JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 1981, p. 522-526
0095-1137/81/110522-05$02.00/0

Vol. 14, No. 5

Bacteriology of Acute Obstructive Suppurative Cholangitis of the Aged

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Received 30 January 1981/Accepted 22 May 1981

Bacteriological examination was performed on bile from 23 patients with acute obstructive suppurative cholangitis. Of 23 bile cultures, 15 yielded aerobic and anaerobic bacteria and 8 yielded aerobic bacteria only. No specimen grew anaerobic bacteria only. A total of 20 cultures yielded a polymicrobial flora, and 3 cultures grew one single aerobic bacterium. *Escherichia coli, Klebsiella* sp., enterococci, *Bacteroides fragilis*, and *Clostridium perfringens* were the predominant bacterial flora in bile of these patients. Bacteremia was documented in 10 of the 12 patients cultured. All bacteremias involved aerobic bacteria and were polymicrobial in three patients. The frequent presence of anaerobes in bile of patients with acute obstructive suppurative cholangitis suggests that antimicrobial therapy should provide adequate coverage for anaerobic bacteria and enteric organisms.

The bacteria commonly described in biliary tract infections include *Escherichia coli, Klebsiella* sp., and enterococci. Recently, it has also been recognized that anaerobes, and especially *Bacteroides fragilis*, may be more commonly involved in biliary tract infections than had been appreciated (4, 5, 7, 12). Acute obstructive suppurative cholangitis, which is the most severe and fulminant form of biliary tract infections, appears to be related to complete obstruction of bile flow within the common duct in the presence of pathogenic bacteria. Anaerobic bacteria have been isolated frequently from various parts of the biliary tract under different conditions (3, 8); if the flow of bile which contains anaerobes is obstructed, then it is reasonable to assume that these anaerobic bacteria may assume a pathogenic role. In this study, investigation of bacteria from bile from 23 patients with acute obstructive suppurative cholangitis was performed with improved anaerobic techniques.

MATERIALS AND METHODS

Medical records of all patients who underwent biliary tract surgery in Tokyo Metropolitan Geriatric Hospital between 1972 and 1979 were reviewed. Twenty-three patients had a diagnosis of acute obstructive suppurative cholangitis. No patient had had previous biliary tract surgery. The features essential for diagnosis were abdominal pain, fever, chills, leukocytosis, jaundice, lethargy, shock, complete biliary obstruction, and pus in the common duct at surgery, which was determined by the operating surgeons and was verified on the gram-stained smears in the laboratory. No patient with recurrent pyogenic cholangitis or ascending cholangitis associated with liver flukes as seen in Southeast Asia was included. Fourteen patients had not received antibiotics before surgical procedures. Seventeen patients underwent emergency surgery within 48 h after onset of the illness. Bile was collected either by direct puncture of the gallbladder with a sterile syringe during the initial stage of laparotomy (cases 1 through 22) or by puncture of the common duct at percutaneous transhepatic cholangiography (case 23). The specimens were sent to the bacteriology laboratory either in a syringe with a rubber stopper on the needle or in an anaerobic transporter (Anaerobic Porter, Clinical Supply Co., Kawashimacho, Gifu, Japan).

Bacteriological examination was carried out with the methods described in an earlier report (12). Gram stains were performed on all bile samples without centrifuging the specimens. Blood cultures were obtained from 12 patients before surgery and inoculated at the bedside with one or more of the following: brain heart infusion broth (Eiken, Tokyo, Japan), thioglycolate broth (Eiken), tryptic soy broth (Eiken), and Columbia broth (BBL Microbiology Systems, Cockeysville, Md.).

RESULTS

Table 1 shows the microbiological and clinical data from each of 23 patients. All subjects were elderly patients; 12 were male and 11 were female, and their ages ranged between 63 and 89 years, with an average of 74.9 years. Obstruction of the bile duct was caused by a gallstone(s) in 19 patients and by carcinoma in 4 patients. Mac-

TABLE 1. *Clinical and microbiological summary of 23 patients with acute obstructive suppurative cholangitis*

Case no.	Age (yr) and sex[a]	Previous biliary tract disease	Maximum temp (°C)	Bilirubin (mg/dl)	Leukocytes/ mm³	Shock	Preoperative chemotherapy	Type of biliary obstruction	Bile culture		Liver abscesses
									Aerobe	Anaerobe	
1	82, F		38.2	3.4	21,300	+		Pigment stone	*E. coli, Klebsiella* sp., enterococcus, *P. morganii, P. vulgaris*	*B. fragilis*	
2	89, F	+	38.0	5.7	12,600			Pigment stone	*E. coli, Klebsiella* sp., enterococcus	*C. perfringens*	
3	80, M	+	40.2	4.2	15,800	+	Ampicillin, 2 g for 4 days	Cholesterol stone	*E. coli, Klebsiella* sp., enterococcus, *Enterobacter* sp., *P. morganii*	*B. fragilis*	
4	77, M		39.6	4.3	11,500	+		Stone[b]	*E. coli, Klebsiella* sp.		+
5	78, F		41.6	8.0	10,300		Cefazolin, 3 g for 3 days	Mixed stone	*E. coli, Citrobacter* sp., enterococcus, *S. epidermidis*		
6	64, F		38.3	2.0	5,400			Stone[b]	*E. coli, Klebsiella* sp., enterococcus		
7	77, F		38.5	10.2	8,000		Cephalothin, 6 g for 3 days	Pigment stone	*E. coli*	*B. fragilis, Peptococcus* sp.	
8	75, M		37.6	ND[c]	15,000	+		Mixed stone	*E. coli, Klebsiella* sp.	*C. perfringens*	
9	68, M		38.0	ND	14,000			Stone[b]	*E. coli, Klebsiella* sp., enterococcus	*B. fragilis, C. perfringens*	+
10	80, F		39.1	ND	7,600	+	Ampicillin, 1 g for 1 day	Pigment stone	*E. coli*, enterococcus	*B. fragilis, Peptococcus* sp.	
11	83, F		39.1	3.6	24,300	+		Pigment stone	*E. coli*	*B. fragilis*	
12	83, F	+	37.3	3.7	12,500	+		Cholesterol stone	*E. coli, Klebsiella* sp.	*C. perfringens*	
13	76, F	+	39.5	7.5	37,600	+	Chloramphenicol, 1 g for 1 day	Pigment stone	*E. coli, Klebsiella* sp.	*B. fragilis, C. perfringens*	+
14	69, M	+	41.8	28.4	44,800	+	Unknown[d]	Pigment stone	*Klebsiella* sp., *Citrobacter* sp.	*C. perfringens, Peptostreptococcus* sp.	+
15	71, M	+	40.2	2.7	44,100	+	Cefazolin, 3 g for 7 days	Stone[b]	*E. coli, P. aeruginosa, P. morganii*, enterococcus	*B. fragilis*	
16	83, M	+	38.2	9.5	13,400		Cefazolin, 3 g for 1 day	Stone[b]	*Enterobacter* sp., enterococcus, unidentified gram-negative rod		+
17	63, M		39.4	6.2	17,500			Mixed stone	*Klebsiella* sp.		
18	63, F	+	38.4	15.0	11,800			Mixed stone	*E. coli, Klebsiella* sp.	*B. fragilis*	
19	93, F	+	39.0	8.6	13,600			Pigment stone	*E. coli, Klebsiella* sp., enterococcus, α-streptococcus	*C. perfringens, Peptostreptococcus* sp.	

TABLE 1.—*Continued*

Case no.	Age (yr) and sex[a]	Previous biliary tract disease	Maximum temp (°C)	Bilirubin (mg/dl)	Leukocytes/mm^3	Shock	Preoperative chemotherapy	Type of biliary obstruction	Bile culture: Aerobe	Bile culture: Anaerobe	Liver abscesses
20	78, M	+	37.7	14.6	25,000	+		Carcinoma of gallbladder	*E. coli*, *Klebsiella* sp.		
21	78, M	+	39.6	6.4	10,900		Ampicillin, 1 g for 3 days	Carcinoma of common duct	*E. coli*		
22	66, M	+	36.9	16.9	6,100			Carcinoma of hepatic duct	*Citrobacter* sp., *P. morganii*, *P. aeruginosa*	*C. perfringens*	+
23	67, M	+	39.1	13.6	8,600			Pericholangial invasion of gastric carcinoma	*E. coli*		

[a] F, Female; M, male.
[b] Gallstone analysis was not done.
[c] ND, Not done.
[d] Antibiotic regime was not done.

roscopic and chemical examination of gallstones from 14 patients revealed that 8 patients had pigment stones, 4 had mixed stones, and 2 had cholesterol stones.

Of 23 cultures, 15 yielded aerobic and anaerobic bacteria and 8 yielded aerobic bacteria only. No specimen grew anaerobic bacteria only. A pure culture of one single aerobic bacterium was found in three specimens. Twenty cultures yielded polymicrobial growth. A total of 58 strains of aerobic bacteria and 21 strains of anaerobic bacteria were recovered. *E. coli* (19 strains) was the most common organism, *Klebsiella* sp. (14) was the second, and enterococcus (10) was the third. *Bacteroides fragilis* (9) ranked fourth and was the most common anaerobic isolate. In this study, *B. fragilis* includes the five species of *Bacteroides* formerly known as subspecies of *B. fragilis* (*B. fragilis* subsp. *fragilis*, *B. fragilis* subsp. *thetaiotaomicron*, *B. fragilis* subsp. *vulgatus*, *B. fragilis* subsp. *distasonis*, and *B. fragilis* subsp. *ovatus*). *Clostridium perfringens* was recovered from eight patients and ranked fifth. Anaerobic bacteria were found in 14 of 19 patients with a common duct stone(s) and in 1 of 4 patients with a malignant biliary tract obstruction.

Bacteremia was documented in 10 of the 12 patients cultured (83% of the patients examined) and was polymicrobial in 3 patients. The predominant blood isolates included *E. coli* (6 isolates) and *Klebsiella* sp. (4 isolates). No anaerobe was recovered from a blood culture. Even an appropriate antimicrobial therapy did not always guarantee protection against bacteremia.

After laparotomy, six patients were noticed to have liver abscesses, but no specimens were collected for culture.

Eight patients died. Four patients died within 2 days after the operation, and four patients died 5, 7, 22, and 23 days later, respectively. Autopsy was performed on six of the eight patients who died. Clinical and postmortem findings indicated that biliary tract infections and shock were important factors in the deaths of those who died within 7 days after the operation. Two patients (cases 7 and 20) who died 22 and 23 days later had had severe pneumonia in their postoperative course. Of the 15 patients who survived, 8 had postoperative wound infections. The organisms isolated from the postoperative wounds were generally found in the bile flora and had been cultured at the time of cholecystectomy. Wound infections were contaminated with *Proteus morganii* in two patients and with fungus and enterococcus in one patient. Seven patients had uneventful courses (Table 2).

TABLE 2. *Postoperative course of 23 patients*

Case no.	Postoperative chemotherapy	Bacteria isolated from postoperative wound infection	Outcome
1	Cephalothin		Died (5 days after operation)
2	Cephalothin	ND[a]	Survived
3	Cephalothin		Survived
4	Cephalothin, thiamphenicol		Survived
5	Ampicillin		Survived
6	Cephalothin	*E. coli, Klebsiella* sp., enterococcus	Survived
7	Cephalothin, ampicillin		Died of pneumonia (23 days after operation)
8	Cephalothin		Died (12 h after operation)
9	Cephalothin	*E. coli, P. morganii*, enterococcus	Survived
10	Cephalothin		Died (7 days after operation)
11	Chloramphenicol		Died (2 days after operation)
12	Cephalothin	*Klebsiella* sp.	Survived
13	Cephalothin, chloramphenicol		Survived
14	Tetracycline, chloramphenicol	*Klebsiella* sp., enterococcus, fungus	Survived
15	Cephalothin		Died (2 days after operation)
16	Cephaloridine		Survived
17	Carbenicillin	*Klebsiella* sp.	Survived
18	Cephalothin	*E. coli, P. morganii*	Survived
19	Cephalothin		Survived
20	Cephalothin, gentamicin		Died of pneumonia (22 days after operation)
21			Died (2 h after operation)
22	Cephalothin		Survived
23	Cephalothin		Survived

[a] ND, The wound was infected, but cultures were not done.

TABLE 3. *Blood cultures obtained from 12 patients*[a]

Case no.	Bacteria isolated from blood
1	*Klebsiella* sp.
3	*E. coli*, enterococcus, *P. putrefaciens*
4	None
5	*E. coli*
8	*Klebsiella* sp.
9	None
12	*Klebsiella* sp.
13	*E. coli*
14	*Klebsiella* sp., *Aeromonas* sp.
15	*E. coli, P. aeruginosa*
18	*E. coli*
21	*E. coli*

[a] Blood cultures were not obtained from the other 11 patients.

DISCUSSION

Numerous reports describe the bacteriology of biliary tract infections, but few distinguish adequately between acute obstructive suppurative cholangitis and other forms of biliary tract infections. Saik et al. performed clinical and bacteriological studies on 28 patients with cholangitis who had undergone biliary tract surgery. They found that 16 of the 28 patients had growth of more than one organism in bile culture (11). The major bacteria isolated were primarily gram-negative enteric coliforms and *Streptococcus* sp. With regard to anaerobic bacteria, Saik et al. found two strains of *Bacteroides* and one strain of *Clostridium* (11). Patients with suppurative cholangitis of varying degrees of severity seem to be included in their series, whereas all of the patients in our study had the complex of fever, jaundice, and abdominal pain (with or without hypotension), suggesting cholangitis, with complete biliary obstruction and common duct pus.

There is general agreement that a polymicrobial biliary infection, involving both aerobes and anaerobes, tends to occur frequently in the presence of a common duct stone and has somewhat more severe clinical manifestations (1, 12). Our bacteriological findings indicate a considerably high incidence of polymicrobial infection (20 of 23 patients; 86.9%), especially that involving both aerobes and anaerobes (15 of 23 patients; 65.2%) in acute obstructive suppurative cholangitis.

Although bacteremia was present in only 10 of the 23 patients, blood cultures were not performed in 11 patients (Table 3); therefore, there was an 83% incidence of bacteremia in the patients cultured. *Aeromonas* sp. and *Pseudomo-*

nas putrefaciens were isolated from the blood of one patient each, but not from bile (cases 3 and 14). This discrepancy is difficult to explain. However, it is probable that these bacteria might have been overlooked in the bile cultures, since case 14 yielded four different types of bacteria from bile and case 3 yielded as many as six types. The isolation of *Aeromonas* sp. and *P. putrefaciens* from the biliary tract was described by von Graevenitz et al. (13, 14), and *Aeromonas* bacteremia from hepatobiliary disease was reported by DeFronzo et al. (2).

Despite frequent isolation of anaerobes from bile cultures, no anaerobic bacteremia was found in our patients. A low incidence of anaerobic bacteremia in biliary tract sepsis was also indicated by England and Rosenblatt (4). Similar results were noted in an animal model of intra-abdominal sepsis. Rats, which were implanted intraperitoneally with a gelatin capsule containing an inoculum of pooled cecal contents, developed peritonitis with bacteremia during the early stage after implantation and then developed intra-abdominal abscesses (15). The dominant bacteria in abscess contents were *B. fragilis* and *Fusobacterium* sp., with lower concentrations of *E. coli* and enterococci. In contrast, blood cultures drawn 24 to 72 h after implantation yielded primarily *E. coli*. *B. fragilis* bacteremia was found in 2 of 10 animals (10). However, subsequent studies indicated that *B. fragilis* appeared in the bloodstream very rapidly after implantation and was cleared from the blood of most animals by 24 h (9). In our patients, not all blood samples for culture were drawn immediately after onset of the disease. It is possible that the delay in blood culture may have resulted in missed *B. fragilis* bacteremia.

In patients with acute obstructive suppurative cholangitis, anaerobes in the biliary tract may not merely be commensals, but may play a role in the purulent process. Lykkegaard Nielsen et al., who have studied an animal model of biliary tract infection, demonstrated that a combined *B. fragilis* and *E. coli* infection leads to a greater mortality and to a more frequent occurrence of liver abscesses than a purely aerobic or purely anaerobic infection (6).

Since acute obstructive suppurative cholangitis is commonly polymicrobial with mainly enteric facultative bacteria and anaerobes, antimicrobial therapy, which is directed at either the bacteremia or the postoperative infection, should provide adequate coverage for enteric coliforms, enterococci, and anaerobic bacteria.

ACKNOWLEDGMENT

We are grateful to Sydney M. Finegold for reviewing the manuscript.

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