Clinical Features of Group B *Streptococcus* Prosthetic Joint Infections and Molecular Characterization of Isolates[▽]

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Twelve group B *Streptococcus* (GBS) prosthetic joint infection (PJI) cases are reported. The mean patient age was 55 years. Eleven infections were caused by GBS alone. The associated isolates belonged to phylogenetic lineages different from those that cause neonatal meningitis. The clinical outcome was favorable for the eight patients for whom follow-up data were available.

Prosthetic joint infection (PJI) is associated with significant morbidity and requires early diagnosis and appropriate treatment (2). Gram-positive cocci, particularly *Staphylococcus aureus* and *Staphylococcus epidermidis*, cause approximately 65% of PJI cases (17). However, some cases of PJI are caused by bacteria of genitourinary and/or gastrointestinal origin.

Group B *Streptococcus* (GBS) is one of the most important pathogens in newborns and pregnant women and is also a pathogen in nonpregnant adults with underlying medical diseases and the elderly (6). Several types of GBS osteoarticular infections have been reported, such as septic arthritis, osteomyelitis, and spondylodiscitis, though few cases of PJI have been studied (10–12). This retrospective study analyzed the clinical features of GBS PJI and the molecular characterization of the strains isolated from these infections.

GBS strains were isolated from operative soft tissue, bone, and/or joint specimens from 12 patients with PJI between January 2002 and December 2006 at Nantes University Hospital. GBS was the causative agent in 6% of the PJIs, as defined by clinical, radiological, biological, and microbiological criteria (13). PJI was diagnosed for 10 patients based on their having at least two GBS culture-positive samples. Intraoperative evidence of purulence supported the diagnosis for 2 patients with single culture-positive specimens.

All clinical samples were inoculated on solid and liquid aerobic and anaerobic culture media. Identification of beta-hemolytic Gram-positive cocci was performed by latex agglutination and with the Vitek2 system (bioMérieux, Marcy-l'Etoile, France). Strains were first serotyped with a latex agglutination

kit (Pastorex Strepto; Bio-Rad, Marnes-la-Coquette, France), and the serotype was then confirmed by a PCR-based serotyping method (5). Susceptibility to antibiotics was determined using the Vitek2 system and interpreted according to the manufacturer's instructions (3).

The presence of GBS genetic markers previously reported in GBS neonatal central nervous system (CNS) infections was determined by PCR (5, 8, 15). The markers analyzed were mobile genetic elements, including the GBSi1 group II intron downstream of the C5a-peptidase gene *scpB* and IS1548 associated with the *hylB* gene, and prophage DNA fragments F5, F7, and F10. Positive-control strains for PCR were included as described previously (8, 15).

Extracted DNA was digested with SmaI and subjected to pulsed-field gel electrophoresis (PFGE). The PFGE patterns were interpreted according to the criteria described by Tenover et al. (14). Multilocus sequence typing (MLST) was performed as previously described (9).

The mean age of the 12 patients was 55 ± 21 years, and eight were male. There were seven hip and five knee PJIs. The patients had elevated leukocyte and platelet counts (means of 13,410/mm³ and 399,000/mm³, respectively) and C-reactive protein (CRP) levels (mean of 88 mg/liter) at the time of diagnosis. Six had associated comorbidities (Table 1). Prior to diagnosis, no previous sample was positive with GBS for any of the 12 patients. A gastrointestinal source was suspected for one diabetic woman who had gastroenteritis a few weeks before PJI was diagnosed. At presentation, the primary symptom was pain in the affected joint. The median time from prosthesis implantation to onset of symptoms was 4 months and 15 days, with four patients presenting within the first month, four patients presenting between 1 month and 1 year, and four patients presenting more than 1 year from surgery.

Most of the patients received oral amoxicillin alone (four cases) or in combination with a fluoroquinolone (five cases) or clindamycin (one case). Ten were treated for 3 months. Surgical intervention included debridement (seven cases), removal of prosthesis (four cases), and amputation (one case). There

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TABLE 1. Clinical and microbiological features of GBS prosthetic joint infections

Patient	Sex ^a	Age (yr)	Joint	Comorbidity(ies)	Joint age	Surgical strategy	No. of samples (no. positive)	Leukocyte count (10 ³ /mm ³)	Platelet count (10 ³ /mm ³)	Treatment ^b (duration)	Outcome ^c
1	F	44	Right hip	Carcinoma	21 days	Debridement	1 (1)	4.61	618	AMX, 6 g (5 wk); GEN (48 h)	Lost to follow-up
2	M	26	Left knee	Osteosarcoma	13 years	Amputation	4 (4)	11.1	439	AMX, 3 g (3 mo)	Alive, favorable
3	F	85	Left knee	None	21 mo	Debridement	2 (2)	12.8	338	SXT, 800 mg (until death)	Lost to follow-up
4	F	80	Right knee	None	6 mo	Two-step removal of prosthesis	6 (6)	8.4	464	AMX, 8 g; MXF, 400 mg (3 mo)	Alive, favorable
5	M	83	Left hip	None	1 mo	Debridement	8 (8)	20.1	689	AMX, 6 g; MXF, 400 mg (3 mo)	Alive, favorable
6	M	18	Left hip	Sarcoma	3 mo	Debridement	4 (4)	10.6		AMX, 3 g; LEV, 1 g (3 mo)	Alive, favorable
7	M	65	Right hip	Diabetes mellitus, diverticulum	10 mo	Two-step removal of prosthesis	2 (2)	13.0		AMX, 6 g; MXF, 400 mg (3 mo)	Alive, favorable
8	M	56	Right knee	None	14 mo	One-step removal of prosthesis	1 (1)	15.1	182	AMC, 8 g (3 mo)	Alive, favorable
9	F	62	Right knee	Gastroenteritis, diabetes mellitus	18 mo	Two-step removal of prosthesis	5 (5)			AMX, 6 g; CLI, 1.8 g (3 mo)	Alive, favorable
10	M	44	Right hip	Polyposis	3 mo	Debridement	3 (3)	6.7		AMX, 12 g (3 mo)	Lost to follow-up
11	M	61	Left hip	None	1 mo	Debridement	4 (4)	18.6	522	AMX, 8 g; MXF, 400 mg (3 mo)	Lost to follow-up
12	M	40	Right hip	None	15 days	Debridement	6 (6)	20.9	502	RIF 1.2 g; MXF, 400 mg (3 mo)	Alive, favorable

^a F, female; M, male.^b AMX, amoxicillin; GEN, gentamicin; SXT, co-trimoxazole; MXF, moxifloxacin; LEV, levofloxacin; AMC, amoxicillin plus clavulanate; CLI, clindamycin; RIF, rifampin.^c For patients who were not lost to follow-up, the median follow-up time was 6 years.

was a favorable outcome for eight patients (median follow-up, 6 years). Four patients were lost to follow-up.

GBS was recovered from 1/1 to 8/8 perioperative samples (mean, 3.8). For two patients, GBS was isolated from only one sample, but intraoperative evidence of purulence was observed. One patient (patient 12) was coinfecting with methicillin-susceptible *S. aureus*.

Molecular analysis showed that most of the GBS isolates belonged to three serotypes, Ia, III, and V, and all were susceptible to β -lactams and vancomycin (Fig. 1). Two were positive for the GBSi1 group II intron. The prophage DNA frag-

ment F10 was found in seven isolates, which grouped into serotypes Ia, III, and V. No other virulence marker was found.

Eight isolates belonged to clonal complex 1 (CC1) (5/8 isolates) or CC23 (3/8 isolates), as shown in Fig. 1 (14). Surprisingly, two isolates (recovered from patients 3 and 9) belonged to serotype Ia and CC23 and had different sequence type (ST) groups (ST280 and ST23) but identical PFGE patterns. In contrast, five isolates (from patients 6, 1, 2, 4, and 8) belonged to CC1 and ST1 and had closely related PFGE patterns but grouped into different serotypes (III, $n = 2$; V, $n = 3$).

Risk factors reported in invasive GBS infections, such as

FIG. 1. Characteristics of 12 *Streptococcus agalactiae* prosthetic joint infection clinical isolates. Pulsed-field gel electrophoresis banding patterns after SmaI digestion are shown. Percentages of similarity are shown above the dendrogram. ERY, erythromycin; CLI, clindamycin; TET, tetracycline; SXT, co-trimoxazole; S, susceptible; R, resistant.

systemic lupus erythematosus, alcoholism, intravenous drug abuse, or chronic underlying diseases, were not found in our patients (6).

Serotypes Ia, III, and V were most prevalent, as previously reported (4, 7, 9). The isolates belonged mostly to CC1 and CC23, with the CC1 isolates exhibiting the lowest degree of genetic diversity. No epidemiological link was detected for the patients whose isolates were similar by PFGE pattern and/or MLST. Unrelated isolates had different serotypes. As recently described for GBS, semiautomated repetitive extragenic palindromic element PCR (rep-PCR) with the Diversilab technology (bioMérieux) underlines the absence of correlation between these typing methods (1).

Remarkably, the strains of the hypervirulent ST17 clone, described for CNS neonatal infections, were not found here. Neonatal infections originate from vaginal GBS ST17 strains, but ST1 and ST23 PJI strains are more likely to originate from genitourinary and intestinal flora. Similarly, the same genetic features are rarely found in GBS strains involved in neonatal CNS infections and adult PJI. Although the F10 prophage fragment has been strongly associated with serotype III in GBS neonatal infections (15), among the PJI isolates, identification of this virulence marker appeared to be independent of serotype. Of interest is that the F10 virulence marker was found in five isolates from six patients without comorbidities; however, two patients with isolates harboring both the F10 and GbSII markers developed an acute sepsis (patients 5 and 12, with joint ages of 15 days and 1 month, respectively). Further prospective studies should be performed to confirm the presence of this prophage DNA F10 fragment and other virulence markers among PJI strains.

The 12 GBS clinical isolates were susceptible *in vitro* to a range of antibiotics usually used to treat PJI. Surgical intervention and prolonged oral antibiotic therapy resulted in favorable outcomes for the eight patients for whom follow-up data were available (16).

In conclusion, GBS should be considered a potential pathogen in PJI. In our PJI cohort, most GBS isolates were limited to two phylogenetic lineages (CC1 and CC23). The genetic elements found in isolates from PJI are different from the elements found in isolates from neonatal infections. Further molecular studies should focus on genetic determinants of virulence in PJI isolates.

S.C. and P.B. conceived and designed the study and the experiments; S.C. (PFGE) and N.V.D.M. (virulence markers, serotyping, and

MLST) performed the experiments; M.I., S.C., S.T., D.B., and D.L. collected the clinical data; S.C., P.B., R.Q., and A.R. analyzed the data; and S.C., D.L., R.Q., and P.B. wrote the paper.

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