

Case Study

Acute Cholecystitis and the Controversies of Treatment

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Key Learning Points

- 1. Acute cholecystitis is often a complication of gallstones disease**
- 2. Most of patients with symptomatic gallstones disease are prone to further complications and cholecystectomy is indicated**
- 3. Laparoscopic early cholecystectomy in acute cholecystitis is superior to delayed cholecystectomy in terms of symptom control, hospital stay and re-admissions, with similar morbidity and mortality and should be attempted in all cases of acute cholecystitis. Difficult cases should be managed by experienced surgeons, in advanced centers, and bail-out procedures should be attempted as per Tokyo guidelines.**
- 4. Percutaneous cholecystostomy should only be used in patients unfit for surgery who fail to improve**
- 5. The data available to support optimal antibiomatic treatment is scarce, and local microbiology guidelines should be used.**

Article Information:

Date Received

Date Accepted

Date Available Online

Keywords:

Acute cholecystitis

Cholecystectomy

Introduction

Acute cholecystitis – inflammation of the gallbladder – is most often a complication of cholelithiasis (gallstones). Cholelithiasis is one of the most common disorders of the gastrointestinal tract, affecting 10% of the western population.¹ Approximately 80% of patients with cholelithiasis will remain asymptomatic, but in those with symptoms of biliary colic, approximately 20% will go on to develop cholecystitis if they are left untreated.² Though 90% of cases of cholecystitis will be due to cholelithiasis, acalculous cholecystitis also occurs. The majority of acalculous cholecystitis occurs in patients with multiple trauma or burns, with major surgery, and sepsis among the other risk factors. Immunocompromised patients may also develop primary infective cholecystitis due to opportunistic pathogens.³ However, this report will focus on acute calculus cholecystitis.

Case presentation

Mr PJ, a previously well 42 year-old bus driver, presents with right upper quadrant (RUQ) pain. The pain was of sudden onset four days ago when it had woken Mr PJ from sleep. It had gradually increased in severity since then and had woken him again on the morning of admis-

sion. This had forced him to go to accident and emergency.

The pain is constant, described as “tight and bloating”, worse on deep inspiration or coughing with a severity of 7/10. It is associated with nausea, though there has been no vomiting. There is no radiation and no association with food, trauma. There have been episodic fevers and sweating over the previous 3 days, but not on presentation. There has been no change in bowel habit and the patient described his appetite as good. Stool and urine colour is unchanged and there has been no dysuria.

There is no past medical history of gallstones or pancreatitis and the patient has never had this particular pain before. There was a history of similar pain ten months ago though it was less severe and was located in the left iliac fossa. At that time the patient had also noticed some blood in his stool and colonoscopy had revealed slight diverticular disease and a simple

anal polyp.

Investigations:

The blood test results demonstrated a WCC of $21.3 \times 10^9/L$, a CRP of $>160 \text{ mg/L}$ and a Bilirubin of $43 \mu\text{mol/L}$. Abdominal ultrasound reported pain on pressure, numerous sub-1cm stones, focal wall thickening in the gallbladder body and pericholecystic fluid. There was no intrahepatic duct dilation and no liver abnormalities.

Differential diagnosis:

The history favours acute cholecystitis. Ascending cholangitis, biliary colic, pancreatitis and renal causes are also possible. Aortic aneurysm and acute coronary syndrome also have to be ruled out, though the patient has few cardiac risk factors. The investigations reflect the differential diagnoses.

Treatment - Medical Management:

Treatment of acute cholecystitis may be conservative or surgical. In selected cases a radiological drain might be required. Medical management is appropriate in the majority of cases. Patients placed on low fat diet, rehydrated with i.v. fluids in an attempt to rest the gallbladder.

Analgesia is usually in form of paracetamol combined with opioids or non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs can reduce gallbladder inflammation by reducing prostaglandin production in the gallbladder wall. Indomethacin has been shown to have the added value of improving gallbladder emptying as it has a prokinetic effect.⁴

The use of antibiotics in acute cholecystitis is an area of debate and as such is covered in discussion. In practice, patients are usually treated empirically for biliary sepsis.⁵

Treatment - Surgical Management:

About 20% of patients presenting with acute cholecystitis need emergency surgery, most commonly because of gangrenous cholecystitis or perforation induced peritonitis. This report will focus on conventional, non-emergency treatment.

Percutaneous cholecystostomy involves the placement of a drain into the gallbladder under local anaesthetic. It is used in patients with serious comorbidity who would be at high risk of mortality from major surgery or in patients waiting for delayed cholecystectomy in which medical management is not sufficient. The latter

is true in the case of Mr PJ. It is a minimally invasive technique, has a high success rate and will usually lead to the resolution of cholecystitis.⁶ It has subsequently become a valuable alternative procedure for decompressing an acutely inflamed gallbladder.

Cholecystectomy is the surgical removal of the gallbladder and is widely considered to be the standard treatment for cholecystitis. It may be performed early or late, by open or laparoscopic techniques. This will form the basis of the discussion below, along with the issue of antibiotic therapy.

The National Institute for Health and Care Excellence (NICE) guideline for Gallstone disease: diagnosis and management recommends early laparoscopic cholecystectomy (to be carried out within 1 week of diagnosis) for people with acute cholecystitis.⁷ The Tokyo guidelines 2018 also recommend early laparoscopic cholecystectomy for acute cholecystitis, and also recommended careful selection based on estimated pre-operative and intra-operative surgical difficulty and safe steps and bail-out procedures (subtotal laparoscopic cholecystectomy or open cholecystectomy) in attempt to reduce vasculo-biliary injury.⁸

Outcome and follow-up:

Mr PJ was observed on the ward for 4 days, his pain was reduced to paracetamol and codeine and he was treated with co-amoxiclav (1.2g tds i.v.) and metronidazole (500mg tds i.v.) for biliary sepsis as per local guidelines. On the 4th day of admission percutaneous cholecystostomy was inserted to drain his gallbladder and on the 7th day he was discharged, with a plan to perform an outpatient laparoscopic cholecystectomy in six weeks. The drain was performed as the patient failed to improve and inpatient cholecystectomy was not feasible.

Discussion

There are three key issues in the management of acute cholecystitis: that of antibiotic use, the surgical approach and the timing of surgery.

Antibiotics

The use of antibiotic therapy should ideally be based on clinical findings such as a raised WCC, the presence of pyrexia, radiographic findings such as air in the gallbladder or gallbladder wall and the clinical picture. Although the initial inflammation of the gallbladder may be sterile,

secondary infections with bugs from gut flora may occur. In practice, however, most patients who are hospitalized for an episode of acute cholecystitis are given antibiotics independent of these signs. Unfortunately, there are few studies on the efficacy of antibiotics in cholecystitis and available studies are now dated. However, one observational study of 302 patients showed no decrease in the development of complications following antibiotic therapy for cholecystitis, though there were lower rates of bacteraemia and wound infection.⁹ Antibiotic use is therefore only recommended for those with diabetes, immunodeficiency, or as prophylaxis for patients undergoing cholecystectomy. The routine use of antibiotics independent of these indications demonstrates how practice is often not dictated by clinical evidence. Clearly more data are needed to guide the most appropriate use of antibiotics in cholecystitis.⁵

When required, empirical antibiotics should include activity against the most common biliary pathogens. In the pathogenesis of cholecystitis these are: *E. Coli*, *Enterococcus*, *Klebsiella* and *Enterobacter*.¹⁰ Second generation cephalosporins such as cefuroxime or a quinolone and metronidazole cover the most virulent of these. Activity against *Enterococci* is usually not required.¹¹ Antibiotic therapy should be adjusted when culture and sensitivity results become available.

Two questions surround cholecystectomy: that of approach – laparoscopic or open; and that of timing – early or delayed.

Approach

Reports of complications following early laparoscopic cholecystectomy (LC) originally led to scepticism about this approach. However, an RCT in 1998 concluded that laparoscopy was as safe, effective and associated with shorter hospitalisation time and earlier return to work than open cholecystectomy (OC).¹² The question of approach was formerly addressed in the Tokyo Guidelines, released in 2018.⁷ This confirmed both the benefits and surgeons' preferences for LC over OC. It noted that the skills required for LC are very different for that of OC and as such only surgeons skilled in LC should perform it. Surgeons should also be aware of the complications of the laparoscopic approach, especially

that of bile duct injury which is increased in LC due to the narrow view and lack of tactile manipulation.

The surgical demands of LC are especially pertinent in cases of gangrenous cholecystitis, where the need for conversion from LC to OC is higher. A 2008 meta-analysis therefore studied whether LC remains the treatment of choice in severe gangrenous and empyematous cholecystitis.¹³ 1408 patients were included in the study and it was found that conversion rates to open procedure were threefold higher in severe than in mild to moderate cholecystitis. However, it was concluded that LC is still the treatment of choice for acute cholecystitis independent of severity, though the surgeon should have a low threshold for conversion to open procedure.

Timing

The most pertinent question in the surgical treatment of acute calculous cholecystitis concerns timing.¹⁴ Generally, the timing of cholecystectomy is divided into 'early': up to a week after the onset of symptoms, and 'delayed': 6-12 weeks after the resolution of symptoms.

Classically, early LC for an acutely inflamed gallbladder is more technically demanding than when the inflammation has settled. This difficulty results from inflammatory adhesions and distortion of the usual biliary architecture, especially Calot's triangle. Historically, therefore, surgeons tended to delay surgery until the resolution of inflammation when laparoscopic landmarks are more visible. As techniques and equipment improved, however, it was found that early LC was associated with a lower risk of conversion to open surgery relative to delayed LC. It is thought that this is due to the formation of 'oedema planes' in the first 72 symptomatic hours, allowing relatively easy gallbladder dissection.³

A Cochrane review formally analysed studies comparing early and late LC in 2006.¹⁵ Five randomised controlled trials (RCTs) of 451 patients were included, four of which were of high methodological quality. The review demonstrated that early LC was as safe as delayed LC across all endpoints. No mortality was reported in any of the RCTs and there were no statistically significant differences between early and delayed groups in terms of conversion rates to open procedure, recovery time or complications (bile duct injury,

bile leak or infection). Though the two approaches may seem equivalent, it is important to note that early treatment significantly reduces overall hospital stay, simply by treating the disease on admission. This translates to substantial there were no statistically significant differences between early and delayed groups in term of conversion rates to open procedure, recovery time or complications (bile duct injury, bile leak or infection). In addition, 17.5% of patients undergoing delayed LC eventually needed emergency surgery because of recurrent or non-resolving cholecystitis. Rates of conversion to open procedure in emergency surgery were almost double those in early LC. Effectively, therefore, early LC prevents complications of cholecystitis before they can arise and subsequently decreases the need for conversion to open procedure.¹⁶

It should be noted that 451 patient is a relatively small population size for a meta-analysis, producing correspondingly wide confidence intervals. This may be responsible for the lack of significance between early and delayed LC endpoints. However, a more recent prospective randomised study lends further support to the Cochrane review, showing early LC is safe and feasible for acute cholecystitis with the additional benefit of shorter total hospital stay. Apart from a shorter operating time, treating patients with delayed laparoscopic cholecystectomy does not offer additional benefit.¹⁷

The breadth of evidence therefore strongly favours early LC over delayed LC and NICE guidelines recommend this. Nevertheless, early cholecystectomy has not been adopted routinely. This may be because of lack of awareness, fear of complications, local setup, surgical skills and theatre availability. In the UK, for example, a cross-sectional study demonstrated that only 11% of surgeons perform early LC routinely. Inadequate human resources and the lack of operating theatres are the most likely reasons for this. It has been suggested that the establishment of national protocols to increase the implementation of early surgery would both benefit patient care and save considerable healthcare costs (equivalent to 25000 bed-days a year).¹⁶

Conclusion

The evidence base for antibiotic use in acute chole-

cystitis is limited and the trend is therefore to treat empirically regardless of indications. Cholecystectomy remains the treatment of choice for cholecystitis. The laparoscopic approach is favoured independent of disease severity, though rates of conversion to open procedure increase with severity and experienced surgeons are required. Early surgery should be carried out where possible, as it has similar complications and outcomes to delayed surgery with dramatically decreased hospital stays. National guidelines are required to ensure the implementation of this plan.

Conflicts of interest

None.

Funding

None.

Consent

Patient consented.

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