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The Occurrence of Acalculous Cholecystitis in a Drug Hypersensitivity Reaction: A Case Report

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Abstract: ***Acalculous cholecystitis (AC) is defined as necro-inflammatory disease in gallbladder in the absence of gallstone which is caused by multifactorial. This case report aimed to show a severe systemic drug allergic reaction which attributed to AC. We reported a 23-year-old male who experienced acute systemic hypersensitivity reaction after 12 hours taking paracetamol. The patient showing generalized urticaria, epigastric and right upper quadrant of abdominal pain. Laboratory findings showed leukocytosis. Abdominal ultrasound showed the thickening of gallbladder wall, without the presence of gallstone and widening of bile duct. The patient was suspected of having vasculitis which complicated to gallbladder ischemia as underlying cause of AC.***

Keywords: acalculous cholecystitis, drug allergy, hypersensitivity reaction

1. Introduction

Acalculous cholecystitis (AC) is a rare and life-threatening disease. [1, 2] AC is defined as a necro-inflammatory disease in gallbladder in the absence of gallstones. The pathogenesis of AC is multifactorial. [3, 4] One of the underlying pathogens of AC is ischemia which can be caused by vasculitis in hypersensitivity reaction. [3-6] Vasculitis causes damage to blood vessels both venules and arterioles. It disturbs the perfusion of the affected organ. We reported a rare case of AC in patient who experienced hypersensitivity reaction to paracetamol.

2. Case Illustration

A 23-year-old man came to the Emergency Department with complaints of generalized body rash and itchy twelve hours after consuming paracetamol. The patient also complained of epigastric and right upper quadrant abdominal pain that appeared together with the rash. There were no factors that aggravate or alleviate the abdominal pain. The patient also complained of nausea and vomiting. Abdominal pain felt with VAS 4/10. Complaints of fever, shortness of breath, diarrheas were denied. The patient had taken paracetamol several times but never experienced abnormal reaction. The patient had experienced allergic reaction two times, but the causes were not identified. Histories of asthma, food allergies or drug allergies were denied. His mother and sister had history of asthma.

Vital signs were in normal limits. Epigastric and right upper quadrant of abdominal pain was found in abdominal palpation. There were generalized papular and annular urticarial plaques (Figure 1). Laboratory findings found leukocytosis (16, 570/uL), neutrophilia (83.8%), and normal eosinophil level (0.2%).

The patient was diagnosed with anaphylaxis reaction due to paracetamol allergic. Paracetamol treatment was immediately stopped. The patient was given intravenous fluid, intramuscular epinephrine injection, intravenous esomeprazole 1x40mg, and oral loratadine 2x10mg. The patient was observed for the vital signs and symptoms. Abdominal pain and urticaria in this patient persist after 24 hours of observation.

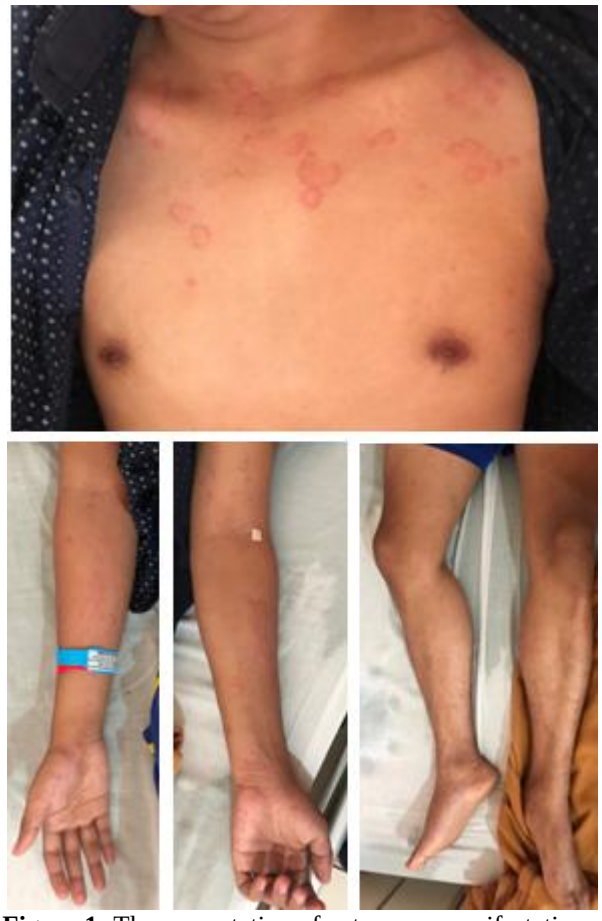

Figure 1: The presentation of cutaneous manifestation

The patient suspected of having vasculitis. We underwent abdominal ultrasound examination to evaluate of abdominal pain. Abdominal ultrasound revealed the thickening of gallbladder wall, no gallstone, and no widening of bile duct.

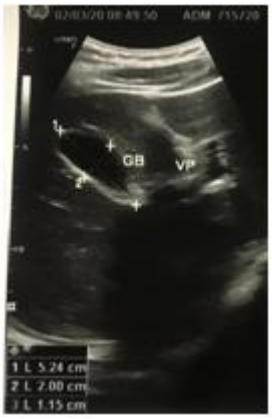

Figure 2: Abdominal ultrasound showed the thickening of gallbladder wall, no gallstone, and no widening of bile duct.

The patient was diagnosed with acute AC and vasculitis. Patients were given additional therapy such as intravenous methylprednisolone 2x62.5mg and intravenous antibiotic to treat acute AC. The patient was treated for eight days, the he was discharged after symptoms improved.

3. Discussions

The patient in this case, a 23-year-old male, was initially diagnosed with anaphylaxis reaction due to paracetamol allergy. This was based on the history of taking paracetamol 12 hours before the onset of cutaneous and gastrointestinal symptoms. A few numbers of anaphylaxis reactions due to paracetamol allergy have been reported by Khan et al, only 0.8%. [7] Most patients with anaphylaxis showing cutaneous (76.7%), cardiac (68.9%), and gastrointestinal (64.3%) manifestations. [7] The most gastrointestinal manifestation occurred were vomiting (13.2%) and abdominal pain (8.5%). [7] The patient was treated according to the guideline for management of anaphylaxis reaction. [8, 9] The main therapy for anaphylaxis is administration of intramuscular epinephrine.[8, 9] Second generation H1-antihistamine and proton-pump inhibitor were given only for symptomatic management.

The vital signs were stable during 24 hours of observation. However, the symptoms of urticaria and abdominal pain still persist. Urticaria in allergic reaction generally disappeared within 24 hours. If the urticaria lesion persists for more than 24 hours, this condition must be considered as vasculitis as a pathogenesis of the urticarial reaction. [10, 11] Urticarial vasculitis showed the episode of recurrent urticarial lesion and it usuallyaccompanied by other systematic disorders. [12, 13]

Vasculitis shows an inflammation of the blood vessel walls caused by a various of non-specific reaction, one of which is hypersensitivity reaction. [10] Some evidence showed the participation of small blood vessel in the allergic reaction, as well as the understanding that some clinical symptoms that cannot be explained, may be due to allergic. [10] The presence of sensitizing antigens causes arteriolar constriction and stoppage of circulation. Leukocytes attached to the endothelium of blood vessels and migrated through capillary walls and venules in large quantities. In addition, some leukocytes are agglutinated causing emboli that block some capillaries and venules. Drugs, invective agents, antibiotics, and malignant tumors act as antigens. Vascular damage is probably the result of antigens and antibodies reaction in the vessel wall. [10] To confirm the type of vasculitis, a skin biopsy is needed, but it was not done in this case due to limited facilities.

Abdominal ultrasound results obtained thickening and edema in the gallbladder wall without stones and bile duct dilatation. In this patient, there was AC. Acute AC is defined as an acute necro-inflammatory disease of the gallbladder in the absence of gallstones and has a multifactorial pathogenesis. [1, 3, 4] Gallstones were the main cause of acute cholecystitis, non-gallstones or AC occurs for only approximately 10% of acute cholecystitis, hence, it is often overlooked and leading to a delayed diagnosis that increase the morbidity and mortality than calculous cholecystitis. [6, 14, 15] Ischemia plays an important role in the pathogenesis of AC. [5]

Gallbladder has a terminal artery. If visceral hypoperfusion occurs due to various things, there is a decrease in gallbladder perfusion and results in gallbladdermucosal ischemia. [6] Halaka et al reported differences in capillary flow in calculous cholecystitis and AC. In calculous cholecystitis, capillary flow appears regular, but in contrast capillary flow is less and irregular in AC. [16] Therefore, AC is also referred as ‘acute ischemic cholecystitis’. Ischemia that occurs in the gallbladder mucosa can cause hypomotility resulting in gallbladder stasis that causes intraluminal exposure of the gallbladder wall, ultimately can cause ischemia, inflammation, and potentially necrosis. In addition, if ischemia, inflammation, or infection occurs continuously, it can cause perforation. [6, 17] AC is more dangerous because of the high potential for necrosis and perforation, especially in late diagnosis.

Actually, there are no specific criteria for diagnosing AC. [15, 17] However, a study stated that the diagnosis of AC was usually based on radiological results. Ultrasonography has been used as first choice to evaluate suspected acute AC because of its advantages. [1]In this case, diagnosis of AC was established based on the presence of 3 major criteria such as thickening of gallbladder wall >3mm, edema of the gallbladder wall, sonography murphy sign; and one minorcriteriasuch as gall bladder distension 5.24 cm (>5cm in transverse diameter) on ultrasound examination. [18] The presence of leukocytosis >10, 000/uL also supported the diagnosis of AC. [17, 19]

It can be concluded that hypersensitivity to the drug can be an unknown factor in some patients with AC. The patient in this case most likely suffered from AC since he was first admitted to the hospital because of a hypersensitivity reaction caused by paracetamol. Some of the supporting reasons were: (1) the patient had just taken paracetamol 12 hours before the initial episodes of rash, epigastric and right upper quadrant abdominal pain appeared, (2) manifestation of rash and abdominal pain persisted more than 24 hours after initial treatment, (3) abdominal ultrasound and laboratory findings supported AC.

The presence of persistent urticaria, the recent use of paracetamol, and the development of AC allowed us to consider that AC in this patient was related to vasculitis due to paracetamol-induced hypersensitivity reactions. Vasculitis causes gallbladder blood flow disruption leading to gallbladder ischemia which plays an important role in pathogenesis of AC.

In this case, thereof most likely causative factor of AC is drug hypersensitivity. Therefore, the suspected drug must be stopped and clinical improvement should be observed. The main treatment is to eliminate the causative factors, so the patient does not need surgery. [10, 20, 21] The treatment of vasculitis is corticosteroid because it has a specific effect on vascular lesion and helps healing and sclerosis. [10]

Second-generationH1-antihistamines are the first-line treatment for acute urticaria with a good side effect profile. [22] The administration of intravenous antibiotics plays a major role in the treatment of AC in hospital setting. If the infection is mild-moderate, antibiotics such as cefazolin, cefuroxime, and ceftriaxone are preferred. [14]Therefore, in this case, we provide therapy for vasculitis in the form of intravenous methylprednisolone and second-generation of H1-antihistamine, loratadine. Antibiotic was given to treat AC.

4. Conclusion

The present report underlines the importance of assessing patients who have systemic hypersensitivity reaction comprehensively. Vasculitis due to drug-induced hypersensitivity reactions can cause organ ischemia that leads to acute AC which is dangerous because of its high potential for necrosis and perforation. The clinicians should be aware for the occurrence of AC in patients with systemic hypersensitivity reaction. Early diagnosis and prompt treatment can decrease the morbidity and mortality in AC patients.

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