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Resistant pathogens in biliary obstruction: Importance of cultures to guide antibiotic therapy

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Abstract

Background. Cholangitis, infection of the bile ducts, is a serious condition that necessitates prompt and efficacious treatment for a good clinical outcome. A single center retrospective study of cholangitis was conducted to better define the spectrum of responsible pathogens and their antibiotic sensitivities.

Methods. We studied all patients at our hospital who had cholangitis from January 1998 to June 2004. Patients were identified by ICD-9 codes and the cause of the cholangitis, the treatment and culture data were noted by review of the medical record.

Results. Thirty patients presented with cholangitis as noted by the clinical symptoms of jaundice, fever and abdominal pain. The cause of the biliary obstruction was gallstones in 18 patients, benign biliary strictures in 5 and malignant obstruction in 7. All the patients with malignant obstruction with cholangitis had stents; there were no cases of cholangitis in malignant obstruction unless prior instrumentation had been performed. The most common isolates were Enterococcus > E. coli > Enterobacter > Klebsiella. Sixty-four percent of blood cultures and all but one of the bile cultures grew organisms. Seventy-two percent of patients had positive blood cultures with at least one resistant organism present and 36% had organisms resistant to multiple antibiotics. Fifty percent of patients with benign biliary disease and positive blood cultures had multiple organisms growing in their blood. Three-quarters of the isolates were resistant to one or more antibiotics and one-quarter of isolates were resistant to three or more antibiotics. Resistant organisms were found regardless of the cause of the biliary obstruction.

Discussion. For all causes of cholangitis, there is a high incidence of positive blood cultures and a high rate of antibiotic resistance. For optimal treatment, blood and/or bile cultures should be routinely performed to optimize antibiotic therapy.

Key Words: *Antibiotic resistance, biliary infection, cholangitis*

Introduction

Increasingly medical centers guide antibiotic therapy through the use of hospital antibiotic formularies or clinical pathways. Review of culture and sensitivity data in various clinical settings is needed to help guide these antibiotic choices. While biliary tract infections are common, cholangitis, infection of the bile ducts, is less frequently encountered. Cholangitis is associated with a high mortality making appropriate and prompt treatment important to improve outcome.

Cholangitis involves both obstruction and infection of the bile ducts. Usually the bile ducts are sterile. However, the presence of gallstones within either the gallbladder or biliary tree is associated with bacterial colonization of the bile [1]. In patients without stone disease, previous biliary intervention is associated with high rates of bacterobilia [2,3]. Under conditions of normal bile flow, bacteria in the biliary system are of no clinical significance. Upon bile duct obstruction, bacteria proliferate within the stagnant bile while biliary pressures increase. Eventually, the bacteria presumably translocate into the circulation causing a systemic infection.

This associated inflammatory response can be quite severe leading to profound sepsis. The impressive presentation of these toxic patients underscores the importance of appropriate antibiotic therapy at the time of presentation. Much of the data on bacterial causes of cholangitis is dated and there has been a wide range of proposed antibiotics for the treatment of biliary infections. We wished to review our experience with cholangitis, focusing on characterization of the bacterial pathogens and antibiotic sensitivities. A single center retrospective review of cholangitis was conducted to better define the clinical presentation and spectrum of pathogens responsible for bile duct infections to better guide future antibiotic therapies.

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Methods

Patients with cholangitis were identified through search of ICD-9 codes 576.1 (Cholangitis) and 576.9 (Bile duct, infection). We examined the charts of all 30 patients with cholangitis who were admitted to Ann Arbor VAMC between 1 January 1 1998 to 1 June 2004. Cholangitis was confirmed with the presence of jaundice, fever, abdominal pain, and biochemical and radiographic evidence of biliary obstruction. Data obtained included: demographic information (age, sex), clinical presentation (complaints and lab values), radiographic evaluation (diagnosis and treatment), clinical history (comorbidities and history of previous biliary disease, etc.), bile and blood culture results, surgical course, and long-term follow-up data. This study was reviewed and approved by our Institutional Human Subjects Review Board.

Clinical characteristics were compared using Fisher's exact test for dichotomous variables and the Wilcoxon rank-sum test for continuous variables. Statistical analysis was performed using SAS v.8.0 (SAS Institute, Cary, NC). Data is expressed as value $\pm$ standard deviation.

Results

The median patient age was 70 years with a range of 49–87 years old. The mean follow-up was 18 months. All but one of the patients were male. The cause of the biliary obstruction was gallstones in 18 patients, benign biliary strictures in 5 and malignant obstruction in 7. All three groups of patients had elevated white blood cell count and bilirubin (Table I). Data in Table I are expressed as mean $\pm$ standard error of the mean (SEM). The serum bilirubin, alkaline phosphatase and white blood cell counts were similar regardless of the type of obstruction. The serum glutamic-oxaloacetic transaminase or [SGOT] levels were significantly lower with benign biliary strictures and cholangitis.

Table I. Clinical presentation of cholangitis

	CBD stones	Benign stricture	Malignant stricture	All cholangitis
Age (years $\pm$ SEM)	69 $\pm$ 3	65 $\pm$ 3	71 $\pm$ 4	69 $\pm$ 2
Fever (>101.6°F)	67%	80%	71%	77%
Abdominal Pain	78%	50%	71%	70%
Jaundice (Bili >4)	72%	60%	67%	69%
Vomiting	33%	0%	57%	37%
Hypotension	33%	25%	29%	30%
WBC ($\times$1000 $\pm$ SEM)	17.8 $\pm$ 3.1	16.1 $\pm$ 1.8	16.6 $\pm$ 1.4	17.2 $\pm$ 1.9
Bili (mg/dl)	6.1 $\pm$ 0.9	4.6 $\pm$ 1	5.7 $\pm$ 1.6	5.8 $\pm$ 0.7
Alk Phos (U/l)	370 $\pm$ 51	472 $\pm$ 149	533 $\pm$ 87	421 $\pm$ 45
SGOT (U/l)	190 $\pm$ 35	54 $\pm$ 3*	184 $\pm$ 61	165 $\pm$ 26

* $p < 0.05$ compared to CBD stone, malignant stricture, and all cholangitis groups.

The significance of this is unclear and may be related to the fact that this group had the smallest number of patients. The possibility exists that this group may have had less hepatocellular damage with the biliary obstruction than the other two, yet more patients would need to be studied for any conclusions to be drawn. The poor overall medical condition of the majority of patients with cholangitis in this series is exemplified by the fact that only 13% had no significant medical comorbidity (Table II).

There was a 13% 30-day mortality for all patients with cholangitis. The 30-day mortality was high regardless of the cause of the biliary obstruction (11% for stone disease, 20% for benign strictures and 29% for malignant obstruction). One patient presented with a liver abscess at the time of initial presentation with cholangitis. Forty-three percent (13) of the patients died during the period of follow-up. Of those who died, there was a mean survival from time of diagnosis of cholangitis to death of 4 months. All of the patients with malignant biliary obstruction died. Of the six patients with malignancies, three had Stage IV pancreatic cancer, three had unresectable hilar cholangiocarcinoma (Klatskin tumors with two being Stage III and one Stage IV), and one patient had gallbladder cancer with liver metastasis (Stage IV). Six patients died who did not have a malignant biliary obstruction, and three of these deaths were directly related to cholangitis.

Ninety percent (27) of patients underwent ERCP. Many patients had multiple ERCPs and a total of 52 were done on this group of 30 patients. Forty-four percent (8/18) of the patients with gallstone disease had a stent placed at the initial ERCP and later had stone extraction and sphincterotomy. Six patients went on to have a percutaneous transhepatic cholangiocatheter (PTC) placed (several due to unsuccessful attempts at ERCP and several due to the location of biliary obstruction).

Thirty percent (9) of patients had significant hemodynamic instability and a prolonged ICU course related to the biliary obstruction. Five patients with choledocholithiasis had a cholecystectomy in the distant past. Twelve patients who had choledocholithiasis were referred for surgery. One refused, three had a laparoscopic cholecystectomy, two had a

Table II. Medical comorbidities in patients with cholangitis

Medical comorbidities	Percent of patients
Hypertension	57%
Cardiac disease	40%
Diabetes	37%
Malignancy (non-biliary)	33%
Pulmonary disease	17%
Renal failure	17%
Liver disease	13%
Vascular disease	10%