Biliary pain

BACKGROUND Gallstones are a common cause of abdominal pain. Gallstones are present in 20% of women and 8% of men, but might not cause symptoms.

OBJECTIVE This article discusses the aetiology of biliary colic and related disorders. The differential diagnosis is examined and relevant investigations are outlined. Some less common aspects of this disease complex are described for context.

DISCUSSION The only effective treatment for symptomatic gallstones is cholecystectomy, for which the laparoscopic approach is now the gold standard.

Gallstone disease is a common cause of upper abdominal pain, and biliary colic will enter the differential diagnosis in many cases of acute abdominal pain. Gallstones are common in western populations and are present in 20% of women and 8% of men in the USA and Europe. The higher incidence in women is thought to relate to oestrogen (including the contraceptive pill). Obesity and a high kilojoule diet – common in the community – also increase the risk.[1]

Biliary colic is sometimes termed 'gallbladder colic' as it is thought to relate to the impaction of gallstones in the neck of a contracting gallbladder. Hence, symptoms are often present shortly after a meal. The symptoms typically last from 30 minutes to a few hours and then resolve, although attacks may occur on a daily basis. Most patients however, would not experience severe symptoms on a daily basis unless the underlying disease was merging into the syndrome of acute cholecystitis.[1]

In biliary colic, the pain is classically felt in the epigastrium; is constant and (often) severe. Radiation to the inter-scapular region is common as are nausea and vomiting. The patient is typically afebrile with tenderness in the epigastrium and (less commonly) the right subcostal region, but no peritonism. Routine blood tests are usually unremarkable in the uncomplicated case.

In acute cholecystitis, the primary pathological feature is inflammation of the gallbladder wall. It is thought that this is often a chemical cholecystitis initially (in the setting of an obstructed gallbladder concentrating the bile) and later merges into a bacterial cholecystitis. The patient has ongoing pain in the right upper quadrant which may radiate 'around' to the right flank or lower ribs, and there is tenderness below the right costal margin. A fever is usual, as is a moderate leucocytosis.

Differential diagnosis

Many cases of biliary colic are 'textbook' cases and ultrasound confirms cholelithiasis. Often however, the clinical presentation is not typical, although gallstones are present. In such cases, the demonstration that other common diseases are absent will make the gallstones a more likely culprit.

Peptic disease is perhaps the major differential for recurrent upper abdominal pain in an otherwise well patient. In cases where gallstones are present, but the clinical picture is not clear-cut, an upper gastrointestinal tract endoscopy is a useful investigation. If major peptic disease (eg. chronic duodenal ulcer) is present, then that becomes the presumptive diagnosis. If less severe disease is present (eg. antral gastritis), then a trial of effective therapy (proton pump inhibitor, +/- *Helicobacter pylori* eradication) is indicated.

Irritable bowel syndrome (IBS) is a differential of almost any cause of abdominal pain. It is well described that IBS has many and varied symptoms, and that these may change over time in a given patient. Features such as daily pain for years, prominent bloating, relief of pain with defaecation, and pain constantly present 24 hours a

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day are more suggestive of IBS and therefore predicate a cautious approach to the idea of surgical intervention.

Acute pancreatitis is another common differential for severe epigastric pain and vomiting. The typical history is of severe epigastric pain that radiates 'straight through' to the back (ie. upper lumbar region) and is often associated with nausea and vomiting. Abdominal tenderness may be marked, but the patient will not have peritonism. Amylase and lipase will usually confirm the diagnosis, but it is possible to miss the rise in these enzymes especially if the presentation has been delayed. In cases where the clinical suspicion is high – but the blood tests are nondiagnostic – a contrast enhanced computerised tomography (CT) scan will show a swollen pancreas with peri-pancreatic oedema.

Chronic pancreatitis is a less likely source of confusion, representing an ongoing illness that classically follows a relapsing course. However, this will not always be the case, and it may be that the initial diagnosis of chronic pancreatitis is made on CT scan. If gallstones are present (as for acute pancreatitis) then cholecystectomy is indicated as the gallstones are potentially the cause of the pancreatitis.

Cholesterolosis of the gallbladder can cause typical biliary pain in the absence of demonstrable gallstones. This condition is characterised by the accumulation of lipid filled histiocytes in the mucosa which gives rise to the appearance of a 'strawberry gallbladder'. The condition is present in 10% of autopsy cases, so it appears this is typically asymptomatic.[1] Symptomatic cases are associated with a degree of acute-on-chronic inflammation in the wall of the gallbladder. It is thought that the condition occurs due to the absorption of lipid from supersaturated bile. Sometimes the diagnosis is suspected because the mucosa is prominent on ultrasound (although that is a very 'soft' finding in most cases), or because of the presence of small mucosal polyps and cholesterol crystals on ultrasound.

Investigating gall bladder disease

Ultrasound

In most cases, the first investigation will be an upper abdominal ultrasound. This test is well tolerated and widely available. Where present, stones will be detected in more than 95% of cases (Figure 1). The investigation is chiefly limited by patient size, which must be remembered when a scan is reported as negative in an obese patient whose clinical presentation is suggestive of gallstone disease. The sensitivity of ultrasound for bile duct stones is poor – as low as 23% in some series.[2]

Biliary sludge

'Biliary sludge' is a common finding on ultrasound and may be the only abnormality reported. The sludge comprises crystals of cholesterol that may be suspended in the bile and tiny gallstones which are typically dependent. Therefore, sludge represents the earliest form of cholelithiasis. Obviously, the sludge cannot block the neck of the gallbladder and cause classic biliary colic, but it can be associated with pain which is typically due to acute on chronic inflammation with or without cholesterolosis. If sludge is present and the clinical picture is consistent with a biliary cause, then cholecystectomy is indicated.

Magnetic resonance cholangio-pancreatography

Magnetic resonance cholangio-pancreatography (MRCP) has become the standard investigation for suspected bile duct stones, and has in that sense replaced diagnostic endoscopic retrograde cholangio-pancreatography (ERCP) (Figure 2). It is sensitive and specific, and being noninvasive is free of the risks that pertain to ERCP. Although not often used simply to diagnose gallstones in the gallbladder, MRCP is very effective and may prove useful in a difficult case, especially in an obese patient. Magnetic resonance cholangio-pancreatography is not currently included in the Medical Benefits Schedule and patients will therefore have a significant out-of-pocket cost for this investigation when ordered privately.

CT cholangiography

Computerised tomography cholangiography combines the imaging quality of modern helical CT scanners with improved intravenous cholangiography agents. The technique involves an injection of contrast that is excreted in bile as the patient is imaged in the CT scanner. Contrast sensitivity is a contraindication, and as the test relies upon the excretion of contrast in bile, obstructive jaundice is a relative contraindication. In general, it is not possible to obtain good images of the biliary tree if the bilirubin is above 40 µmol/L (roughly twice the upper limit of the normal range). This technique can give excellent pictures of the biliary tree but will not show the gallbladder at all unless the cystic duct is patent – and hence is less useful in cases of biliary colic or cholecystitis.

Nuclear medicine biliary scanning

Nuclear medicine biliary scanning is often referred to as 'HIDA' scanning, although HIDA is just one of a series of technetium labelled compounds that may be used. In this technique, the radio labelled tracer is injected

intravenously and excreted in bile. Images are obtained using the gamma camera over a period of time and can be relied upon as functional rather than anatomical images (ie. they lack anatomic detail). The test may be combined with a fatty meal or cholecystokinin (CCK) challenge to provoke gallbladder emptying. The gallbladder ejection fraction can be computed and compared to the normal range. Sometimes the patient's pain will be provoked by the fatty meal or CCK injection. In uncomplicated cholelithiasis this test will be normal. If the cystic duct is blocked then the gallbladder will not fill. In some cases the gallbladder fills but does not empty and may be reported as 'nonfunctioning'. It is thought that this often relates to acute or chronic inflammation of the gallbladder wall. A decreased ejection fraction may be an earlier stage of this process, or may be a variant of normal.

Endoscopic retrograde cholangio-pancreatography

Endoscopic retrograde cholangio-pancreatography has been regarded as the gold standard for imaging of the bile duct but has been supplanted by the advent of MRCP. Significant complications of ERCP (bleeding, pancreatitis, cholangitis, perforation) occur in 10% of cases and the procedure related mortality is of the order of 1%. The 30 day mortality is up to 15%, but this reflects the underlying disease rather than late complications of the procedure.[2] Endoscopic retrograde cholangio-pancreatography has little role in the diagnosis of cholelithiasis; its main role being a therapeutic procedure in patients with known bile duct stones (*Figure 3*).

Management

The only effective management for symptomatic gallstones is cholecystectomy.[2] The management of a patient who is waiting for a cholecystectomy can be problematic. Attacks of pain may be very frequent and/or very severe. Any dietary trigger that the patient identifies should be avoided; it is probably worthwhile to recommend to all patients that they avoid fatty foods (especially fried food and rich dairy products). Pain needs to be treated on its merits and may on occasion necessitate an injection of opioid analgesic, attendance at an emergency department or admission to hospital. Antispasmodic agents such as hyoscine butylbromide can be very effective in some cases, but many patients do not gain any benefit. If attacks are occurring everyday for several days, then consider the possibility that the pathological process is merging into that of cholecystitis – a repeat ultrasound with urgent surgical review for

Figure 1. Ultrasound showing large gallstone with soft tissue mass at fundus (histology showed adenomyoma)

Figure 2. Gallstones seen on pre-operative MRCP

Figure 3. ERCP. Note: three stones on ERCP (the third is at the bottom of the duct). These could not be removed at ERCP and therefore a stent has been placed

those with an inflamed gallbladder is recommended.

Over the past 15 years, laparoscopic cholecystectomy has replaced open cholecystectomy as the elective operation of choice. There have been concerns raised that the laparoscopic operation may be associated with a higher rate of injury to the bile duct, but the evidence does not support this hypothesis. Operative cholangiog-

raphy remains a contentious issue with its proponents arguing that it diminishes the risk of a severe bile duct injury whereas its detractors point out that it is still possible to injure the bile duct despite having done a cholangiogram.[3] To this point in time, there is no evidence to show that cholangiography is harmful and there appears to be no reason to object to its routine use, except perhaps the technical difficulty associated with the laparoscopic cannulation of the cystic duct.

One clear advantage of operative cholangiography is the detection of unsuspected bile duct stone. In such cases the surgeon may attempt to remove the stone via the cystic duct using a basket to remove the stone by opening the bile duct and performing a laparoscopic exploration (*Figure 4a-e*) or to place a stent across the ampulla to decompress the duct and to facilitate post-operative ERCP. If cholangiography is omitted, then these stones will be undiagnosed until/unless the patient develops a complication.

There has been ongoing interest in the use of drugs that may dissolve gallstones (litholytic agents such as ursodeoxycholic acid) used either alone or in combination with extra-corporeal lithotripsy, but the results have been disappointing and these methods have been abandoned. Litholytic agents may be useful in patients with cholestatic liver disease, especially those who
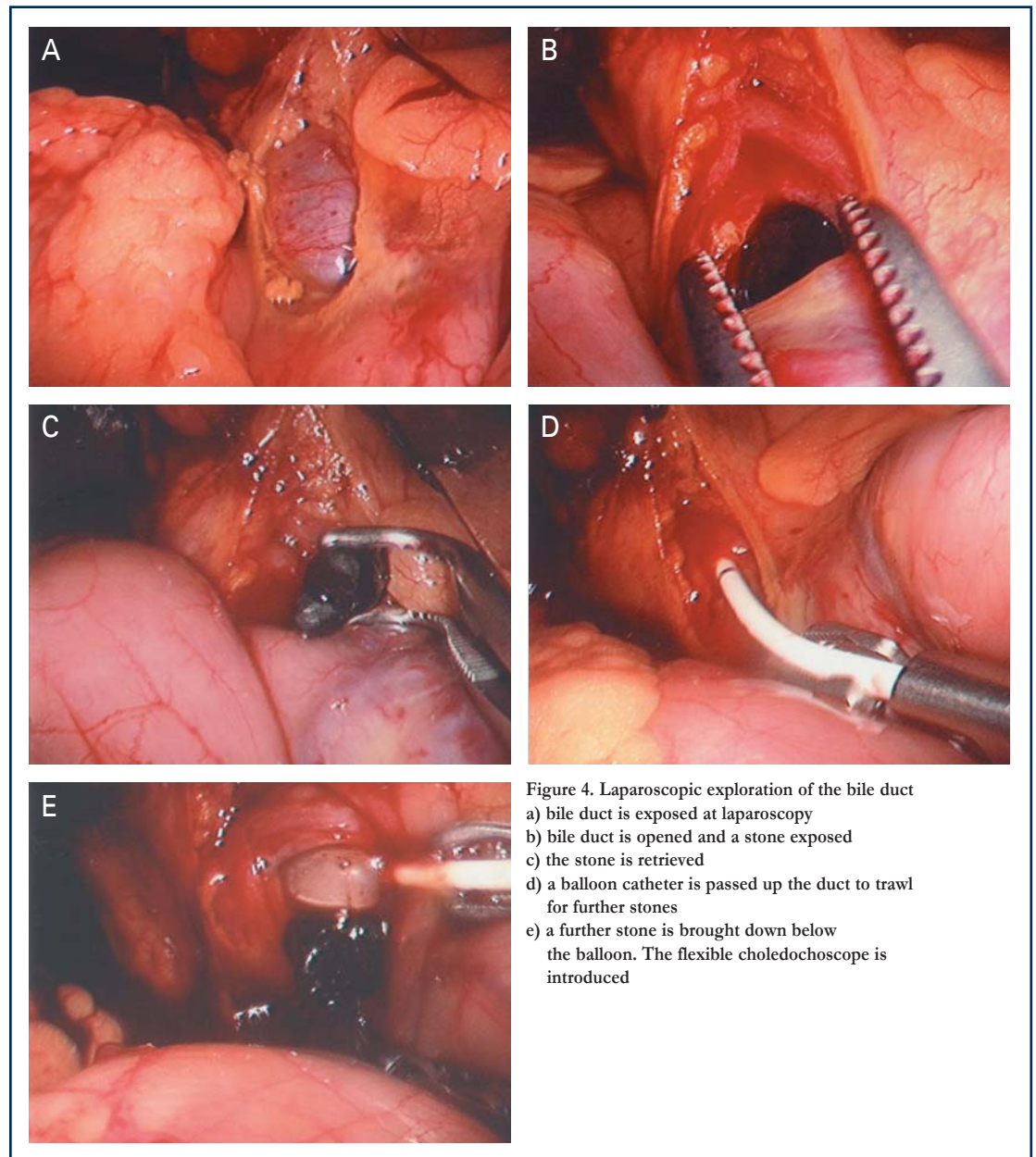

Figure 4. Laparoscopic exploration of the bile duct
a) bile duct is exposed at laparoscopy
b) bile duct is opened and a stone exposed
c) the stone is retrieved
d) a balloon catheter is passed up the duct to trawl for further stones
e) a further stone is brought down below the balloon. The flexible choledochoscope is introduced

repeatedly form intra-hepatic stones, but this is a separate issue to 'routine' cholelithiasis.

Asymptomatic gallstones

Asymptomatic gallstones are a common incidental finding when imaging is ordered for other clinical presentations. The conventional advice has been that cholecystectomy is not indicated prophylactically. This approach has largely been predicated upon the results from the era of open cholecystectomy – which is a more morbid operation than the laparoscopic one – but it remains the consensus position. Some patients will be anxious about the risk of gallbladder cancer and it is true that there is a small increase in absolute risk in the setting of chronic cholecystitis, however, it must be remembered that this is a rare tumour. For anxious patients a laparoscopic cholecystectomy is a reasonable option given that morbidity is low. A calcified or 'porcelain' gallbladder (in contrast to a calcified gallstone) is at high risk of malignancy and cholecystectomy is mandatory.

Patients with bile duct stones

Suspect bile duct stones when the patient:
- presents with cholangitis
- presents with jaundice
- presents with pancreatitis
- has a dilated bile duct on ultrasound
- has an obstructive pattern on liver function tests.

These patients warrant a preoperative MRCP or CT cholangiogram to determine whether bile duct stones are present. If bile duct stones are present, then preoperative ERCP is indicated with the aim of clearing the bile duct before surgery.

If ERCP is not possible (eg. there is previous surgery such as a distal gastrectomy) or not successful (eg. the ampulla is hidden within a duodenal diverticulum) then the surgical strategy will need to take account of this. In most cases this will mean the bile duct will be explored (open or laparoscopically) at the time of cholecystectomy.

Patients with no gallstones but 'poor ejection fraction'

This is a contentious area. Some argue that a gallbladder that empties poorly on biliary scan is always pathological and is a cause of symptoms, whereas others argue that this finding is really a normal variant. It seems most likely that poor gallbladder contraction is sometimes a result of pathology in the gallbladder wall and therefore some patients with this finding will benefit from cholecystectomy. Jones et al[4] treated 36 patients who had 'recurrent typical biliary colic' but no gallstones on ultrasound with laparoscopic cholecystectomy, and noted that 29 of the 33 patients who had undergone preoperative biliary scanning had a decreased gallbladder ejection fraction (mean 9%, normal >35%). Twenty-six of the 28 patients (one lost to follow up) with low ejection fraction were improved, but this is not appreciably different from the overall result of 32 of the 35 patients being improved by the surgery. Approximately one-third of patients had ongoing nonspecific symptoms such as bloating or flatulence.

Conclusion

Biliary colic is typically felt as constant epigastric pain lasting between 30 minutes and several hours and is frequently associated with nausea, vomiting and radiation to the interscapular region. Laparoscopic cholecystectomy is the appropriate definitive treatment. Ongoing pain, fever and leucocytosis are suggestive of acute cholecystitis. Cholangitis, jaundice, pancreatitis, an obstructed pattern on liver function tests or a dilated bile duct on ultrasound raises the possibility of bile duct stones.

In most cases gallstones are readily diagnosed on upper abdominal ultrasound, but diagnosis may be more difficult in an obese patient and bile duct stones may not be seen on ultrasound. In such instances other investigations such as MRCP, CT cholangiography or nuclear medicine scanning may be required. With the advent of MRCP, ERCP now has little role in the diagnosis of cholelithiasis. Its main role is as a therapeutic procedure in patients with known bile duct stones.

Conflict of interest: none

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