

Right hypochondrial pain: a case study

Abstract

This article will review the pathophysiological manifestations of a patient who acutely presented to a surgical assessment unit with severe right hypochondrial pain radiating into the right scapula with associated symptoms including nausea, dark urine and pale stools. After further tests and investigations a diagnosis of cholelithiasis was given. Cholelithiasis, commonly referred to as gallstones, has a prevalence of approximately 20% in western societies affecting over 5.5 million United Kingdom adults. However, 80% of patients with gallstones are asymptomatic, but despite this, since the 1990's there has been a 53% increase in hospital admissions; with over 70000 cholecystectomies performed in 2016/17, making this one of the most commonly performed operations, costing the NHS in excess of 110 million pounds.

Evaluation into underlying pathology, pathophysiology and clinical manifestation of symptoms of this case study will be detailed; establishing the importance of the application of a systematic approach when formulating end diagnosis alongside considered differential diagnoses. Furthermore, appropriate investigation, treatment pathways developed from evidence-based practice will be reviewed, evaluated and right hypochondrial pain discussed.

Keywords:

Hypochondrial pain, cholelithiasis, gallstones, cholecystitis, cholecystectomy

CPD reflective questions

Consider lifestyle advice to give to patients regarding symptom management of gallstones?

Consider your communication to patients, regarding the diagnosis, and pre or post interventional treatment?

What concerns should be raised regarding patients presenting with new onset jaundice with consideration to differential diagnoses?

Introduction

Gastrointestinal disturbance and abdominal pain are the third highest presenting complaint to accident and emergency departments in the United Kingdom (UK); with over 800,000 reported cases in 2016/17 (National Health Service, NHS Digital, 2018). Of these cases over 50% presented with upper abdominal pains (Leath and Lowery, 2018), with biliary pathology being the lead causative factor (Beckingham and Ryder, 2001). Patient X presented with severe right hypochondrial pain radiating into the right scapula; associated symptoms included nausea, dark urine and pale stools. Differential diagnoses were considered (Table 1), but after clinical assessment, laboratory results and imaging a diagnosis of cholelithiasis was given.

Prevalence of gallstones

Cholelithiasis, commonly referred to as gallstones, has a prevalence of approximately 20% in western societies (Rance and Jones, 2015) affecting over 5.5 million UK adults (Beckingham and Ryder, 2001). The majority, approximately 80% of individuals are asymptomatic (National Institute for Health and Care Excellence, [NICE], 2014) with the incidence of developing symptoms 2-4% per annum. Despite only 20% of individuals being symptomatic, in the UK alone there has been an 53% increase in hospital admissions since the 1990's (Kang et al, 2003); with over 70000 cholecystectomies performed in 2016/17 (NHS Digital 2017) making this one of the most commonly performed operations, costing in excess of 110 million pounds (NICE, 2014). Mortality from non-complicated gallstones is extremely rare, less than 0.6% (Stinton and Shaffer, 2012); that said morbidity and mortality risk increases ten-fold with some of the potential complications such as pancreatitis or cholangitis paired with a pre-morbid aging population (European Association for the Study of the Liver, [EASL], 2016).

Gallbladder anatomy

The gallbladder is approximately 9cm in length and positioned above the transverse colon, inferior and posterior to the liver, within the right hypochondrium (Clavien and Baillie, 2006). The main function is that of a bile reservoir, to store and release the bile salts produced by the liver. (Dooley et al. 2011). The motility is controlled by a number of mechanisms involving nerves, peptides and hormones primarily Cholecystokinin (CCK). Clavien and Baillie (2006) explain after ingestion of food, CCK initiates a cephalic response which stimulates contractions in the smooth muscle of the gallbladder walls, alongside relaxation of the sphincter of Oddi, allowing bile to flow through the common bile duct (CBD) into the duodenum.

Bile

Bile is a complex fluid with water making up 85-95%, other components include cholesterol, acids, phospholipids, bilirubin, proteins and muco-proteins (Dooley et al. 2011). Bile has two main functions, aiding in digestion and eliminating certain waste products such as haemoglobin and excess cholesterol from the body.

Formation of gallstones

When there is an imbalance of these substances' crystallisation can occur, leading to sludge and ultimately stone formation. Based on their composition there are two main aetiologies of stone; cholesterol and pigment (Kumar and Clark, 2012). Cholesterol stones form when there are excessive amounts of cholesterol within the bile; due to one or a combination of three defects, accelerated nucleation, cholesterol supersaturation of gallbladder bile or gallbladder hypomotility (Shaffer, 2018). Pigment stones are split into two sub-types based on their chemical compounds. Brown stones, which form as a result of bile stasis or infection in the bile ducts and are predominately unconjugated bilirubin and calcium salts. Black stones consist of insoluble bilirubin pigment polymer and calcium phosphate salts, primarily associated with chronic haemolysis or liver damage (Clavien and Baillie, 2006).

Cholesterol stones account for 90% in western societies (EASL, 2016). Shaffer (2005) explains gallstone formation is multifactorial but the 21st century lifestyle of processed food, little physical activity and rise in obesity is one theory behind cholesterol stones accounting for such high percentage. This is reiterated by Stender, Nordestgaard and Tybjaerg-Hansen (2013) who concluded that risk of symptomatic gallstones increased by 7% for every 1kg/m squared increase in body mass index (BMI). Other key risk factors include genetics, advancing age and gender. Multiple studies are in agreement that females have a 2 to 3 times higher risk than males, believed caused by higher oestrogen levels, increasing biliary cholesterol secretion and altering gallbladder motility (Dooley et al, 2011). Factors including hormonal changes, pregnancy and use of hormone derived medications such as oral contraceptive pill have been proven to increase risk of stone formation (Sun et al, 2009). Patient X had both modifiable and non-modifiable risk factors (See Appendix 1) supporting a diagnosis of gallstones.

Pain

Pain is the most common presenting complaint of non-complicated gallstones (Shaffer, 2018). Biliary natured pain, known as biliary colic, tends to follow certain patterns; characteristics are described as episodic, sudden onset, constant, right hypochondrial pain that increases in intensity, reaches a crescendo then spontaneously resolves (Kumar and Clark, 2012). Soliman et al, (2018) concluded intermittent bouts of pain that resolve within 1 hour is indicative of gallstones, another positive predictor in this study was pain in the evening or night, which was suffered by the majority, 88% of the subjects studied. Patient X was admitted late evening describing an exact mirror of the described biliary colic pain, which radiated into the back. Radiated pain alongside biliary colic are the two most significant positive predictors for gallstones (EASL, 2016). This is supported by Berhane et al, (2006) where all 220 patients displayed right upper quadrant pain, with 63% suffering radiating pain. This study also displayed that 66% of individuals pain preceded ingestion of fatty foods. Thistle et al. (2011) challenges this, concluding post prandial pain did not predict post cholecystectomy relief; in fact, pain within 30 minutes of eating was a negative association. That said, post prandial pain is regularly referred to in key literature as an indicator for gallstones (Kumar and Clark 2012; EASL, 2016). Marciani et al, 2013 found that long chain fats with high emulsification caused a 42% bile volume change, with the school of thought that the sudden change in volume over stimulates CCK causing excessive stimulation of the smooth muscles, manifesting into a spasmodic effect.

There are two major causes of pain manifestation that either originate from the gallbladder or involve the gallbladder, both altering the natural mechanisms. The first being intermittent or complete blockage of any of the ducts by gallstones, impairing bile filtration and gallbladder motility; the second being the stones and or inflammation, cause irritation and infection of the surrounding tissues leading to localised peritoneal irritation and subsequently if untreated peritonitis (Kumar and Clark, 2012).

Acute cholecystitis

Localised peritonism is more indicative of acute cholecystitis, one of the considered differentials. As a result of this inflammatory process individuals are likely to present with fever, pain lasting several hours or days, previous episode of biliary pain and tenderness on

palpation known as Murphy's' positive (Gomes et al, 2017). Murphy's sign is a clinical examination tool where when the subcostal region of the right hypochondrium is palpated on inspiration the gallbladder to descent towards the examiners hand, evoking pain and a sudden cessation of inspiration (Douglas, Nicol and Robertson 2013). Trowbridge, Rutkowski and Shojania (2003) conducted an extensive data analysis and concluded Murphy's sign to be highly specific and sensitive with a high positive predictor rate for the diagnosis of cholecystitis. This is further supported by Singer et al, (1996) study, where Murphy's sign had a sensitivity of 97.2% and a positive predictive value of 93.3%. However, this study was relatively small, only having 53 subjects all from one demographical area, questioning its transferability to an international level. This question reiterates Douglas, Nicol and Robertson (2013) findings who display a more clinically realistic figure with pooled sensitivity of 50-97% and specificity of 50-80%, suggesting Murphy's sign should not be used exclusively as a tool for diagnosis or exclusion.

Cholecystitis can be in acalculous or calculous origin; patient Xs history was suggestive of gallstones, a calculus pathology. Acalculous cholecystitis is rare affecting less than 10% with an extremely high morbidity and mortality risk (Dooley et al, 2011). Individuals affected are likely to have predisposing co-morbidities or be acutely unwell. A complex multifactorial pathogenesis including ischaemia, empyema, bile stasis and bile infiltration manifest in an acute necro inflammatory process (Huffman and Schenker, 2010).

Calculus cholecystitis

Calculus cholecystitis is prolonged obstruction of the cystic duct by impacted stones (Dooley et al, 2011). The obstruction increases intraluminal pressure, compromising blood flow and lymphatic drainage which triggers an acute inflammatory response by stimulating the synthesis of prostaglandin I2 and E2 (Bellows, 2018). Indar and Beckingham (2002) continue explaining the stagnant supersaturated bile becomes extremely noxious to surrounding structures, causing ulceration to the mucosa and susceptibility to bacterial invasion of various microorganisms. If untreated, activation of the systemic inflammatory cascade by endotoxins or exotoxins occurs (Sartelli et al, 2014). This complex process involves humoral and cellular responses, manifesting in acceleration and exaggeration of macrophage-derived cytokines release and effect. Tissue necrotic factor (TNF), Interleukin 1 alpha and beta (IL1) are key cytokines. The action of TNF and IL1 orchestrates a febrile response via the sympathetic nervous system, they also aid the triggering of a thrombolytic cascade leading to a hypercoagulable state and increased vascular permeability. The amplified pro-inflammatory and anti-inflammatory cytokine production induces widespread dysregulation of innate systems and ultimately multi organ failure (Widmaier, Raff and Strang, 2011).

In this case study, the absence of pyrexia, with stable vital signs and a negative Murphy's sign, cholecystitis was deemed unlikely. However NICE (2017) reiterate clinicians should not depend purely on history and examination to diagnose or exclude conditions without the support of biochemistry, haematology or imaging. First line investigations included an Ultra-Sound Scan (USS) alongside biochemistry and haematology tests; deemed mandatory in acute abdominal pain presentations (RCS, 2014).

Abdominal ultrasound

USS is seen as the gold standard investigation for abdominal pain of biliary nature (NICE 2014), with a positive predictive value of 92% and negative predictive value of 95% (Kumar and Clark, 2012). Summers et al (2010) supports the use of USS in biliary presentations concluding an 88% sensitivity and 87% specificity even when used in an emergency setting by non-radiologists. Furthermore, USS does not require ionising radiation, are non-invasive, quick, readily available, are transferable to the patient's location, relatively low cost and have the ability to evaluate adjacent organs (Bortoff et al, 2000).

Common bile duct size

As suspected, patient X's USS confirmed the presence of gallstones. In the absence of wall thickening, distension, oedema or pericholecystic fluid, cholecystitis was disregarded (Bortoff et al. 2000). It did however display an 8mm common bile duct (CBD). A CBD greater than 6mm, is classified as dilated and increases likelihood of CBD stones (EASL, 2016), estimated to be present in 10-20% of symptomatic individuals (Williams et al, 2017). Factors such as age, previous cholecystectomy and BMI all significantly affect the diameter of the CBD (Peng et al. 2015) therefore, individualistic interpretation is required. In this case, with stated factors considered and in combination with liver function test (LFT) derangement there was high probability of the presence of CBD stones.

Liver function derangement

LFT derangement can be described as hepatocellular where alanine transaminase (ALT), aspartate aminotransferase (AST) and bilirubin are elevated; or cholestatic with predominant elevation of alkaline phosphate (ALP), gamma-GT (GGT) and bilirubin (Ramnarace, 2018). This suggested pattern is supported by Peng et al. (2005) and Ahn et al (2016) whose studies both concluded GGT to be the highest predictive value for CBD stones with a sensitivity 80-86% specificity 74.5%-76%. Gurusamy et a,. (2015) Cochrane review adds support finding ALP has a 92% sensitivity and 79% specificity in detection of CBD stones. However, Resnick et al, (2016) found that in fact a sharp rise in ALT and AST were present in early presentations with enzymes including bilirubin having a slower onset of elevation, questioning the reliability of categorising LFTs into specific clinical pictures. Dooley et al, (2011) continue explaining with LFTs it is the overall trend, patterns amongst the different enzyme levels, amount changed from the classified normal limits and alterations from the individuals' baseline that is the more reliable method in distinguishing severity and underlying pathologies of jaundice.

Jaundice

Hyperbilirubinaemia, commonly known as jaundice; is defined as an increased concentration of circulating bilirubin above the normal laboratory upper limit. Patient X had a bilirubin of 31 however had no visible clinical signs such as yellowing to the skin and sclera; for these signs to be apparent a 50% increase to approximately 40mmol/l is required (Beckingham and Ryder, 2001). Bilirubin is the end result of the catabolism of haem (Ramnarace, 2018). As each red blood cell traverses through the reticuloendothelial system, when the cell membrane is too fragile to allow this it can rupture, subsequently releasing cellular contents including haemoglobin into the blood (Feldman, Freidman and Brandt, 2006).

Haemoglobin is phagocytosed by macrophages, and split into its haem and globin portions. Two reactions occur to the haem molecules, the first oxidation reaction is catalysed by the microsomal enzyme haem oxygenase and results in biliverdin, the cytosolic enzyme biliverdin reductase enables reduction of biliverdin to pigments called bilirubin (Abbas et al, 2016). Classified as unconjugated bilirubin it binds to serum albumin to be transported to the liver where it is conjugated with glucuronic acid becoming water-soluble to enable excretion (Widmaier, Raff and Strang, 2011).

Jaundice aetiology is classified as haemolytic, hepatocellular or cholestatic, depending on which part of the physiological mechanism the pathology affects. (Kumar and Clark, 2012). Haemolytic occurs when there is an increased rate of haemolysis caused by certain genetic disorders such as sickle cell anaemia, leading to higher levels of unconjugated bilirubin then the liver is able to excrete (Abbas et al, 2016). Hepatocellular occurs as a direct consequence of damage to the liver itself, inhibiting one or more of its normal functions and ability to conjugate or excrete bilirubin adequately (Novo and Welsh, 2017). Considering differential diagnosis with patient X the above pathologies were excluded on the basis of lack of pre-existing co-morbidities and absence of risk factors.

Cholestatic jaundice

Cholestatic jaundice occurs when there is marked disruption to the secretion and flow of bile at any level of the bile excretory pathway, depending on the level of the obstruction it can be classified as intra or extrahepatic. Intrahepatic is due to a functional impairment of the parenchymal cells and intrahepatic ducts, extrahepatic is due to an excretory block outside of the liver such as strictures or stones causing partial or complete blockage (Dooley et al, 2011). Obstruction leads to an accumulation of conjugated bilirubin resulting in symptoms such as dark urine, pale stools and pruritis; symptoms reported by patient X. The increase of conjugated bilirubin in the urine without urine-urobilinogen results in darkened colour. As increased bilirubin is excreted in the urine, less reaches the gastrointestinal tract giving stools a pale clay like appearance due to the absence of bile pigments which give faeces their normal colour, the absence of bile can also inhibit fat digestion further attributing to change in colour and consistency of faeces (Pavlidis and Pavlidis, 2018). Pruritis exact mechanism is widely debated but is thought to be related to the deposited bile acids and salts in the skin alongside the release of endogenous opioids (Clavien and Baillie, 2006).

Following a symptomatic episode of cholelithiasis there is a 50% chance of recurrent symptoms with a 10–15% readmission rate (RCS, 2013) therefore definite treatment in the form of an early cholecystectomy is recommended (NICE 2014); this was the advice given to patient X. Laparoscopic is now the standard method even in the presence of moderate complications with over 93% of cholecystectomies performed laparoscopically (EASL, 2016). EASL (2016) guidelines explore advantages which include lower rates of complications, reduced hospital stay and operation time, quicker convalescence and increased cost effectiveness.

Traditionally with suspicion of CBD stones further imaging was deemed essential prior to surgery (Dooley et al. 2011) however, guidance from the Royal College of Surgeons (2013) state patients with deranged LFTS, in the absence of frank jaundice have under 15% risk of the presence of CBD stones at the time of intervention and may proceed to laparoscopic cholecystectomy (LC) with bile duct exploration (LCBDE) as a one-stage intervention or two-

stage endoscopic retrograde cholangio pancreatography (ERCP) followed by LC, both methods equilibria. A meta-analysis by Singh and Kilambi (2018) reiterated that LCBDE displayed no significant difference in complication or mortality rates, has increased stone clearance ability and lower rates of technical difficulty. LCBDE has also displayed cost effectiveness and improved median length of hospital stay from 4 to 2.5 days (Mattila et al. 2017). Furthermore, Dassari et al. Cochrane review exploring surgical versus endoscopic treatment of CBD stones found ERCP to have over 10% risk of serious complications such as pancreatitis, haemorrhage, cholangitis and duodenal perforation. That said, LCBDE requires a longer anaesthetic time, is yet to be as readily available and only performed in specialist centres, meaning likely longer waiting times for one-stage intervention (Williams et al. 2017). As clinician's the decision of any intervention should be made on an individualised basis considering clinical information, benefit and risks; both of the chosen intervention, the likelihood of recurrent symptoms and serious complications both with managing conservatively and any suggested interventions (EASL 2016).

Communication

Biliary symptoms are often varied and can resemble many disorders the diagnosis and differential diagnosis in this case was established primarily through detailed history of presenting complaint and clinical examination, later supported by investigations. Fisherman and Cullen (2014) reiterate the importance of the initial consultation stating up to 90% of sound clinical reasoning and subsequently appropriate investigation and management comes from history alone. High standard, unambiguous, communication both verbal and non-verbal are paramount in all aspects of healthcare, especially the initial patient consultation. Effective two-way communication increases the likelihood patients will share pertinent information, feel involved in the decision-making process, trust the practitioner, follow advice given, adhere to treatment plans and enhance the overall recovery process (Chandra, Mohammadnezhad and Ward, 2018). Furthermore, an observational study by Little et al. (2001) found good communication the single strongest predication of overall patient satisfaction and management of patient expectations. Throughout this consultation patient X was listened to, updated regularly of any results, given full explanations behind the decisions being made and shared decision making was both supported and encouraged; not only ensuring Patient X had a positive experience and understanding of the condition but adhering to both professional regulations and NICE Guidance (2012). This stresses the importance of engendering excellent communication skills for all health care professionals.

Conclusion

This article has reflected on a patient who presented acutely with severe right hypochondrial pain, radiating into the right scapula, with associated symptoms including nausea, dark urine and pale stools. Evaluation into underlying pathology, pathophysiology and clinical manifestation of symptoms has been detailed; establishing the importance of the application of a systematic approach when formulating end diagnosis alongside considered differential diagnoses. Furthermore, appropriate investigation, evidenced based treatment pathways has been reviewed and evaluated. Collectively these factors, alongside effective communication ensure sound clinical reasoning and high quality patient centred care.

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Table 1. Case study template
Age: 35
Gender: Female
Presenting Complaint: Right hypochondrial pain
<p>History of Presenting Complaint and Symptoms:</p> <ul style="list-style-type: none"> • 3 weeks of intermittent pain, increased severity in the last 24 hours, not settled as normal with simple analgesia. • Pain described as sudden onset, constant dull ache, increasing into a sharp spasmodic stabbing sensation, 9/10 at the worse, currently 4/10. • In the last 24 hours pain has radiated into the right scapula. • Pain appears worse following a meal. • Nausea but no vomiting, appetite reduced when pain present. No recent weight loss. • No fevers/ shakes/ sweats. Fells well in self between pain bouts. • Bowels open daily, looser then normal- reports pale stools, no blood or mucus. • No urinary frequency, burning or urgency- reports urine darker than normal last 24-48 hours. • No PV discharge or irregular bleeding. LMP 3/52 ago.

Past medical history: Anxiety & depression	
Drug history: Sertraline; levonorgestrel (ocp); multi vitamins (otc);	
Allergies: NKDA	
Social History: Lives with partner and son (3 years old) Unemployed- previously worked in retail	
Family History: Mother- T2DM, Gallstones, MI; Paternal Grandmother- T2DM, Breast Cancer	
Risks: Non-Smoker; No illicit drug use; Less than 8 units of alcohol a week; Obese BMI 40	
Investigations and examination findings: <ul style="list-style-type: none"> • BP- 148/82 • P- 102 • R- 16 • S- 98%RA • T- 36.8 • BM- 4.2 	
Clinical Examination:	
General Inspection	Good Pallor Looks settled, no obvious signs of distress, SOB or acute pain at present Moving freely No adjuncts No obvious hernias or deformities
Abdo	Soft, No guarding or peritonism Maximum tenderness in the right hypochondrium No masses/ fullness/ hernias Murphy's negative Bowel sounds present
CVS	Heart sounds I+II+0
Resp	Able to talk in full sentences Bilateral equal air entry Normal resonance, no added sounds
Investigations/Imaging: <ul style="list-style-type: none"> • Urinalysis- NAD • Urine Amylase- 241 • BHCG- Negative • Erect CxR- No consolidation or free air under the diaphragm • USS- Within the gallbladder there are multiple calculi, no pericholecystic fluid or thickening is noted. The common bile duct measure 8mm, there is no intrahepatic duct dilation. Where visualised the liver, spleen, aorta and both kidneys appear normal. 	
Laboratory Results:	

FBC	WCC- 8.39 HB- 142	
CRP	2	
U&Es	Sodium- 137 KCL- 3.8 Urea- 3.9 Creatinine- 80 eGFR- >60	
LFTs	Alk Phos- 106 ALT- 471 GGT- 169 Bili- 31	
Amylase	71	
Serum Glucose	5.8	
Diagnosis(s): Biliary Pathology/ Gallstones		
Differential Diagnosis(s):		
<ul style="list-style-type: none"> • Gastritis • Cholecystitis • Pancreatitis • Obstructive Jaundice • Cholangitis 		
Potential management /referrals/communication:		
<ul style="list-style-type: none"> • Analgesia and Anti-emetic • IV Fluids • Bloods including FBC, U&Es, CRP, LFTs and Amylase • Urine dip, urine amylase and BHCG • Abdominal ultra-sound scan • Gallstone information leaflets including dietary advice and laparoscopic cholecystectomy • Full explanation & listing for elective laparoscopic cholecystectomy +/- CBD exploration <p>(In this case the on-call consultant was an HBP specialist- if another speciality were on-call referral would have been place to the HBT team)</p>		