

Streptococcus bovis group and biliary tract infections: an analysis of 51 cases

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Abstract

Streptococcus bovis is a well-known cause of endocarditis, but its role in other infections has not been well described. We analysed prospectively all patients with biliary tract infections caused by *S. bovis* group during the period 1988–2011. We selected those cases associated with cholangitis and cholecystitis, defined according to Tokyo guidelines. Identification of the strains was performed using the API 20 Strep and the GP card of the Vitek 2 system, and was confirmed by molecular methods. Our series included 51 cases (30 cholangitis and 21 cholecystitis). The associated microorganisms were: *Streptococcus infantarius* (biotype II/1) 29 cases (57%), *Streptococcus gallolyticus* subsp. *pasteurianus* (biotype II/2) 20 cases (39%) and *Streptococcus gallolyticus* subsp. *gallolyticus* (biotype I) two cases (4%). The only difference found between *S. infantarius* and *S. gallolyticus* subsp. *pasteurianus* was a greater association of the first with malignant strictures of the bile ducts: 48% (14/29) versus 5% (1/20), $p < 0.001$. Thirty-seven of the cases also had bacteraemia, causing 20% (37/185) of all *S. bovis* bacteraemia, with differences between *S. gallolyticus* subsp. *gallolyticus* (2/112; 2%) and the other two microorganisms: *S. infantarius* and *S. gallolyticus* subsp. *pasteurianus* (35/73; 48%; $p < 0.001$). The vast majority of biliary tract infections due to *S. bovis* group are caused by *S. infantarius* and *S. gallolyticus* subsp. *pasteurianus* (*S. bovis* biotype II), and nearly half of the bacteraemia due to these two species has a biliary source (43% of the *S. infantarius* and 56% of *S. gallolyticus* subsp. *pasteurianus*).

Keywords: Biliary tract infection, *Streptococcus bovis*, *Streptococcus gallolyticus*, *Streptococcus infantarius*, *Streptococcus pasteurianus*

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Introduction

The *Streptococcus bovis* group (SBG) includes several species and subspecies of microorganisms that can cause humans infections. This group was previously classified in two biotypes, I and II (this latest divided in two subtypes (II/1 and II/2); the current classification comprises different species: *Streptococcus gallolyticus* subsp. *gallolyticus* (formerly *Streptococcus bovis* biotype I), *S. gallolyticus* subsp. *pasteurianus* (formerly *S. bovis*

biotype II/2) and *Streptococcus infantarius*, subsp. *coli* and subsp. *infantarius* (formerly *S. bovis* biotype II/1).

The SBG has been primarily associated with endocarditis and colorectal neoplasia [1,2]. This association with colorectal neoplasms is higher than in controls [3], and this association is stronger with advanced neoplasms [4], especially with *S. gallolyticus* subsp. *gallolyticus* [5]. The SBG has also been linked to osteoarticular infections, urinary tract infections, meningitis, peritonitis and spontaneous bacteraemia in cirrhotic, neonatal infections and non-colorectal cancer [6–11]. Over 20 years ago, Ruoff *et al.* [12] reported the association between *S. bovis* biotype II and biliary tract infections. Since then, this association has received little attention [13–16]; the percentage of SBG bacteraemia with biliary origin has been estimated in several reports at between 0 and 38% [17–27]. However, the features associated with this infection, risk factors, underlying

diseases, and the relationship with the new taxonomic species of SBG has not been well determined.

For this reason, the aim of this study is to describe clinical, microbiological features and risk factors of the biliary tract infections associated with SBG in our institution.

Materials and Methods

The study was performed at the Hospital Lucus Augusti (formerly Hospital Xeral-Calde, Lugo), a large community teaching hospital with 740 beds, serving a mixed urban and rural area of 265 000 inhabitants, and is the reference centre for two regional hospitals that provide health care to an area of 118 000 inhabitants. Between 1 January 1988 and 31 December 2011, all adult patients with positive blood cultures were followed prospectively. During this period we detected 11 750 bacteraemias, of which, 185 were caused by SBG (1.6%). Of these 185 cases, 112 were identified as *S. gallolyticus* subsp. *gallolyticus*, 27 as *S. gallolyticus* subsp. *pasteurianus* and 46 as *S. infantarius*, subsp. *coli* and subsp. *infantarius*.

Furthermore, since 2003 we have also followed all patients with SBG isolated in any other type of sample other than haemoculture. We isolated SBG in bile in 17 patients, which was 3.4% of the microorganisms isolated in bile (495 cases).

All patients with biliary tract infection and SBG isolated in blood cultures or bile were included in the study. The diagnosis of acute cholangitis and acute cholecystitis was made, according to Tokyo guidelines [28,29], on the basis of the clinical findings in combination with laboratory data and imaging findings.

Isolates were stored in skimmed milk Difco™ (Becton-Dickinson, Sparks, MD, USA) at -70°C . Identification of the strains was performed using the API 20 Strep gallery and card Vitek 2 system GP (both from bioMérieux, Marcy l'Etoile, France). For molecular identification, the complete 16S rRNA gene sequence was determined as previously described by Beck *et al.* [23]. Antimicrobial susceptibility testing was performed using the disc diffusion technique according to CLSI guidelines [30] and the E-test method (AB Biodisk, Solna, Sweden), following the manufacturer's recommendations.

Results

General characteristics of the series

During the study period, SBG was isolated in 51 patients diagnosed with biliary tract infection according to Tokyo guidelines. The mean age of the patients was 73.6 years (range 44–93 years), and 65% were male. The biliary tract infections

diagnosed were: 30 cholangitis and 21 cholecystitis (Table 1). The causes of cholangitis were: malignant biliary stricture in 17 cases [pancreatic cancer (eight cases), cholangiocarcinoma (four cases), ampulloma (two cases), gastric cancer (two cases), duodenal cancer (one case)]; choledocholithiasis in nine cases, and benign strictures or fistulas caused by previous surgery in four cases. The causes of the cholecystitis in all 21 patients was cholelithiasis.

Clinical manifestations and complications

The most common clinical manifestations were fever (84%), abdominal pain (63%) and jaundice (29%). Seventy-nine percent of patients presented with leucocytosis. Major complications were: abdominal or liver abscesses (11 cases), pancreatitis (five cases), surgical wound infections (four cases), gallbladder perforation with peritonitis (three cases) and septic shock (three cases).

The most frequent associated co-morbidities were: cancer (22 cases, 17 of them digestive non-colorectal, two prostate, two breast, one leg sarcoma), diabetes mellitus (20 cases), ischaemic heart disease (11 cases) and chronic obstructive pulmonary disease (nine cases). Colorectal adenomas were detected in four patients.

Five patients with biliary infection by SBG died (10%): two of them from sepsis and the other three due to their underlying disease (pancreatic cancer).

Treatment

Empirical antimicrobial treatment was appropriate in 87% of patients. All isolates were susceptible to penicillin, ceftriaxone and vancomycin, and 69% and 75% of them were susceptible to clindamycin and levofloxacin, respectively. Surgery was performed in 15 cases (29%); any other drainage was carried out in 17 cases (33%), and a biliary stent was placed or replaced in five cases (10%).

Microbiological characteristics

Streptococcus bovis group organisms were isolated in 51 patients with biliary infection: 34 from blood cultures, 14 from bile and three in both samples. The SBG accounted for 3.3% of biliary infections documented microbiologically. SBG was isolated from polymicrobial infections in 30 patients (59%): in 18 cases with two microorganisms and in 12 cases with three or more microorganisms. SBG was isolated with other microorganisms in 71% (10/14) of bile samples and in 54% (20/37) of haemocultures. Most frequently associated microorganisms were: *Escherichia coli* (24 cases) and *Enterococcus* spp. (11 cases). The only statistically significant difference between the polymicrobial biliary infections due to SBG compared with SBG monomicrobial biliary infections was the lower percentage of

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