature by Genga *et al*[5] revealed that the most common presentations in Africa were joint and skin.

Gastrointestinal manifestations are common in lupus, with up to 40% of patients experiencing them during their lifetime[6,7]. Examples include oral ulcers, lupus hepatitis, intestinal pseudo-obstruction, lupus enterocolitis, amongst others[6,7]. An acute abdomen usually poses diagnostic challenges in lupus. The potential causes of acute abdomen in lupus are spontaneous peritonitis pancreatitis and acalculous cholecystitis. Al-Hakeem *et al*[8] reported that 15% of patients with SLE presented with abdominal pain, which was attributed to cholecystitis in a review on 88 lupus patients done over 15 years. Acalculous cholecystitis accounts for 10% of all cases of acute cholecystitis and is characterized by necro-inflammatory pathogenesis affecting the gall bladder. It has multifactorial aetiologies, one of which is lupus and is associated with high morbidity and mortality. There are a few case reports of acalculous cholecystitis in the setting of lupus[9,10]. The pathogenesis of acalculous cholecystitis revolves around local inflammatory response that results from gallbladder stasis and ischemia[9-11]. In the setting of lupus, the cause is mainly attributed to vasculitis, thrombosis, or as part of an adverse reaction to the drugs used for treatment. Vasculitis can either directly affect the gall bladder or involve the mesenteric vein. When vasculitis directly affects the gall bladder, it leads to acute arteritis with periarterial fibrosis. Vasculitis can rarely cause mesenteric inflammatory veno-occlusive disease affecting mesenteric vein and its branches sparing the arterial vasculature[12]. The thrombotic disease is commonly observed in the background of antiphospholipid antibodies, presenting as thrombi in gall bladder veins with no evidence of vasculitis[12]. We suspect the patient had a vasculitis as clinical and radiology evaluations did not reveal evidence of thrombosis. Due to financial constraints, the antiphospholipid antibodies screening tests were not done.

Critically ill patients presenting with sepsis and acute abdomen diagnosis of a calculous cholecystitis should be suspected. Diagnostic evaluation should include haemograms, inflammatory markers, blood cultures, renal tests, liver tests, and pancreatic enzymes. Our patient had leukocytosis and elevated CRP suggestive of sepsis. Liver function tests suggested an obstructive picture that our patient had. Differentials include pneumonia and urosepsis. The urinalysis ruled out urosepsis, and a chest X-ray was reported as normal. Abdominal imaging includes either ultrasonography or contrast-enhanced abdominal Computed Tomography (CT) scan not only to the diagnosis of suspected acalculous cholecystitis but to rule out other potential causes of acute abdomen. Ultrasound findings have a sensitivity ranging from 30-92% with a specificity of 89 to 100%[13,14]. Sonographic Murphy's sign is indicative of gallbladder inflammation but very user-dependent. Gall bladder thickening has a high sensitivity but low specificity[13,14]. False positives mimicking gall bladder thickening include ascites, hypoalbuminemia gall bladder stones, and sludge. A significant limitation of ultrasonography is the ability to detect gall bladder abnormalities in a large number of critically ill patients, even in the absence of acalculous cholecystitis. One study recorded one ultrasonographic gall bladder abnormality in 84% and up to three abnormalities in 57% of the 44 patients recruited. The final tally of diagnosis of acalculouscholecystitis was two[15].

The precision of the CT scan appears to be comparable with ultrasonography[16]. The CT scan findings suggestive of acalculous cholecystitis include gall bladder wall thickening (>3mm), gallbladder distention (>5cm), subserosal edema, hyperdense bile (sludge), hyperdense bile (sludge), pericholecystic fluid, mucosal sloughing and intramural gas[17]. Of the above findings, those with the highest specificity include gas in the gall bladder wall, lack of gallbladder wall enhancement, and edema around the gallbladder at 99, 95, and 92%, respectively[17]. It is important to note that these findings have reduced sensitivity at 11, 38, and 22%, respectively. CT scan results should be interpreted with caution as critically ill patients have a high prevalence of gall bladder abnormalities: one case series noted the rate at 96%[17]. Clinicians should not use imaging alone to make the diagnosis due to the low sensitivity of most of the gall bladder abnormal findings. They should be interpreted in the context of the clinical presentation of the patient. Our patient's diagnosis was made based on symptoms of acute abdomen, sepsis, deranged liver function tests, and CT scan abdomen demonstrated gallbladder wall thickening with pericholecystic edema without any evidence of stone or biliary sludge.

The treatment for acute acalculous cholecystitis associated with lupus is controversial. Data on the

mortality rate of a calculous cholecystitis is at 30% but can go as high as 75% if treatment is delayed[17]. Traditionally early cholecystectomy was indicated in unselected AAC patients as they can rapidly progress to gall bladder necrosis, gangrene, and perforation, which are markers of poor prognosis[17]. However, new evidence shows that successful treatment outcomes are possible with a combination of corticosteroids, antibiotics, and supportive treatment[18,19]. Liu *et al*[19] compared treatment outcomes in 22 patients with lupus associated Acalculous Cholecystitis (ACC). They divided the patients into two treatment arms one with moxifloxacin alone and the other corticosteroid moxifloxacin combination. One patient in the combination arm had an inadequate response and had to undergo surgery. The moxifloxacin monotherapy arm had a higher failure rate; six of the ten had to accept cholecystectomy in the antibiotic group due to inadequate response[19]. During treatment, corticosteroids arm noted a reduction in the indexes of SLE activity such as SLICC/ ACR damage indexes, antinuclear antibody, anti-double stranded DNA antibody, and anticardiolipin antibody. They attributed the results to the pathogenesis of ACC in lupus being partly an inflammatory process with vasculitis; thus, the role of high-dose methylprednisolone as an anti-inflammatory[19]. Several case reports that have described successful outcomes of ACC with high dose steroids treatment[20,21]. Shin *et al*[20] recommended that if the patient's general condition is good, has no severe complications, has no other risk factors for ACC, and no evidence of infection, then one may consider high-dose steroid therapy as a first line of treatment. Based on the recommendations from Shin *et al*[20] as our patient met all of the criteria apart from evidence of infection together, we decided to start with high dose steroid treatment. Our patient also had markers suggesting high lupus activity, such as reduced complement, haemoglobin, and platelet levels. Our decision to combine with antibiotics was based on leukocytosis and results of the review by Liu *et al*[19]. The choice of antibiotic should be determined by the source of infection if its community-acquired versus healthcare-associated. Other factors that will determine the choice of antibiotics include bacterial cultures and the patient's risk factors for infection and possible risk of adverse outcomes[22]. Our empiric choice of ceftriaxone and metronidazole was based on the possibility that the source of the infection was community-acquired. Indications for an emergency cholecystectomy include emphysematous cholecystitis, gallbladder necrosis, and perforation[23].

Acute abdomen poses a diagnostic challenge, especially in the setting of lupus. Though rare clinicians should always have a high index of suspicion of lupus associated ACC due to its high mortality rates, one should suspect it if a lupus patient presents with fever, abdominal pain, leukocytosis, and elevated liver tests. Lupus activity tests such as anti-double stranded DNA and complement levels can help augment the diagnosis. Imaging should be interpreted in the context of the clinical presentation of the patient. There is evidence from literature that a majority of the gall bladder abnormalities have low sensitivity rates.

Conclusions

This case demonstrates there may be a role of corticosteroid therapy for lupus associated ACC. There is limited research on the comparison of the effectiveness of corticosteroid treatment with surgery due to low numbers of lupus associated ACC cases. The decision to treat either conservative or surgery should be tailor-made to each patient. There is evidence that supports patients in good general condition, having no severe complications (such as emphysematous cholecystitis, gallbladder necrosis, and perforation), has no other risk factors for ACC and no evidence of infection can benefit from high dose corticosteroids (0.5–1.5mg per kilogram of body weight per day for 3-5 days) as first-line treatment. More research still needs to be done on this rare manifestation of lupus. The need for the surgical and rheumatology teams to work together is paramount to improve outcomes of patients with lupus associated ACC.

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