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CLINICAL CASES

Refractory abdominal pain resistant to medical management as the main manifestation of ischemic gallbladder

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Abstract

In the present paper, we discuss the importance of clinical evaluation by presenting three cases whose diagnosis was acute cholecystitis. Their clinical presentation was characterized by abdominal ischemic pain, with no data of acute complicated cholecystitis in imaging or laboratory studies. However, during surgical procedures, the gallbladders of all three patients were found in an ischemic phase. We observe that conventional studies are not able to identify gallbladder ischemia before the surgery. Contrasting computed tomography must be used, but we emphasize that clinical suspicion must be obtained.

Keywords: *Acute cholecystitis. Abdominal pain. Ischemic pain. Ischemic gallbladder. Gangrenous cholecystitis. Acute complicated cholecystitis.*

Introduction

Acute cholecystitis corresponds to the inflammatory process of the gallbladder typically associated with stone formation[1]. The gallbladder is located in its fossa, located on the visceral side of the liver, measuring between 7 and 10 cm in length and 4 cm wide[2,3], and its hepatic side is attached to the liver by connective tissue of the capsule fibrous liver. The gallbladder is divided into three parts: fundus, body, and neck, from where it joins the cystic duct. The cystic duct forms folds with the mucosa in its proximal part, performing the function of a valve, keeping the cystic duct open so that bile can pass into the gallbladder from the bile duct, or pass into the duodenum when it contracts[2]. The gallbladder causes a clinical condition characterized by cramping pain, typical of hollow viscera, whose clinical pattern is intermittent and subsides due to fatigue of the visceral smooth muscle. This pain is produced by the direct effect of muscle contraction on mechanosensitive pain receptors or in response to chemical stimuli. In the case of ischemia, the pain changes its pattern, becoming more intense, constant, and resistant to medical management. This pain is the result of anaerobic metabolism derived from the lack of oxygen in the tissues, which causes the accumulation of lactic acid in the tissues, in addition to the release of different inflammatory substances, such as bradykinin and proteolytic enzymes that cause cellular damage; all of this together stimulates the pain nerve endings in the smooth muscle. Likewise, distension and contractions of smooth muscle can promote ischemic-type pain due to the collapse of blood vessels[4].

Case report 1

The patient was a 65-year-old female with a history of type 2 diabetes mellitus and long-standing systemic

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arterial hypertension, both under medical treatment; three cesarean sections and hysterectomy secondary to uterine myomatosis. The last surgical intervention was performed 37 years ago. The patient went to the emergency department due to sudden-onset abdominal pain, associated with eating food, lasting approximately 12 h, located in the epigastrium, Visual Analog Scale (VAS) intensity 10/10, oppressive and burning type, radiating to the right hypochondrium. Moreover, the ipsilateral subscapular region, without identified exacerbators or mitigating factors, accompanied by general malaise, nausea, hyporexia, and vomiting of gastrobiliary content on seven occasions, managed empirically by the patient with oral butylhyoscine on one occasion, without improvement. Vital signs upon admission: blood pressure (BP) 180/95 mmHg, heart rate (HR) 89 bpm, respiratory rate (RR) 20 rpm, Temp 36.6°C, $SatO_2$ 99%. Upon physical examination, the patient showed poor general condition and pain, a balloon-like, distended abdomen, without visible masses or visceromegaly, with multiple striae and scars from previous cesarean sections, peristalsis present, soft and depressible, without palpable masses or visceromegaly. Abdominal tenderness to medium and deep palpation in epigastrium and right hypochondrium, mostly noticeable with pron maneuver, frank Murphy sign, positive McBurney and Rovsing, tympanic, with pain on percussion in right quadrants. Acute cholecystitis is suspected as the main symptom. Blood tests showed 15,300 leukocytes with neutrophilia. There were no liver enzymes elevation, kidney function parameters, bilirubin and coagulation times presented normal values. Ultrasound of the liver and bile ducts shows a distended gallbladder, dimensions of 85 × 37 × 46 mm, homogeneous and anechoic content, thin wall of 2.1 mm. No stone is seen in the bile ducts. The simple computed tomography of the abdomen shows a gallbladder with a thin and regular wall, without stones inside, measuring 91 × 46 × 43 mm, a cystic duct with the presence of a hyperdense image of oval morphology and defined edges of 2.8 mm (Fig. 1). Presumptive diagnosis: hydropic gallbladder secondary to cystic duct stone. The patient was admitted to the hospital 4 h after admission to the emergency room, with no improvement in pain despite management with antispasmodics and antibiotic therapy, so surgical time for laparoscopic cholecystectomy was scheduled.

During surgery, microabscesses were observed on the surface of both lobes of the liver and seropurulent fluid in the right subphrenic and subhepatic spaces. Fluid is aspirated and when the vesicle is detached from its bed, a hydrocholecyst is observed with patches of ischemia, fibrin, and seropurulent material in the periphery (Fig. 2). The patient had a post-operative course without complications and was discharged 5 days after her surgery, adequately tolerating the oral route, with surgical wounds without signs of infection and without signs of abdominal alarm.

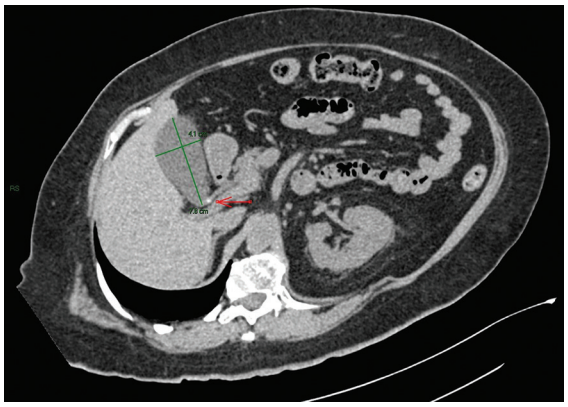

Figure 1. Clinical case 1: simple abdominal tomography in an axial section at the level of the gallbladder shows the increase in the dimensions of the gallbladder in longitudinal and transverse axes, with stone in the neck region (arrow), as well as striation of perivesicular fat.

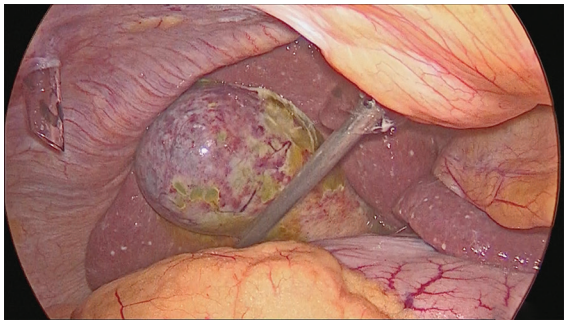

Figure 2. Clinical case 1: The laparoscopic image shows multiple areas of transmural ischemia in the gallbladder body.

Case report 2

The patient was a 50-year-old female with a surgical history of a cesarean section, with no other significant personal history. He went to the emergency room due to abdominal pain of insidious onset, with 2 days of evolution, predominantly in the epigastrium, VAS intensity 10/10, oppressive, radiating to the right hypochondrium,

exacerbated by the ingestion of cholecystokinetic foods, accompanied by nausea without vomiting. Moreover, the sensation of unquantified thermal rise managed with oral butylhyoscine prescribed by a private doctor, without improvement in pain. Vital signs upon admission with BP 125/87 mmHg, HR 87 bpm, RR 17 rpm, Temp 36.7°C, $SatO_2$ 93%. Upon physical examination, the abdomen was globose, without visible masses or visceromegaly, scar from a previous cesarean section, normal peristalsis, with excess adipose panniculus, without masses or palpable visceromegaly, painful on superficial and deep palpation in the epigastrium, Irradiating to right the hypochondrium and Rovsing moneuvers were positive, without signs of peritoneal irritation, tympanic. Acute cholecystitis is diagnosed. Blood count without leukocytosis, only with an increase in the percentage of neutrophils (86%), blood chemistry with mild hyperglycemia (134.54 mg/dL), preserved kidney function, elevated liver function tests above the 99th percentile, hyperbilirubinemia at the expense of bilirubin direct (1.16 mg/dL), ultrasensitive C-reactive protein (CRP) (280 mg/L), and quantitative procalcitonin (0.85 ng/mL) elevated coagulation times presented normal values. Simple computed tomography of the abdomen shows a gallbladder measuring 122 × 48 × 50 mm, a 5-mm thickened wall, and heterogeneous contents (Fig. 3). Initial management was symptomatic treatment with antispasmodics and prophylactic antibiotics. The patient presented partial improvement in the abdominal pain. The patient is admitted to the hospital floor for a surgical procedure the next day. Laparoscopic cholecystectomy was performed, finding hydropiocholecyst with ischemic patches in the gallbladder and thickened cystic with necrotic-looking mucosa when performing a cross-section, in addition to seropurulent fluid in the cavity (Fig. 4). During the post-operative period, the patient had elevated quantitative procalcitonin for 2 days, with an adequate response to broad-spectrum antibiotics, and was discharged on the 3rd post-operative day, adequately tolerating the oral route, with no clinical signs of infection or abdominal alarm.

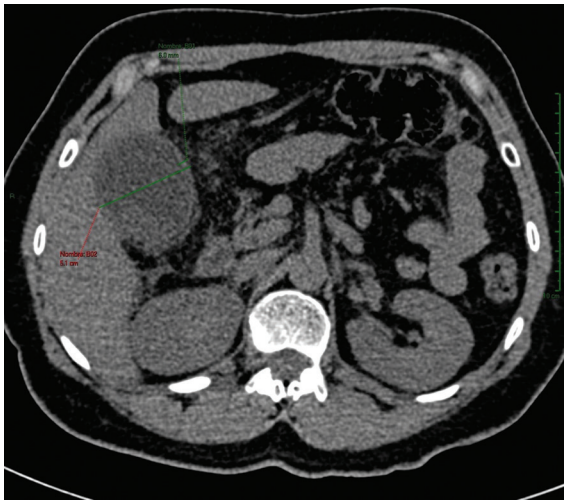

Figure 3. Clinical case 2: simple tomography of the abdomen in an axial section at the level of the gallbladder shows an increase in the dimensions of the gallbladder in longitudinal and transverse axes, as well as a "double rail" sign.

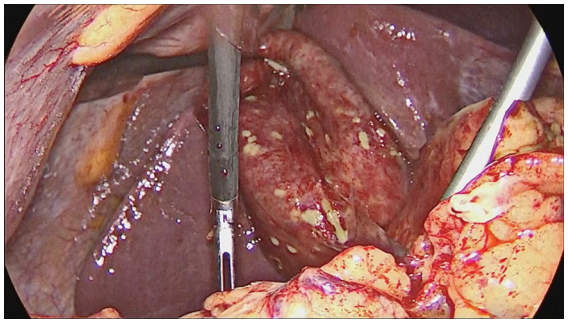

Figure 4. Clinical case 2: The laparoscopic image shows the body of the gallbladder with small patches of necrosis, some of them covered with fibrin.

Case report 3

The patient was an 84-year-old female with a history of long term type 2 diabetes mellitus and systemic arterial hypertension, both of long duration, chronic obstructive pulmonary disease treated with supplemental oxygen at home, allergic rhinitis, and colostomy secondary to diverticular disease with abdominal hernia repair 11 years ago. She went to the emergency department with a 1-day history of sudden abdominal pain associated with eating, located in the epigastrium, with an intensity of 10/10 on the VAS scale, stabbing, radiating to the right upper quadrant and right lower quadrant, without exacerbators. nor extenuating circumstances, accompanied by anorexia and nausea, leading to vomiting of gastro-alimentary content on one occasion. Admission vital signs: HR 59 bpm, RR 22 rpm, BP 149/93 mmHg, Temp 35.9°C, $SatO_2$ 92%. Globular, distended abdomen, a surgical scar in the left abdomen, without visible masses or visceromegaly, preserved peristalsis, generally tenderness on deep

palpation with predominance in the upper quadrants, Murphy maneuver positive, without signs of peritoneal irritation, tympanic. Blood tests showed 17,940 leukocytes with neutrophilia, hyperglycemia of 196.43 mg/dL, no alterationes in renal or liver function markers, lactate dehydrogenase with elevated levels (275.21 U/L), no hyperbilirubinemia. CRP-ultrasensitive, quantitative procalcitonin and coagulation times in normal parameters. Simple computed tomography of the abdomen reports a gallbladder with a thin, regular wall, measuring 104 × 58 × 50 mm, with heterogeneous content (Fig. 5). Presumptive diagnosis: hydropic gallbladder probably secondary to gallstones. The patient was admitted to the hospital floor fasting and with symptomatic treatment with antispasmodics and prophylactic antibiotics, without notable improvement in the clinical picture. A laparoscopic cholecystectomy was performed the next day, in which a hydropiocholecyst was found, a tense gallbladder with ischemic patches, fibrin, and pus in the morrison and subphrenic spaces. The patient did not present any complications during the post-operative period; he was discharged adequately tolerating the oral route, with no evidence of infection or abdominal alarm.

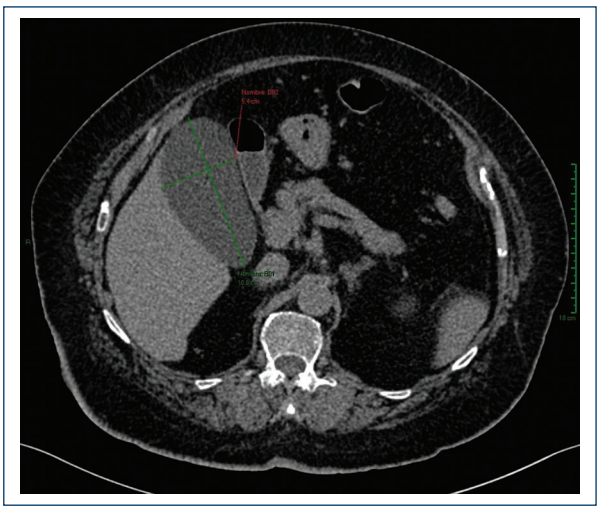

Figure 5. Clinical case 3: simple tomography of the abdomen in an axial section at the level of the gallbladder shows an increase in the dimensions of the gallbladder in longitudinal and transverse axes, as well as heterogeneous content inside (arrow) that suggests gallbladder lithiasis.

Discussion

The gallbladder and cystic duct are supplied by the cystic artery, which most commonly arises from the right branch of the hepatic artery. Venous drainage of the bile ducts and the neck of the gallbladder is provided by the cystic veins, which drain into the hepatic portal vein[2,3]. Obstruction of the outflow of bile material during gallbladder contraction leads to distension of its lumen, causing gradual thickening of the wall due to submucosal edema[1]. This clinically translates as colicky pain, which subsides due to fatigue of the smooth muscle, so it is intermittent[4]. Patients with uncomplicated acute cholecystitis present with a sudden onset of cramping pain, predominantly in the right upper quadrant or epigastrium, radiating to the right scapula or posterior thorax, which may be accompanied by fever, nausea, vomiting, and anorexia. The findings in imaging studies in acute uncomplicated cholecystitis are thickening of the gallbladder wall ≥ 3 mm[5] or ≥ 4 mm[6], elongation of the gallbladder in its long axis ≥ 8 cm and in its short axis ≥ 4 cm; stones or stone remains, free fluid around the gallbladder, and striations in the perivesicular adipose tissue[5,6]. Ultrasound of the liver and bile ducts has a sensitivity of 81% and specificity of 83% for acute uncomplicated stone cholecystitis; MRI has a sensitivity and specificity of 85% and 81%, respectively[6]. Ultrasound is the imaging study of the first choice when acute cholecystitis is suspected[6] due to its lower cost, greater accessibility, and better sensitivity to detect gallstones compared to computed tomography. Regarding acute cholecystitis, a retrospective study of more than 2800 cases concluded that simple computed tomography of the abdomen is not inferior to ultrasound for diagnosing it, having a sensitivity of 55% and 61%, respectively, and specificity of 92% and 91%, respectively, in addition to the fact that computed tomography has the advantage of ruling out differential diagnoses. Similarly, it was concluded that contrast-enhanced computed tomography is not superior to non-contrast computed tomography[7].

Complications of cholecystitis are due to increased intraluminal pressure, inflammation of the gallbladder wall, vascular compromise, hemorrhage, and gangrenous changes, which can lead to perforation of the gallbladder. Within the pathological evolution of acute cholecystitis, edematous cholecystitis comprises the first 2-4 days[8]. After 3-5 days, cholecystitis evolves to necrotizing and subsequently suppurative stages, in approximately 7-10 days[9]. Gangrenous cholecystitis is a severe complication of cholecystitis, which consists of inflammation, ischemia, and necrosis of the gallbladder wall. It occurs in approximately 22-39% of patients with acute cholecystitis, with identified risk factors

being advanced age, male sex, and diabetes mellitus[5]. The pain present in this type of patient is characterized by following an ischemic type pattern, which is of great intensity, constant, and does not yield to medical management with analgesics. It is accompanied by poor general condition and signs of systemic inflammatory response syndrome. Upon physical examination, studies have observed that almost 100% of patients with gangrenous cholecystitis present a positive murphy sign; however, this is expected due to the high sensitivity but low specificity of said sign, 86-97% and 35-48%, respectively[7,8]. The Tokyo guidelines for diagnosis and staging of the severity of acute cholecystitis recommend dynamic computed tomography of the abdomen with contrast as the imaging study to detect gangrenous cholecystitis, where the finding of the gallbladder wall with little contrast impregnation has a sensitivity of 73% and specificity of 95% for this pathology[6]. Other findings of gangrenous cholecystitis are irregularities in the gallbladder wall, increased density of perivesicular adipose tissue, the gas inside the gallbladder, and perivesicular abscess[5,8]. Attempts have been made to deduce parameters predictive of necrosis based on the patient's clinical history (advanced age, male sex, diabetes mellitus), physical examination (tachycardia, antalgic position), laboratories (leukocytosis, elevated CRP), and imaging studies (thickening of the gallbladder wall > 4.5 mm, perivesicular fluid). Studies have concluded that leukocyte levels, CRP, and gallbladder wall thickening are the findings most associated with more advanced clinical and histopathological stages[9], that the variables male sex, diabetes, fever, erythrocyte sedimentation rate, and white blood cells are significantly more common in patients with gangrenous cholecystitis[10,11], or that elevated CRP levels help identify patients with gangrenous cholecystitis[12]. Gangrenous cholecystitis has also been associated with the presence of striations in the gallbladder wall and intraluminal membranes, which correspond to fibrin exudates[8,11]. All studies were without conclusive results for the pre-operative diagnosis of gangrenous cholecystitis.

Conclusion

Various studies[5,8-12] have attempted to predict gallbladder ischemia using personal history, comorbidities, and laboratory and imaging studies, without conclusive results. Due to the characteristics of the clinical picture of the cases presented, simple computed tomography scans of the abdomen were performed as part of the initial approach to acute cholecystitis. Although the Tokyo guidelines for the diagnosis and severity of acute cholecystitis[6] recommend dynamic abdominal computed tomography with contrast as the study of choice to identify gangrenous cholecystitis, this is not a routine or first-choice imaging study. For the evaluation of abdominal pain, given that it depends on availability, cost, and patient comorbidities, particularly acute kidney function, which may limit the use of contrast media. When faced with abdominal pain in a patient diagnosed with cholecystitis, clinical symptoms are a fundamental component during the evaluation. In this article, we refer to three clinical cases with very similar pain characteristics: persistent, intense and that does not respond easily to analgesics and antibiotics, so we conclude that the diagnosis of acute cholecystitis by an imaging study, accompanied by a change in the pattern of visceral colic pain to an ischemic type pattern, which presents an intense, constant evolution and refractory to medical treatment, is the best clinical predictor of gallbladder ischemia.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type

of generative artificial intelligence for the writing of this manuscript or for the creation of images, graphics, tables, or their corresponding captions.

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