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Acute cholangitis: Diagnosis and management

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Abstract

Acute cholangitis is a serious septic condition of the biliary tract. It is associated with obstruction of the biliary passages. Early diagnosis and assessment of the severity is essential. Aggressive supportive care, commencement of appropriate antibiotics, optimizing the function of various vital organ systems and early biliary drainage are pivotal in reducing the morbidity and mortality associated with this condition.

Keywords: Acute cholangitis diagnosis severity management

Introduction

Infections of the biliary tract are commonly encountered in surgical practice. Acute cholecystitis and acute cholangitis are the common biliary tract infections. The aetiology of acute cholangitis is variable ranging from stone disease to malignancy. Early diagnosis and prompt treatment is essential. The morbidity and mortality associated with acute cholangitis is quite high if diagnosis and treatment is delayed ^[1]. The aetiopathogenesis, diagnosis, severity assessment and management of acute cholangitis is discussed in the paper.

Aetiopathogenesis

Normal defence mechanisms in the biliary system preventing infection

There are a multiple mechanisms which protect the biliary system from infection ^[1, 2, 3].

1. Continuous normal free flow of bile in the biliary passages keeps the intraductal pressure low and flushes out the passages thereby preventing bacterial concentration.
2. Bile salts have bacteriostatic activity.
3. Biliary epithelium secretes IgA which is protective and also secretes mucus which has anti-adherent properties.
4. Kupffer cells in the biliary epithelium and tight junctions between the cholangiocytes prevent translocation of bacteria from the hepatobiliary system into the portal venous system.
5. The sphincter of Oddi prevents any migration of bacteria from the duodenum into the biliary system.

In an obstructed system there is a rise in the intraductal pressure due to stagnation of bile. The tight junctions between the cholangiocytes widen leading to entry by bacteria. The function of the Kupffer cells is also altered accompanied by fall in Ig A levels. This leads to successful bacterial invasion of the biliary passages ^[3, 4].

The normal choledochal pressure is 7 to 14 cms of water. Complications develop when the pressure exceeds 25 cms of water. There is cholangiovenous and cholangiolymphatic reflux. Bacteraemia followed by release of endotoxins occurs. There is release of inflammatory mediators like TNF, IL-1, IL-6, and IL-10 leading to hemodynamic insufficiency ^[4].

The commonest cause of cholangitis is biliary obstruction. Choledocholithiasis, strictures and malignancy are the common causes of obstruction. However there is wide spectrum of causes for biliary obstruction. (Table 1)

Ascending cholangitis can occur due to migration of bacteria from the duodenum into the common bile duct ^[5]. Rarely do bacteria translocate from the portal vein into the bile duct. Other rare causes of cholangitis are primary biliary cholangitis, primary sclerosing cholangitis, Ig G4 related autoimmune cholangitis, and recurrent pyogenic cholangitis or oriental cholangiohepatitis ^[6].

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Understanding the spectrum of bacterial flora causing cholangitis is essential for proper choice of antibiotic therapy. Coliforms are the predominant organisms isolated from bile in acute cholangitis. These include *E. coli* (25-50%), *klebsiella* (15-20%), *enterococcus* species (10- 20%) and *enterobacteriaceae* (5-10%) [6, 7].

Anaerobic organisms like *bacteroides fragilis*, *Cl. Perfringens* are found in elderly population or in those patients who have already undergone biliary tract surgery [8]. In a few cases, parasites have also been identified in bile. These include liver flukes *clonorchis sinensis*, *opisthorchis viverrini*, *opisthorchis felinus* and *ascaris lumbricoides*.

Recurrent acute cholangitis (oriental cholangiohepatitis) is an uncommon condition [9]. It is associated with pigment stones in the intrahepatic ducts predominantly in the lateral segment of the left lobe or in the posterior segment of the right lobe. Though the exact etiopathogenesis is unknown, it is associated with malnutrition and parasitic infestations such as *ascaris lumbricoides* and *clonorchiasis*. Transient portal bacteraemia allows entry of bacteria into the biliary system initiating a cycle of infection and stone formation. In 5% of cases there is a likelihood of development of cholangiocarcinoma [9].

Clinical features

The common symptoms are right upper quadrant abdominal pain, high grade fever for more than 24 hours and jaundice. This is typically described as Charcot's triad. It has a sensitivity of 26.4% and specificity of 95.9% in diagnosing acute cholangitis [9, 10]. When the severity of cholangitis escalates, hypotension and mental obtundation are seen in addition to pain, fever and jaundice. The five features together constitute Reynold's pentad. Charcot's triad is suggestive of acute cholangitis in 26.4 to 72% of cases [9, 10].

Physical examination will reveal high fever, tachycardia, hypotension, jaundice and altered sensorium in severe cases. Abdominal examination will reveal tenderness in the right hypochondriac and epigastric region.

Investigations

Complete blood count, liver function tests, PT/INR and renal profile are baseline haematological investigations. Inflammatory markers such as CRP and ESR are quite helpful [11, 12]. Blood cultures are useful in determining the spectrum of organisms causing cholangitis. Imaging modalities range from ultrasound imaging to MRCP [11, 12]. The main aim of imaging is to identify the obstructing pathology. Collecting a bile sample during a drainage procedure is likely to yield a positive culture in 59-93% of acute cholangitis cases [13].

Diagnosis

The new Tokyo guidelines (TG 13) help in ascertaining the diagnosis of acute cholangitis [9]. These take into consideration three parameters, inflammatory, cholestatic and imaging results [9, 10].

1. Systemic inflammation

A-1 Fever more than 38° C with shaking chills.

A-2 Laboratory data (Evidence of inflammatory response)

WBC <4000/cmm or > 10,000/cmm.

C reactive protein (CRP) ≥ 1mg/dl.

2. Cholestasis

B-1 Jaundice (Total bilirubin ≥2mg/dl)

B-2 Laboratory data

Alkaline phosphatase > 1.5x upper limit of normal (IU)

γ glutamyl transpeptidase > 1.5x upper limit of normal(IU)

AST/ALT > 1.5 x upper limit of normal (IU)

3. Imaging

C-1 Biliary dilatation

C-2 evidence of aetiology in imaging (stone, stricture, stent)

Suspect diagnosis of acute cholangitis: one item in A + one item in B or C.

Definitive diagnosis of acute cholangitis: one item in A + one in B + one in C.

The sensitivity of TG 13 in diagnosis of acute cholangitis is 91.8% and specificity is 77.7% [10]. The false positive rate for TG 13 is 5.9%, 11.9% for Charcot's triad [10].

Assessment of severity

Severity of cholangitis will determine the response to initial medical treatment and the possibilities of organ dysfunction. (TG13 guidelines) Hence it is very important to assess the severity of acute cholangitis [9, 10].

Grade I (mild acute cholangitis)

No organ dysfunction

Does not meet the criteria of moderate acute cholangitis

Responds to antibiotic treatment.

Grade II (moderate acute cholangitis)

No organ dysfunction

Does not respond to initial antibiotic treatment

Two out of the following five criteria should be present

1. WBC > 12,000/cmm or < 4000/cmm
2. High temperature ≥39 °C
3. Elderly (age > 75years)
4. Total bilirubin ≥5mg/dl
5. Hypoalbuminaemia (<0.7 x lower limit of normal)

Grade III (severe acute cholangitis)

Does not respond to initial medical treatment

Organ dysfunction present in at least one of the following organ systems.

1. CVS – dopamine infusion ≥ 5 µg/kg/min
2. CNS- altered consciousness
3. RS- PaO₂ /FiO₂ ratio < 300
4. Renal- oliguria / S creatinine > 2mg/dl
5. Hepatic: INR > 1.5, platelet < 1 lakh.

In acute suppurative cholangitis there is formation of pus in the biliary passages. On ERCP, pus is seen coming from the ampulla of Vater. Severe acute cholangitis or toxic cholangitis is seen in 5% of all cholangitis cases [11, 12].

Treatment

The most important primary step towards treatment is aggressive resuscitation of the patient [13]. Majority of patients are hemodynamically compromised. Hence fluid resuscitation is essential. Supportive infusions of fresh frozen plasmas and vitamin K injections are helpful in preventing coagulopathy. Once haemodynamic stability is achieved then two issues need to be addressed, control of infection and relief of obstruction [13]. The choice of antibiotic for control of infection depends upon multiple factors [14]. These include

1. Renal status
2. Hepatic status
3. Drug allergies

4. Co morbidities
5. Hospital acquired infections.

Initially empiric antibiotic therapy covering gram positive and anaerobic organisms needs to be started. There are a wide variety of antibiotics which can be used. These include piperacillin- tazobactam, ticarcillin- clavulanate, ceftriaxone with metronidazole and ampicillin with sulbactam. In patients sensitive to penicillin, ciprofloxacin with metronidazole, carbapenem or gentamicin with metronidazole can be used [14]. Once blood culture reports are available then specific antibiotic therapy can be commenced. Blood cultures are positive in 21-71% of acute cholangitis patients. Antibiotic therapy should be continued for ten days.

High biliary pressure caused by obstruction needs to be relieved at the earliest. Timing of drainage is dependent upon the grade of severity of cholangitis [15].

Grade I needs drainage within 24 to 48 hours.

Grade II severity needs drainage at the earliest.

Grade III severity cases require optimization of organ systems followed by immediate drainage. This can be achieved by biliary drainage by a therapeutic ERCP. The various therapeutic options are

1. Endoscopic sphincterotomy with stone evacuation followed by stenting
2. Transpapillary biliary stenting for strictures
3. Replacement of blocked old stents with biofilm formation
4. Endoscopic nasobiliary drainage (ENBD)
5. Percutaneous transhepatic biliary drainage (PTBD)
6. Open surgical drainage (T tube placement after laparotomy)
7. Rarely EUS guided drainage.

ENBD has a few advantages [15].

A repeat cholangiogram can be done when the location of the stricture is unknown.

Purulent bile mixed with thick pus can be effectively drained.

The tube can be safely irrigated if clogged.

Bile aspirates for culture can be collected easily.

The main disadvantages are significant discomfort to the patient and chances that a confused patient will pull the tube out.

PTBD

PTBD is usually done after a failed ERCP. It can safely be done in patients with co morbidities especially in those patients who are unfit for ERCP [15]. The disadvantages of PTBD are patient discomfort, increase in hospital stay, and risk of biliary peritonitis, haemorrhage and infection.

PTBD is contraindicated in patients with ascites, coagulopathy and intrahepatic biliary obstruction.

Surgical drainage by way of choledochotomy with T tube placement is indicated when all options have failed [15, 16].

A balloon enteroscopic assisted ERCP with biliary drainage can be done in cases with obstructed Roux-en Y hepatico jejunostomy [16].

EUS guided biliary drainage is considered when ERCP is unsuccessful as in cases of ampullary obstruction, gastric outlet obstruction and in a roux en Y hepaticojejunostomy [16].

Oriental cholangiohepatitis poses both a diagnostic and therapeutic dilemma [17]. Administration of intravenous fluids and antibiotics is followed by intervention for biliary drainage. Stone extraction, stent placement, stricture dilatation and percutaneous biliary drainage after failed ERCP are various options [18]. Segmental hepatic resection for localized disease and liver transplantation for diffuse end stage liver disease can be done [17]. Prognosis depends upon the timing of biliary

drainage, commencement of antibiotics and presence of co morbidities [19]. Poor prognostic factors are advanced age, high grade fever, leucocytosis, raised bilirubin levels and low albumin levels. Co morbidities associated with poor prognosis are cirrhosis, malignancy, liver abscesses, coagulopathy and raised creatinine levels. An IL 7 level less than 6 and a procalcitonin level greater than 0.5 are associated with increased mortality [20, 21]. The mortality after drainage is 10% while after surgical intervention the mortality can rise to 30% [16].

Table 1: Aetiology of biliary obstruction

Cholecholithiasis	Benign or malignant strictures of the bile ducts
Pancreatic cancer/ampullary adenomas	Porta hepatis tumors/metastasis
Obstructed biliary stents (biofilm formation, biliary sludge, duodenal reflux)	Primary sclerosing cholangitis
Mirizzi's syndrome	Lemmel's syndrome (peri-ampullary diverticulum causing distal biliary obstruction)
Round Worms (<i>A lumbricoides</i>)	Tape worm (<i>T Saginata</i>)
AIDS cholangiopathy	Strictured biliary-enteric anastomosis
Choledochoceles	Post ERCP cholangitis

Conclusion

Acute cholangitis is a life threatening condition. Establishing the diagnosis and determining the severity is pivotal for formulating a therapeutic plan. Aggressive resuscitation, commencement of appropriate antibiotics and biliary drainage are the cornerstones of successful management.

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