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The Association of *Streptococcus bovis* Bacteremia and Gastrointestinal Diseases: A Retrospective Analysis

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There is a well-established association between *Streptococcus bovis* bacteremia (SBB) and colorectal cancer. However, SBB is also frequently associated with chronic liver disease and has been described with other gastrointestinal disorders. The aim of the study was to evaluate the prevalence of gastrointestinal disease in patients with SBB. Retrospective analysis of the microbiology database at Jackson Memorial Medical Center, Miami, Florida, between 1992 and 2002, was performed. Patients' clinical records were reviewed, with special focus on underlying gastrointestinal disease or other major comorbidities. Thirty-eight patients (83%) were adults and eight (17%) were pediatric patients. Nineteen patients presented with gastrointestinal disorders associated with SBB (41%). Nine adult patients (19%) had end-stage liver disease (five female). Six patients had alcohol-induced liver disease (one with concomitant chronic hepatitis C), with the remaining three cases related to autoimmune hepatitis, primary biliary cirrhosis, and nonalcoholic steatohepatitis. Colonic neoplasms (adenocarcinoma in 3 and adenomatous polyps in 3) were found in 6 of 10 adult patients in whom colonoscopic evaluation was performed. Seven adult patients had acquired immunodeficiency syndrome (AIDS) (18%). Mortality in the patients with AIDS and SBB was high (71%). No significant association with gastrointestinal diseases was found in the pediatric population. Bacteremia due to *S. bovis* in adults is frequently associated with hepatic dysfunction (1:4), colonic neoplasms (1:6), and AIDS (1:6). This association was valid for our adult population only. SBB is an early clue to the likely presence of these serious underlying conditions and warrants rigorous investigation when recognized.

KEY WORDS: *Streptococcus bovis*; colonic neoplasms; gastrointestinal neoplasms.

Streptococcus bovis is a normal inhabitant of the intestinal tract and may be isolated in 5–16% of fecal samples in normal adults (1). It is a group D nonenterococcal streptococcus. Its association with microbial endocarditis has been known for more than 40 years (2, 3). In this clinical scenario, it is often difficult to determine with certainty an organism's portal of entry unless one can document either a preceding peripheral focus of infection caused by the same organism or an instrumentation procedure known to be associated with bacteremia. Since *S. bovis* is a normal inhabitant of the gastrointestinal tract, it is not coincidental or surprising that a sizable proportion of patients with *S. bovis* bacteremia have concomitant bowel lesions.

Based on this concept, Klein *et al*. reported in 1977 two cases of *S. bovis* endocarditis associated with colonic adenocarcinoma (4). After this initial report, a number of case reports and small series have followed to support this association (5–9).

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Additionally, *S. bovis* bacteremia has also been described with neoplastic polyps (10) and other malignancies of the gastrointestinal tract, such as carcinoma of the esophagus, stomach, pancreas, and gastric lymphoma (11, 12). There are also reports of *S. bovis* bacteremia associated with inflammatory bowel disease (13), chronic liver disease (14), and intestinal parasitosis (*Strongyloides stercoralis* colitis) (15).

The purpose of this report was to evaluate the prevalence of gastrointestinal disease in patients with *S. bovis* bacteremia in a large community teaching hospital.

METHODS

A retrospective analysis of the microbiology database at Jackson Memorial Memorial Center, Miami, Florida, between 1992 and 2002, was performed. The study was reviewed and approved by the Institutional Review Board of the University of Miami School of Medicine. The records of 46 patients with positive blood cultures for *Streptococcus bovis* were reviewed. There were 24 males and 22 females, with a mean age of 44 years (range: 2 days–80 years). Thirty-eight patients (83%) were adults and eight patients (17%) were pediatric.

Patient's clinical records were reviewed, with special focus on underlying gastrointestinal disease and other major comorbidities. The presenting illnesses of the patients with *S. bovis* bacteremia are presented in adults and children separately (Tables 1 and 2).

Patients were considered to have undergone colonic evaluation if they had colonoscopy, sigmoidoscopy, and/or barium enema. Histologic examination of endoscopic biopsies or surgically resected specimens was reviewed.

Liver evaluation was considered to be undertaken if serum chemistries were performed including bilirubin, transaminases, and alkaline phosphatase levels; computerized tomographic or ultrasound scans of the liver; and/or liver biopsy.

TABLE 1. PRESENTING ILLNESSES IN ADULT PATIENTS WITH *Streptococcus bovis* BACTEREMIA

Illness	*Male*	*Female*	*Total*
Infectious disease			
Endocarditis	2	5	7
C. difficile colitis	1	0	1
AIDS	4	3	7
Meningitis	1	0	1
Toxoplasmosis	0	1	1
Neoplastic			
Leukemia or lymphoma	2	0	2
Vaginal carcinoma	0	1	1
Colon carcinoma	2	1	3
Colon polyps	2	1	3
Gastrointestinal			
Diverticulosis	2	0	2
Cirrhosis	4	5	9
Choledocholithiasis	0	1	1
HCV	0	1	1
Neurologic	1	0	1
Sickle cell disease	0	1	1

TABLE 2. PRESENTING ILLNESSES IN PEDIATRIC PATIENTS WITH *Streptococcus bovis* BACTEREMIA

Illness	*Male*	*Female*	*Total*
Meningitis	1	1	2
Gastroenteritis	1	0	1
PDA	0	1	1
Neonatal jaundice	1	0	1
Incarcerated inguinal hernia	1	0	1
Third-degree burns	1	0	1
Born to HIV+ mother	0	1	1

RESULTS

Thirty-eight adult patients (83%) and eight pediatric patients (17%) were included in the study, with a mean age of 44 years (range: 2 days–80 years). The adult population included 19 males and 19 females, with a mean age of 56 years (range: 19–80 years). The pediatric group included five males and three females, with a mean age of 3 months. Five were neonates.

The demographics of this population revealed 17 (37%) African-Americans, 15 (32%) Hispanics, and 14 (30%) non-Hispanic whites. The presenting illnesses of the patients with *S. bovis* bacteremia are shown separately for adults and children in Tables 1 and 2. Of the 46 patients with *S. bovis* bacteremia, 7 (15%) adult patients (2 male and 5 female) were diagnosed as having endocarditis, with a mean age of 62 years (range: 40–80 years). There was no evidence of endocarditis in the pediatric group.

Overall, 19 of the 46 patients (41%) presented with gastrointestinal disorders associated with *S. bovis* bacteremia (Figure 1). Of the 38 adults, 10 patients (26%) completed colonic evaluation. Colonic pathology was identified in 6 (60%) of these 10 adult patients (4 male; mean age, 58 years) (Figure 2). Colon cancer was identified in three (30%) patients, two of them metastatic to the

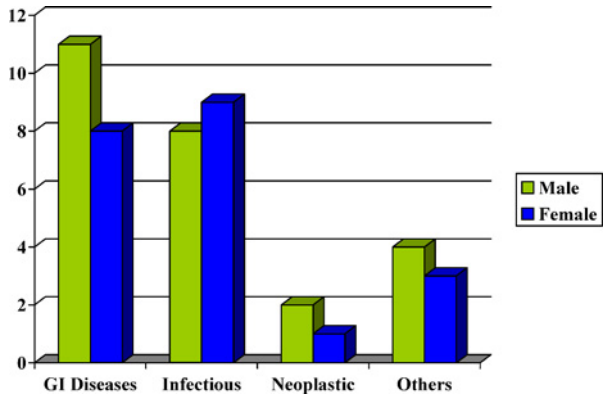

Fig 1. Presenting illnesses in patients with *Streptococcus bovis* bacteremia.

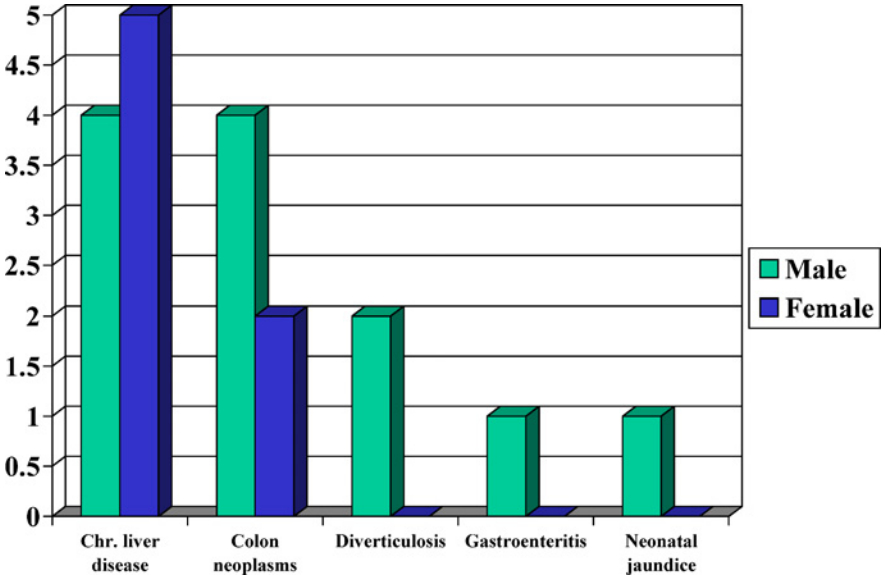

Fig 2. Gastrointestinal diseases associated with *Streptococcus bovis* bacteremia.

liver. Adenomatous colonic polyps were found in an additional three (30%) patients. The two pediatric cases with a gastrointestinal disorder did not have a complete colonic evaluation.

Diverticulosis was found in two adult patients, including one patient with endocarditis and one patient with cirrhosis. One adult case had a diagnosis of *C. difficile* colitis and HIV. None of the seven patients with endocarditis had evidence of colon cancer and only one patient had evidence of colon polyps.

Nine of the thirty-eight adult patients (24%) were identified as having chronic liver disease (five female) (Figure 2). Six of these patients had alcohol-induced liver disease (one with concomitant chronic hepatitis C), with the remaining three cases related to autoimmune hepatitis, primary biliary cirrhosis, and nonalcoholic steatohepatitis. Upper gastrointestinal bleeding secondary to esophageal varices was seen in three patients. Three of these nine patients with chronic liver disease underwent orthotopic liver transplant. Four of the adult patients (11%) had documentation of both colon and liver disease. Patients with liver disease were younger than those with colonic neoplasms (mean age, 49 vs 58 years, respectively).

Acquired immunodeficiency syndrome (AIDS) was identified in seven of the adult cases (18%). Four were male with a mean age of 52 years. Associated clinical entities in patients with AIDS were *C. difficile* colitis (one case), CNS toxoplasmosis (one case), and bacterial meningitis (one case). Mortality in the patients with AIDS and *S. bovis* bacteremia was high (71%).

Other associated presenting illnesses in the adult patients, excluding colonic and liver disease, were as follows: vaginal carcinoma (one case), acute myelogenous leukemia (AML; one case), chronic lymphocytic leukemia (CLL; one case), sickle cell disease (one case), diabetes mellitus (one case), cerebrovascular accident (CVA) with disseminated intravascular coagulation (DIC; one case), and choledocholithiasis (one case) (16). Different clinical entities were appreciated in pediatric population: gastroenteritis (one case), incarcerated inguinal hernia (one case), neonatal jaundice (one case), third-degree burns (one case), congenital heart disease (PDA; one case), and bacterial meningitis (two cases).

Mortality was reported in 13 patients (28%), including 5 adult cases with advanced AIDS, 3 adult cases with endocarditis, 1 adult case with only bacteremia, 1 adult case with metastatic colon cancer, 2 adult cases with decompensated alcoholic liver disease, and 1 pediatric case with third-degree burns (>40% BSA).

DISCUSSION

This retrospective analysis of 46 patients with *Streptococcus bovis* bacteremia confirmed the previously described association with colonic pathology. Complete colonic evaluation was only performed in 10 of the 38 adult patients (26%), and not in the pediatric population. Sixty percent of these 10 patients had colonic pathology, with 30% presenting with colon cancer and 30% with adenomatous polyps. Previous retrospective and prospective

series have shown similar results, with a range from 18–50% incidence of colorectal neoplasia (10, 17–20).

It has been suggested that the association of *S. bovis* bacteremia with colonic neoplasia could be the result of two factors. One is a change in colonic flora in patients with colon cancer. *S. bovis* is found in the gastrointestinal tract of only 5–16% of normal human subjects (1). However, Klein *et al.* (4) found a high fecal carriage rate for *S. bovis* (56%) in patients with colon carcinoma. Whether this increased prevalence is cause or effect is unknown. The second factor is that this bacteria may have a specific propensity for both transmucosal invasion and the development of bacteremia and endocarditis. *S. bovis* accounts for 14% of all microbiologic endocarditis, 24% of streptococcal endocarditis, and 63% of group D streptococcal endocarditis (16). However, the factors promoting fecal overgrowth, access to the portal venous system, entry into the systemic circulation, and lodgement on cardiac valves have yet to be elucidated.

This analysis also showed an association with chronic liver disease in 9 of the 38 adult patients (24%). Six patients had alcohol-induced liver disease, one with concomitant chronic hepatitis C, and three cases related to autoimmune hepatitis, primary biliary cirrhosis, and nonalcoholic steatohepatitis. Each of these liver problems may result in a compromised hepatic reticuloendothelial system (21, 22). Furthermore, alterations in hepatic secretion of bile salts and/or secretory immunoglobulins may promote the translocation of bacteria from the intestinal lumen into the portal venous system (23, 24). Also, the presence of portal hypertension with portosystemic shunting may bypass the hepatic reticuloendothelial system and allow direct access to the systemic circulation.

AIDS was identified in 7 (18%) of the 38 adult patients (1:6) with a high mortality rate (71%). The role of underlying HIV infection in facilitating the development of *S. bovis* bacteremia is unclear. However, it is suggested that alterations in immune regulation and changes in colonic flora may promote this systemic infection.

There was no evidence of significant association of Streptococcus bovis bacteremia and gastrointestinal diseases or HIV/AIDS in the pediatric population. It is important to mention that the majority of our pediatric cases were neonates (62%), with a different set of presenting illnesses, but common for this group.

Streptococcus bovis bacteremia is an early clue to the likely presence of these serious underlying complications in the adult population. This retrospective analysis suggests that all adult patients with documented *S. bovis* bacteremia and/or endocarditis should undergo colonic and liver evaluation as well as an HIV workup.

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