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Clinical and bacteriological investigation of *Streptococcus dysgalactiae* subsp. *equisimilis* infections treated at Tokyo Medical University Hospital

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Abstract

Recently, many studies have focused on *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) due to an increase in severe invasive streptococcal infections caused by this microorganism, infections similar to those caused by group A streptococci. To date, analyses of SDSE isolated from patients in tertiary care hospitals have been limited. In this study, 957 clinical strains of group G streptococcus (GGS) isolated at our university hospital between 2002 and 2012 were investigated. Seventy-six GGS strains, considered to cause invasive infection were isolated from clinical samples that would normally have been expected to be sterile. The total number of GGS strains isolated in our hospital has been increasing each year, with 7 in 2002 and 12 in 2012. Referring to medical records, 22 clinical cases in which GGS was isolated from blood cultures were retrospectively surveyed. The median age of occurrence of invasive GGS infection was 61 ± 23.1 years, which was lower than that observed in previous studies. The most prevalent underlying disease was malignant disease (11 cases). Two patients died from severe GGS infection and 3 others from underlying diseases. Ten preserved SDSE strains isolated from blood cultures were analyzed. The most prevalent type of *emm* and Multilocus Sequence Typing were *stG6792.1* and ST17, respectively, which are frequently isolated from patients with severe invasive streptococcal infection in Japan. All strains had the *scpA*, *ska*, *saga*, and *slo* virulence genes, and 3 strains had *speG*. No differences in the clinical courses of patients infected with strains with or without the *speG* gene were detected, however. Three strains were found to be resistant to levofloxacin, while 4 and 5 strains were resistant to clarithromycin and tetracycline, respectively. Only 1 strain with the *tet*M antimicrobial resistance gene was detected, however. A few SDSE strains were resistant to beta-lactam antibiotics. The present results indicate that the possibility of lethal invasive SDSE infection should be considered in patients with underlying diseases.

Introduction

Streptococci belonging to Lancefield serological group C or G have traditionally been considered to have very low pathogenicity, even though they are beta-hemolytic, and hence regarded as clinically insignificant unless isolated from patients with certain predisposing medical conditions or from the isolates of normally sterile sam-

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ples[1]. However, group G streptococcus (GGS) has recently been shown to cause streptococcal toxic shock-like syndrome (TSLS), which was originally thought to be caused only by group A streptococcus (*Streptococcus pyogenes* : GAS)[2]. Furthermore, a number of cases of bacteremia, necrotizing fasciitis, and thoracic empyema[1)2)] caused by GGS have recently been reported worldwide[3]. Most such disease-causing GGS are thought to be *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE)[4], which Vandamme et al. proposed to be a clinically pathogenic novel subspecies in 1996[5]. Group G streptococci are common members of the normal flora of the human skin, pharynx, gastrointestinal tract, and urinary system, but can sometimes cause pharyngitis, skin and soft tissue infections, septic arthritis, bacteremia, and endocarditis[6]. Cases of streptococcal TSLS progress very rapidly and are fulminant from onset, with the patient possibly developing necrosis of soft tissue, acute kidney injury, adult respiratory distress syndrome, disseminated intravascular coagulation, and multiple organ failure within 24 to 72 hours after onset, leading to shock and death[6]. The onset of invasive SDSE infection is thought to be strongly associated with underlying host factors and general conditions, but not with virulence factors or toxins of the specific strains[3)7)8)].

In Japan, since 2000, there has been an increase in the number of diagnoses of severe invasive group C or G streptococcus infections[3] according to figures provided by the National Institute of Infectious Diseases[6)9)] and other large-scale local hospitals[10]. Only 3 independent facilities[11-14] have reported on the analyses of GGS infections at their own facility. The purpose of this report is to present an analysis of cases of GGS infection at Tokyo Medical University Hospital together with a molecular epidemiological analysis of the strains involved.

Materials and Methods

1. Clinical Samples, Bacterial Strains, and Cases

A search of the database of our microbiology laboratory revealed that 7,618 strains were identified as streptococcus from culture specimens during the approximately 11-year period spanning January 1, 2002 to November 17, 2012. During this time, 47 strains isolated from blood culture specimens from 22 patients were identified as GGS. Of these, 10 were preserved for subsequent molecular epidemiological analysis (Fig. 1).

2. Analysis of GGS Strains

The number and type of isolate according to the Lancefield grouping (A, C, or G) was determined together with the type of clinical specimen in which it was detected, patient age, and the clinical department involved. A total of 22 GGS bacteremia cases were identified. The clinical records were consulted to establish the patient's clinical background, age, sex, underlying diseases, method of transportation to hospital, type of hospital visit, outcome, diagnosis of GGS infectious disease, and antimicrobial agents administered.

3. Antimicrobial Agent Susceptibility Test

Antimicrobial susceptibility tests were performed using microplate panels (MICroFast®5J or MICroFAST® 7J, Siemens, Japan). The Microscan WalkAway 96 Plus automated microbiology testing system (Beckman Coulter, Japan) was used for the analysis.

4. Bacterial DNA Extraction

Bacterial DNA, which is required for all the procedures described below, was extracted as follows : the preserved strains were grown on Pearl Core® heart infusion broth (EIKEN Chemical Co., Japan) ; DNA was

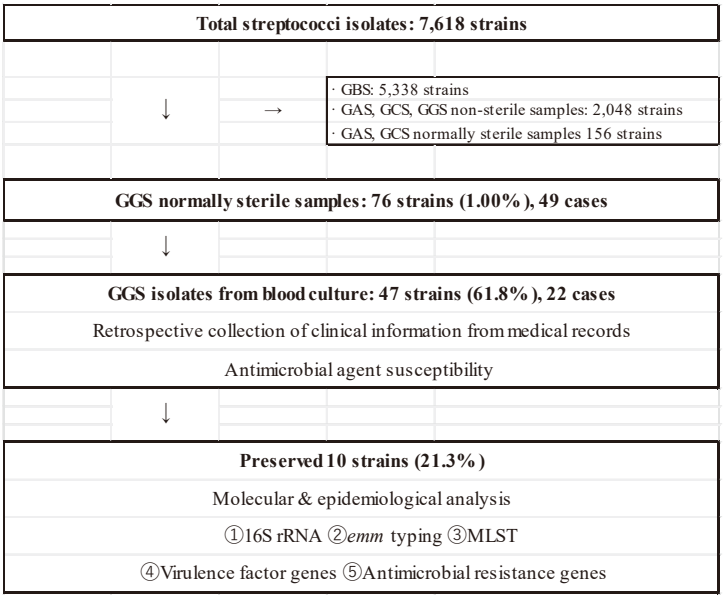

Fig. 1 Flow chart of study

extracted from the growing colonies using the DNeasy® Blood & Tissue Kit (50) (QIAGEN, Japan) in accordance with the manufacturer's protocol[15].

5. 16S ribosomal RNA (rRNA) Analysis

The species of the isolated strains were identified by 16S rRNA gene analysis. Using the universal primers 27F (5′-agagtttgatcctggctcag-3′) and 1492R (5′-ggttaccttgttacgactt-3′), polymerase chain reaction (PCR) was performed as described previously[3][16][17]. Amplified DNA fragments were sent to Solgent Corporation (Korea) for sequencing of the 16S rRNA, and homology searches were then performed using BLAST[18] and le BIBI[19].

6. *emm* Typing

Group G streptococci express a cell surface M-like protein which helps them evade the human immune system and exert pathogenicity. M-like proteins are encoded by *emm* genes, and strains can be typed according to the sequences of these genes[20]. The protocol of *emm* typing is shown on the Centers for Disease Control and Prevention (CDC) homepage[21]. The amplified DNA fragments were sent to Solgent Corporation for sequencing. The homology searches were performed by our team using the CDC database.

7. Multilocus Sequence Typing

In accordance with the procedure mentioned on the Multilocus Sequence Typing (MLST) database homepage[22], PCR was performed with the primers shown in Table 1. Amplified DNA fragments were sent to Solgent Corporation for sequencing. Homology searches were performed using the MLST site and the sequence type numbers of the isolates identified.

8. Analysis of Virulence Genes

The presence of the specific virulence genes *scpA*, *ska*, *slo*, *sag*, *speA*, *speB*, *speC*, *spe G*, *speJ*, *speI*, *speH*, *speL*, and *speM* was determined by PCR with specific primers (Table 1) as described previously[6][23], followed by agarose gel electrophoresis of the amplified DNA fragments.

9. Analysis of Antimicrobial Resistance Genes

Macrolide resistance genes (*erm*A, *erm*B, and *mef* A/E) and the tetracycline resistance gene (*tet*M) were detected by PCR using specific primers (Table 1) as described in previous studies[1][24-26]. This was followed by agarose gel electrophoresis of the amplified DNA fragments.

The study protocol was approved by the Ethics Committee of Tokyo Medical University Hospital (approval no. 2016-107).

Table 1 Primer sequences used for PCR

	Gene	Forward primer	Reverse primer (5′-3′)
	emm	TATT(C/G)GCTTAGAAAATTAA	GCAAGTTCTTCAGCTTGTTT
MLST	*gki*	GGAATTGGTATGGGATCACCAGGAGC	AATTCTCCTGCTGCTGACAC
	gtr	GCACAAGTATTATGGGCACA	CACGGTCTGCGACTTC
	murI	GACCTGCTGAGCAAATTAGAGAATACAC	CAGGACTTGCCGTTGTGTAAAAATGGTG
	mutS	GAAGAGTCATCTAGTTTAGAATACGAT	AGAGAGTTGTCACTTGCGCGTTTGATTGCT
	recP	GCAAATTCTGGACACCCAGG	CTTTCACAAGGATATGTTGCC
	xpt	TTACTTGAAGAACGCATCTTA	ATGAGGTCACTTCAATGCCC
	atoB	ACGTTGCTCAGAAATATGGCAT	AAAGTGTTGCTAGTCCTCTGGTTAC
Virlence genes	*speG*	AAGAAAATTTCTAATGGAAA	GTAGATATCAAAATGACTAA
	speJ	TTTCATGGGTACGGAAGTG	TTATGTATGGAGAATTAGG
	speI	ACTCTACATATGATCCAACA	TTATAAGAAATTCTCTCTCC
	speH	CAAATTCTTATAATACAACC	CTAACTTTTATATCCACTTC
	speL (M3)	GACGAAATTTTGGATAATAG	CTAATCTTTAGAAAAATCTT
	speL (M18)	TTAATTTTCTTTGTTTGTGT	ATGAGAATTTTTTTACACCA
	speM	CTAATTTTTAGAAAAATCTTC	TCGCTTGCTCTATACACTAC
	speA	CTTCAAAATATATATTTTC	TAAATGATTCCCTTCATG
	speB	GATCAAAACTTTGCTCGTAACG	AGGTTTGATGCCTACAACAGC
	speC	GACTCTAAGAAAGACATTTCG	AGTCCCTTCATTTGGTGAGTC
	scpA	CCATTTGATAAACTTGCC	ATTAATCACCTTAGCTCCC
	sagA	ACTTCAAATATTTTAGCTAC	CTTCCGCTACCACCTTGAG
	slo	CTTATCCTATTTCATACACC	CTACTTATAAGTAATCGAACC
	sla	GAAGGGATAAATGATAAAATGG	TTAACATCCTATAGAACCTAC
Antimicrobial resistance genes	*Erm*A	TCTAAAAAGCATGTAAAAGAA	CTTCGATAGTTTATTAATAATATTAGT
	*Erm*B	GAAAAGGTACTCAACCAAATA	AGTAACGGTACTTAAATTGTTTAC
	*mef*A/*mef*E	AGTATC ATTAATCACTAGTGC	TTCTTCTGGTACTAAAAGTGG
	*tet*M	GAACTCGAACAAGAGGAAAGC	ATGGAAGCCCAGAAAGGAT

Results

1. Lancefield Serologic Grouping of Isolates

A total of 7,618 streptococcal strains were identified. The number and proportion of each Lancefield serologic group are shown in Fig. 2. The annual number of isolations of GGS has increased since 2004, with 55 isolated in 2002, and approximately 100 per year after 2006. Similarly, the number of GGS isolates from normally sterile samples also showed a tendency to increase (Fig. 3). Group A streptococcus, group C streptococcus (GCS), and GGS were isolated from 139/954 (14.6%), 17/369 (4.6%), and 76/957 (7.9%) patients with infectious diseases, respectively, and all from samples that normally would have been expected to be sterile, such as blood, pleural effusion, ascites, puncture exudate, and pus obtained from a closed space. As for the age distribution, GAS had a tendency to be isolated from younger patients, whereas GGS tended to be isolated from older patients (Fig. 4). Clinical departments in which streptococci were most frequently detected comprised Dermatology, followed by Otorhinolaryngology, Pediatrics, and Emergency and Critical Care. The rate of detection of GAS was high in the Department of Pediatrics, and that of GGS isolates was high in the Department of Neurology and Geriatric Medicine (Fig. 5).

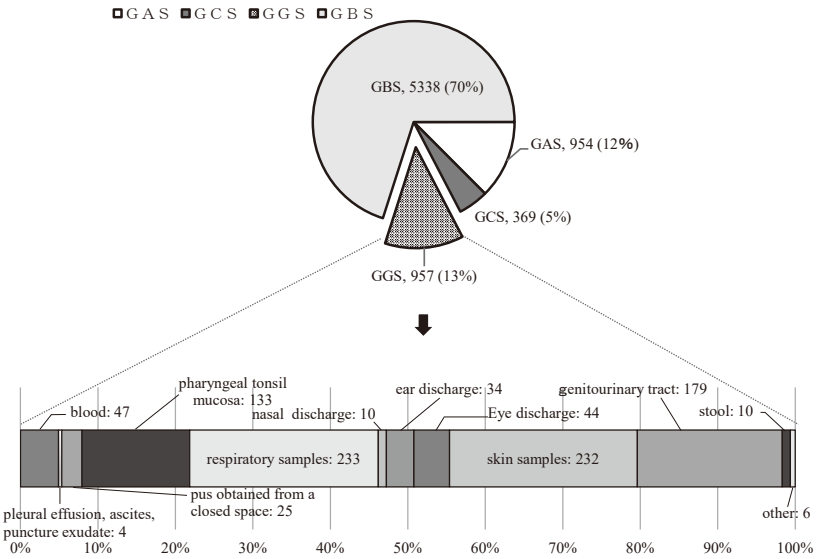

Fig. 2 Proportion of each Lancefield serologic group of streptococci isolated (total 7,618) and breakdown of specimen types containing GGS.

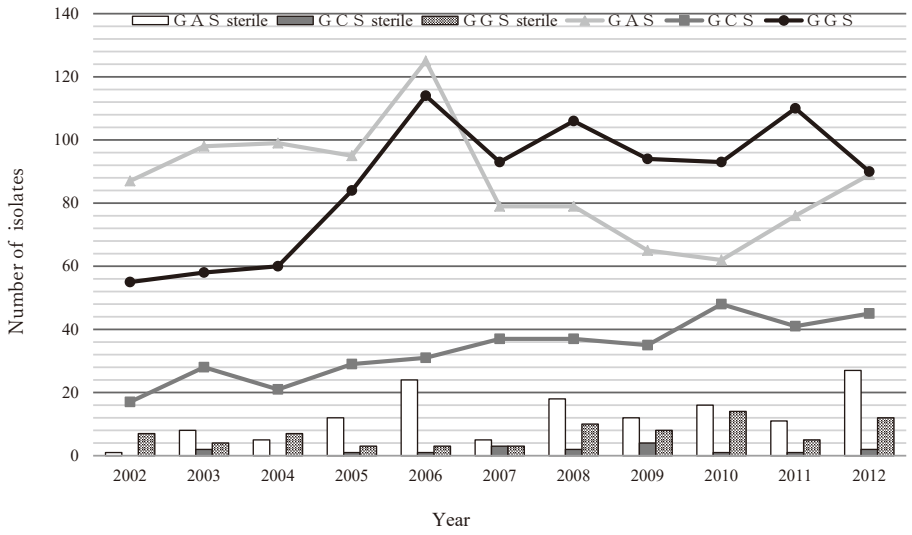

Fig. 3 Annual trends in groups A, C, and G streptococci isolated in total (lines) and from normally sterile samples (bars)
Number of GGS isolates increased from 2005, and was approximately 100 isolates annually from 2006. GGS isolates from normally sterile samples also increased, with approximately 10 isolates annually from 2008.

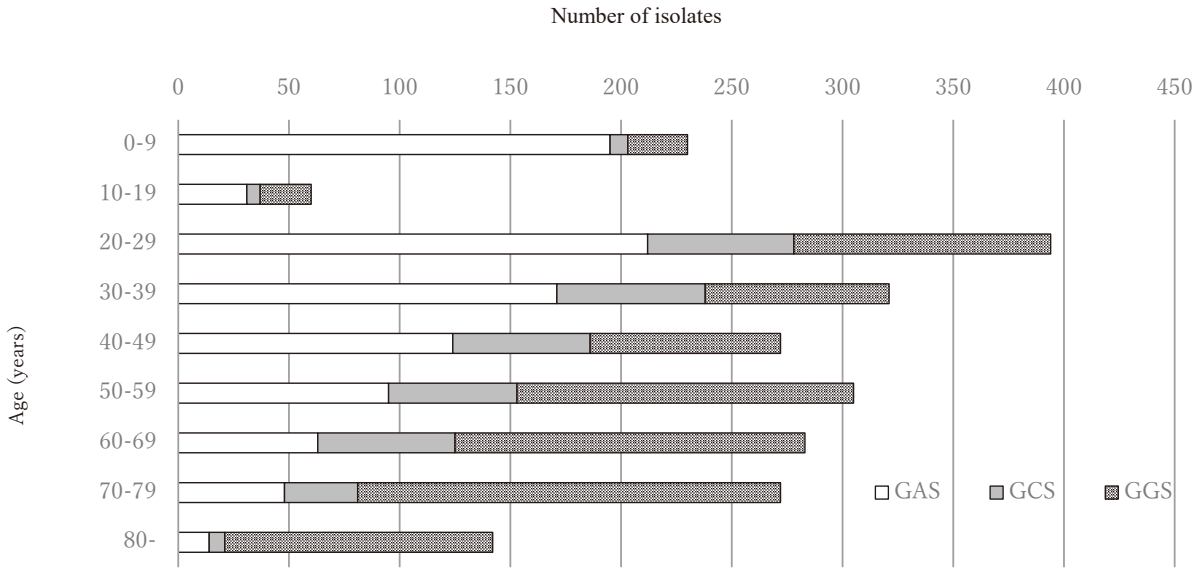

Fig. 4 Age distribution in patients infected with group A, C, or G streptococci
Prevalence of GAS was higher in younger patients, whereas prevalence of GGS was higher in older patients.

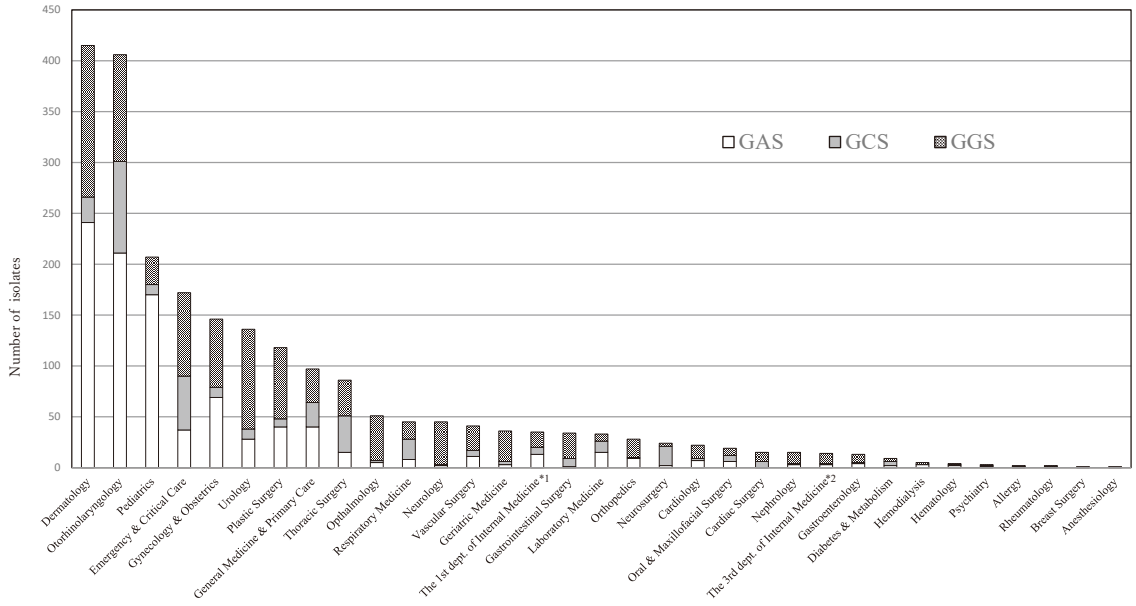

Fig. 5 Detection of GAS, GCS, and GGS at various clinical departments
Clinical department with highest rate of detection of streptococci was Dermatology, followed by Otorhinolaryngology, Pediatrics, and Emergency and Critical Care.
*1 1st Department of Internal Medicine comprised combined departments of Hematology and Respiratory Medicine until 2005
*2 3rd Department of Internal Medicine comprised combined departments of Diabetes, Endocrinology, Metabolism and Hematology until 2005

2. Clinical Backgrounds of Patients

The clinical characteristics and manifestations of the patients are shown in Table 2 and Table 3, respectively. Five of the patients died in hospital, of which 2 were suspected to have died from GGS infection. There were no cases suggesting a fulminant type of streptococcal infection.

3. Antimicrobial Susceptibilities

Except for 1 strain, the GGS strains had high susceptibility to penicillin, with minimum inhibitory concentrations of less than 0.25 μg ; however, 5, 3, and 3 isolates were resistant to cephalosporins, fluoroquinolones, and tetracyclines, respectively. Two other strains were resistant to both macrolides and tetracyclines (Table 4).

Table 2 Clinical characteristics of 22 GGS blood culture-positive patients (all admission cases)

Age (years)	0-97	(Median : 69 ± 21.8)
Sex	Men : 11 (50%)	Women : 11 (50%)
Outcome	Death : 5 (22.7%)	Recovery : 17 (77.3%)
Length of admission (days)	Mean : 54.9 (range : 3-326)	

		Number of patients (%)
Method of transport/type of hospital visit	Ambulance	13 (59.0)
	Hospital transfer	2 (0.09)
	Outpatient	6 (27.2)
	Inpatient	1 (0.05)
Underlying diseases	Malignant disease	11 (50.0)
	Cardiovascular disease	8 (36.3)
	Chronic kidney disease	4 (18.1)
	Diabetes	3 (13.6)
	Hepatitis C	3 (13.6)
	HIV infection	2 (0.09)
	Atrial fibrillation	2 (0.09)

There were equal numbers of men and women. More than half of patients with invasive GGS were brought to hospital by ambulance.

Table 3 Clinical manifestations of 22 patients with GGS-positive blood cultures

Clinical manifestation	No. of cases
Cellulitis	5
Pneumonia, pleuritis	3
Arthritis, spondylitis	2
Mastitis	1
Infectious endocarditis	1
Endophthalmitis	1
Necrotizing mediastinitis	1
Urinary tract infection	1
Bacteremia with an unidentified primary focus	7
Total	22

4. Molecular Epidemiology and Analysis of Strains

The results of the 16S rRNA analysis of the 10 preserved strains showed 99.9% (1,465 base pairs (bp)/1,466 bp) homology with the standard strain SDSE (accession number NC_019042.1 [BLAST], DQ232540 [le BiBi]). As for *emm* typing, 5 strains were typed as *stG679.2*, 2 as *stG6.1*, and 1 each as *stG480.0*, *stG10.0*, and *stC36.0*. As for the MLST, 6 strains were ST17, 2 were ST15, and 1 each were ST25 and ST8. All 10 strains had the *scpA*, *ska*, *saga*, and *slo* virulence genes, and among them, 3 strains also had the *speG* gene. No strain had the *speA*, *speB*, or *speC* genes, which are thought to be associated with fulminant streptococcal infections. None of the strains had the *erm*A, *erm*B, or *mef*A/E macrolide resistance genes, while 1 of the 3 tetracycline-resistant strains had the *tet*M gene (Table 5).

Discussion

In Japan, only a few GGS cases, including TSLS, have been reported since 1996. Starting with the investigation by Ikebe et al. at the National Institute of Infectious Diseases in 2003[6], large-scale investigations[3)8)9)27)28)] have been performed mainly by Ubukata and the Invasive Streptococcal Disease Working Group as part of the 'Research Project for Emerging and Re-emerging Infectious Diseases' run by the Ministry of Health, Labor and Welfare of Japan[28]. However, detailed investigations of SDSE infections at a single facility have been limited, with only 4 reports to date (Takahashi et al., in 2009[11] and Asami et al., 2010[12] at the same facility ; Ichikawa et al., in 2011[13], and Fujita et al., in 2016[14]). However, these studies had several limitations : there was a selection bias, as only elderly patients were enrolled, and a lack of clinical details regarding the invasive infections involved.

The characteristics of the present study were that, even though it was performed at a single facility, it was a 10-year investigation at a tertiary care university hospital situated in a metropolitan area ; and that it employed a large sample size of 7,618 streptococcal specimens obtained from 49 invasive infection cases, which was much larger than in previous studies[13)14)].

Table 4 Antibiotic susceptibility of 22 SDSE strains isolated from blood cultures

Antibiotics administered	Death : 5 patients		Recovery : 17 patients	
	S	I + R	S	I + R
PCG	5 (100%)	0	17 (100%)	0
ABPC	5 (100%)	0	17 (100%)	0
ABPC/SBT*1	4 (100%)	0	12 (92.3%)	1 (7.7%)
CEZ*2	0	1 (100%)	0	4 (100%)
CTM or CTX	4	1 (20%)	13 (76.5%)	4 (23.5%)
FMOX*2	0	1 (100%)	0	4 (100%)
IPM/CS or MEPM	5 (100%)	0	17 (100%)	0
MINO*2	1 (100%)	0	1 (25%)	3 (75%)
CAM*1	4 (100%)	0	11 (84.6%)	2 (15.4%)
TC*1	4 (100%)	0	8 (61.5%)	5 (38.5%)
VCM	5 (100%)	0	17 (100%)	0
LVFX	5 (100%)	0	14 (100%)	3 (13.6%)

PCG : penicillin G, ABPC : ampicillin, ABPC/SBT : ampicillin/sulbactam, CEZ : cephazolin, CTM : cefotiam, CTX : cefotaxime, FMOX : flomoxef, IPM/CS : imipenem/cilastatin, MEPM : meropenem, MINO : minocycline, CAM : clarithromycin, TC : tetracycline, VCM : vancomycin, LVFX : levofloxacin

S : susceptible, I : intermediate, R : resistant

*1/ 17 isolates were tested with MICroFAST®7J.

*2/ 5 isolates were tested with MICroFAST®5J.

Similarly to previous large-scale studies, the number of GGS isolates at our hospital increased from 2004[4]. Compared to the results of earlier nationwide investigations into cases of invasive infection, the median age in such cases at our hospital was lower, at 61 ± 23.1 years compared with 75 ± 15[10], 84[11], and 80 years[12]. Comorbid conditions, including a variety of underlying diseases, were found in the SDSE bacteremia cases seen here, and this was higher than that at other hospitals in Japan (76%-85%)[10)12)28)]. Two patients (9%) among the 22 GGS bacteremia cases were thought to have died from this infection, which was lower than the 27.3% rate reported by Asami et al[12]. Previous studies[28)29)] have suggested that a white blood cell count of less than 5,000/μL or a platelet count of less than 13 × 10^4/μL at the time of a patient's first visit indicates a poor outcome in patients with invasive streptococcal infections. Six patients among the 22 GGS bacteremia cases here were found to have a poor prognosis based on these indices in the results of peripheral blood test results on their first visit. In 2 of these patients, a decrease in white blood cell and/or platelet count was thought to have been caused by an underlying hematological malignancy, whereas in another patient it was thought to have been due to chemotherapy for malignant disease. However, all bar 1 of these 6 patients recovered and were discharged without any post-infection sequelae. The most prevalent clinical manifestation of GGS bacteremia at our hospital was a lack of an identifiable primary focus, followed by cellulitis and respiratory infection, including pneumonia. These results were identical to those of earlier nationwide surveillance studies[10)27)28)].

Our molecular characterization results showing that there were many isolates of types *stG6792.3* and ST17 were also consistent with those of previous nationwide studies[7)10)27)], which showed that those were the most dominant isolates from invasive SDSE infections in Japan. The same results were obtained from a nationwide investigation[3)] concluding that all SDSE isolates had the *scpA*, *ska*, *saga*, or *slo* virulence factor genes. In the present study, 3 strains had the *speG* virulence factor gene, but we did not detect any differences in the clinical courses of the patients concerned compared with those of the other patients. Regarding antimicrobial susceptibilities, the resistance of streptococci to macrolides, tetracyclines, and new quinolones has become a serious problem all over the world[1)8)10)]. Here, 3 of the 22 strains were resistant to the fluoroquinolone levofloxacin, which is a high proportion. Regarding resistance to beta-lactam antibiotics, which is currently not considered a serious problem in other facilities, 6 strains were found to be resistant or partially resistant to beta-lactam antibiotics. None of the strains had macrolide resistance genes, and only 1 of the 3 strains that were resistant to tetracycline had the *tet*M gene. Regarding the rate of possession of the *tet*M gene, it was previously reported to be present in 62% of tetracycline-resistant strains[30)], which is similar to the present results. It was reported that 10.9% of strains had the *erm*A, *erm*B, or *mef*A gene (macrolide resistance genes)[1)]. Another study reported

Table 5 Molecular and epidemiological data on 10 preserved strains and details of clinical cases

Strain no.	Year of isolation	Age	Sex	Clinical manifestation	Underlying diseases*1	Length of admission (days)	Outcome	Possibility of death due to infection	16S rRNA	*emm*	MLST	Antimicrobial agent susceptibility	Antibiotics administered	Virulence facter genes						Antimicrobial resistance genes	
														speG	*scpA*	*ska*	*sagA*	*slo*	Others*2	*tet*(M)	Others*3
1	2009	59	M	urinary tract infection	1, 2	37	Recovery	−	SDSE	*stG6792.3*	ST17	LVFX : R	MEPM	−	+	+	+	+	−	−	−
2	2009	0	F	bacteremia of unknown focus	others	326	Recovery	−	SDSE	*stG6792.3*	ST17	LVFX : R	VCM, CFPM	−	+	+	+	+	−	−	−
3	2010	76	F	endophthalmitis	1, 2	46	Death	possible	SDSE	*stG480*	ST17	no resistance	not administered	−	+	+	+	+	−	−	−
4	2010	97	M	cellulitis	2, 4	13	Recovery	−	SDSE	*stG6792.3*	ST17	no resistance	CAZ, CTRX, ABPC/SBT, ABPC, AMPC/CVA,	−	+	+	+	+	−	−	−
5	2010	79	F	infectious endocarditis	2	30	Death	no	SDSE	*stG6792.3*	ST17	no resistance	ABPC, GM, PCG,CLDM	−	+	+	+	+	−	−	−
6	2012	77	M	cellulitis	2	22	Recovery	−	SDSE	*stG6792.3*	ST17	no resistance	ABPC/SBT, ABPC,CLDM、	−	+	+	+	+	−	−	−
7	2012	88	M	bacteremia of unknown focus	2	3	Death	no	SDSE	*STG6792.3*	ST25	no resistance	MEPM, PCG, VCM	−	+	+	+	+	−	−	−
8	2012	33	M	cellulitis	6	8	Recovery	−	SDSE	*stG6.1*	ST15	CAM : R, TC : R	ABPC, CEZ, CLDM	+	+	+	+	+	−	−	−
9	2012	80	F	cellulitis	others	39	Recovery	−	SDSE	*stG6.1*	ST15	CAM : I, TC : R	LVFX, ABPC/SBT, ABPC, CEZ, CLDM	+	+	+	+	+	−	+	−
10	2012	61	M	necrotizing mediastenitis	2	34	Recovery	−	SDSE	*stC36.0*	ST8	TC : R, ABPC/SBT : I	CFPM, VCM, PCG, AMPC/CVA, AMPC	+	+	+	+	+	−	−	−

Among 10 preserved isolates, *emm stG 6792.3* and ST 17 of MLST were most abundant.

PCG : penicillin G, ABPC : ampicillin, ABPC/SBT : ampicillin/sulbactam, AMPC/CVA : amoxicillin/clavulanate, CEZ : cephazolin, CTM : cefotiam, CTRX : ceftriaxone, CFPM : cefepime, CAZ : ceftazidime, MEPM : meropenem, CAM : clarithromycin, CLDM : clindamycin, TC : tetracycline, GM : gentamycin, VCM : vancomycin, LVFX : levofloxacin

S : susceptible, I : intermediate, R : resistant

*1 : 1. malignant disease, 2. cardiovascular disease, 3. chronic kidney disease, 4. diabetes, 5. hepatitis C, 6. HIV infection, 7. atrial fibrillation

*2 : *speJ*, *spe I*, *speH*, *speL (M3)*, *speL (M18)*, *speM*, *speA*, *speB*, *spe C*, or *sla*

*3 : *erm*A, *erm*B, or *mef*A/E

that strains that do not have these macrolide resistance genes still have MICs to azithromycin of greater than 8 μg/mL[1]. This suggests that these strains may have other mechanisms of antimicrobial resistance than those investigated hitherto[1].

This study had some limitations. At this hospital, identification of species from strains isolated from blood cultures is carried out at the microbiology laboratory. Therefore, some SDSE strains may have been counted as GCS, and streptococci other than SDSE may have been counted as GGS.

Furthermore, the patients in the present study were younger than those in earlier studies, but had underlying diseases, and hence their general condition may have been worse than that in the patients targeted in earlier surveillance studies at multiple facilities or single facilities nationwide. This may have been because our institution is a university hospital located in a metropolitan area, or due to differences in the investigation period. Even if a patient is relatively young, any treatment strategy should still take into account their clinical background, which means that infectious diseases more commonly associated with elderly patients with underling diseases should not be ruled out. However, the relative youth of the patients here meant that treatment was able to yield a full recovery, despite the presence of an invasive infection.

stG6792.3 was first detected in India[11], and is known to be uncommon in the United States[31], Europe[27], Taiwan, and China[23]. It is known that SDSE mutates more rapidly than GAS, and new types of strains are identified every few years. As we treat many foreign travelers at our hospital, it is possible that this will become the first institution in Japan to detect a new type of SDSE strain in the near future.

Conclusion

Patients, regardless of their age, should be treated on the assumption of a possible lethal invasive SDSE infection, taking into consideration underlying diseases and general condition.

Conflict of interest

None to declare.

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東京医科大学病院における *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) 感染症の実態調査

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【要旨】 2002 年から 2012 年に東京医科大学病院（以下「当院」と略す）で分離された G 群溶連菌 (group-G streptococci : GGS）について調査した。GGS は 957 株検出され、通常無菌検体から分離された GGS は 76 件、22 例の菌血症例があった。22 症例は診療録を調査し、分離・保存 10 菌株については、DNA を抽出し分子疫学解析と病原因子・薬剤耐性因子遺伝子を同定した。保存 10 菌株は、16S rRNA 解析で全株 SDSE と同定された。GGS 感染症による死亡は 2 例で、基礎疾患は血液･悪性腫瘍が 11 例と多かった。薬剤感受性ではセフェム系、ニューキノロン系、テトラサイクリン・マクロライド系抗菌薬耐性を示す株がみられた。*emm* 型と MLST は、本邦で侵襲感染症の原因として最も分離される *stG679.2* 型および ST17 が多く、全 10 株が病原因子遺伝子 *scpA*、*ska*、*sagA*、*slo* を、3 株が *speG* を有していた。薬剤耐性遺伝子 *tet*M を有するものが 1 株あった。当院での侵襲性 GGS 感染症例の年齢の中央値は 61 ± 23.1 歳で、他施設の報告と比較して低い一方、救命率は高かった。当院のような高次機能病院では、患者の基礎疾患や全身状態を考慮し、患者の年齢に関わらず侵襲性 SDSE 感染症を想定して診療にあたる必要がある。

〈キーワード〉G 群溶血性連鎖球菌、SDSE、*emm*、病原因子遺伝子、薬剤耐性因子遺伝子