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Case study

Infective endocarditis following urinary tract infection caused by *Globicatella sanguinis*

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ABSTRACT

We report the first case of infective endocarditis following urinary tract infection (UTI) caused by *Globicatella sanguinis* in an 87-year-old Japanese woman with recurrent episodes of UTI. We identified the pathogen using the Rapid ID32 Strep system. Accurate identification of this infection is important and essential for the effective antimicrobial coverage to this pathogen.

Introduction

G. sanguinis was described in 1992 as a new genus and species of catalase-negative, facultatively anaerobic, non-motile, non-hemolytic, Gram-positive cocci (GPC) forming short chains or pairs by Collins, et al. [1]. Only 42 isolates from clinical specimens and 13 case reports about UTI, bacteremia, or meningitis have been reported (Table 1). These reports suggest that *G. sanguinis* can colonize inguinal skin [2] and aged female patients with a history of cerebrovascular disease are susceptible to *G. sanguinis*. However, the epidemiology and the clinical significance of this pathogen remain largely unknown. *G. sanguinis* is an unusual pathogen that it could be misidentified or misdiagnosed with viridans streptococci (or may be overlooked) due to its colonial morphology [3]. We successfully identified the organism using the Rapid ID32 Strep system. We present the first case of an infective endocarditis by *G. sanguinis* following a UTI.

Case report

An 87 year-old Japanese woman was admitted to our hospital with recurrent episode of UTI, with a fever higher than 38.5 °C for 5 days, and with hematuria despite taking oral levofloxacin 500 mg and acetaminophen 1200 mg daily. She had been bedridden at nursing home since a subarachnoid hemorrhage and surgical construction of ventriculo-peritoneal shunt, and she had gastrostomy 10 years ago. On examination, she had body temperature of 36.5 °C, blood pressure 92/35 mmHg, pulse 84 bpm, respiratory rate 16 breaths/min, and pulse oxygen saturation 98% on room air. Physical examination showed Glasgow Coma Scale (GCS) of 7 (E2, V2, M3), inner lip bleeding, and systolic murmur at cardiac apex. Laboratory data at the admission was leucocyte count 35,600/mL, hemoglobin level 10.7 g/dL, platelet count 4.3000/mL, C-reactive protein 21.1 mg/dL, procalcitonin level 20.5 ng/mL, albumin 1.9 mg/dL, blood urea nitrogen 212 mg/dL, creatinine 3.9 ng/mL, uric acid 11.1 mg/dL, and lactate dehydrogenase 299 IU/L. Urine microscopy showed the presence of leukocytosis and numerous bacteria. Abdominal CT scans revealed bilateral hydronephrosis and hydroureters besides distended urinary bladder. After inserting urinary bladder catheter, pyuria and hematuria were obtained. Urinary gram stain showed GPC (1 +) in pairs and short chains and Gram negative rods (GNR) (2+). She was diagnosed with infected hydronephrosis due to neurogenic bladder and started to receive ceftriaxone (CTRX) 2 g every 24 h empirically.

On day 3, her blood cultures from admission were growing aerobic, a-hemolytic GPC in short chains in 2 of 4 bottles (Fig. 1A, B). On day 4, the isolates were identified as *G. sanguinis* with a high certainty (98.8%) by Rapid ID32 Strep (bioMerieux, Lyon, France). In order to double-

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Table 1
Clinical reported 42 cases of *G. sanguinis* infections.

Reference	Country	Age	Gender	Underlying conditions	Presenting signs and symptoms	Site of isolation	Infection	Identification	Antibiotic treatment	Outcome
[2]	France	56	F	N/A	meningitis	CSF	meningitis	16S rRNA sequencing	CTX, FOM	alive
[3]	USA	N/A	F	N/A	N/A	blood	bacteremia	Rapid ID 32 Strep + BBL Crystal Rapid Gram-Positive ID kit + BBL Crystal Gram-Positive ID kit + RapID STR	N/A	N/A
[3]	USA	N/A	F	N/A	N/A	blood	bacteremia	same as above	N/A	N/A
[3]	USA	N/A	M	N/A	N/A	urine	urinary	same as above	N/A	N/A
[3]	USA	N/A	N/A	N/A	N/A	blood	bacteremia	same as above	N/A	N/A
[3]	USA	N/A	N/A	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	69	M	N/A	N/A	urine	urinary	same as above	N/A	N/A
[3]	USA	85	F	N/A	N/A	urine	urinary	same as above	N/A	N/A
[3]	USA	N/A	N/A	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	1	M	N/A	N/A	CSF	meningitis	same as above	N/A	N/A
[3]	USA	84	F	N/A	N/A	blood	sepsis	same as above	N/A	N/A
[3]	canada	N/A	F	N/A	N/A	urine	N/A	same as above	N/A	N/A
[3]	USA	90	F	N/A	N/A	blood	urosepsis	same as above	N/A	N/A
[3]	USA	68	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	canada	82	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	canada	79	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	N/A	N/A	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	1	M	N/A	N/A	blood	septocemia	same as above	N/A	N/A
[3]	USA	N/A	N/A	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	58	M	N/A	N/A	blood	septocemia	same as above	N/A	N/A
[3]	USA	82	F	N/A	N/A	blood	septocemia	same as above	N/A	N/A
[3]	canada	2	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	canada	92	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	canada	N/A	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	70	F	N/A	N/A	blood	endocarditis	same as above	N/A	N/A
[3]	canada	43	F	N/A	N/A	CSF	N/A	same as above	N/A	N/A
[3]	canada	85	M	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	canada	1	F	N/A	N/A	blood	N/A	same as above	N/A	N/A
[3]	USA	3	F	N/A	N/A	blood	septicemia	same as above	N/A	N/A
[4]	Japan	80	F	colon cancer, brain stroke,dementia, HTN	fever, pyuria	urine	urinary	16S rRNA sequencing	ABPC	alive
[5]	Korea	85	F	parkinson's disease, asthma, hypertwnsion, staying at nursing home	pain and swelling of left arm, fever	blood	bacteremia	partial 16S rRNA sequencing	VCM + CTRX	alive
[7]	USA	72	F	obesity, gastrip lap banding, tabacco	Hip pain	Hip synovium	prosthetic joint infection	API 20TREP + Vitek 2 g-Positive ID card + MALDI-TOF MS	VCM	alive
[7]	USA	54	F	obesity, DM, gastric bypass, tabacco	fatigue and fever	blood	bacteremia	MALDI-TOF MS	LZD	alive
[12]	Taiwan	80	F	chronic diarrhea, DM	cardiac arrest	blood	bacteremia	16S rRNA sequencing	N/A	died
[12]	Taiwan	92	F	dementia, CHF	fever, cough	blood	urosepsis	16S rRNA sequencing	CXM = > CAZ	alive
[13]	Denmark	23	F	intravenous drug use. Right-sided endocarditis, hepatitis C	pneumonia	blood	bacteremia	Rapid ID32 Strep, partial 16S rRNA sequencing	CXM = > PC	alive
[13]	Denmark	82	F	alzheimer's disease, hypertension	dehydration	blood	urosepsis	Rapid ID32 Strep, partial 16S rRNA sequencing	PC	alive
[13]	Denmark	56	M	crohn's disease, atrial fibrillation	erysipelas, dyspnoea, fever	blood	bacteremia	Rapid ID32 Strep, partial 16S rRNA sequencing	CXM	alive
[14]	Japan	94	M	dementia, CHF, nephrolithiasis	back pain, fever	blood	bacteremia	16S rRNA sequencing	ABPC/ SBT = > VCM	alive
[15]	Germany	69	F	VPS	meningitis	CSF	meningitis	Rapid ID32 Strep, phoenix PMIC/ID-56	CTRX	alive
[16]	India	70	M	Craniectomy	meningitis	CSF	meningitis	Vitek 2 ID	LVFX, CPZ, SBT, AMK = > VCM, LVFX	alive

DM, diabetes mellitus; CHF, chronic heart failure; VPS, ventriculoperitoneal shunt; CSF, cerebrospinal fluid; VCM, vancomycin; CTRX, ceftriaxone; LZD, linezolid; CXM, cefuroxime; CAZ, ceftazidime; PC, penicillin; ABPC/SBT, ampicillin/sulbactam; ABPC,levofloxacin ampicillin; CTX, cefotaxime; FOM, fosfomycin; LVFX, levofloxacin; CPZ, cefoperazone; SBT, sulbactam; AMK,amikacin; MEPM, meropenem

check the results, we performed 16S rRNA sequencing because the species is rare and for confirmation of the diagnosis. Extended-spectrum b-lactamase producing *Escherichia coli* (ESBL-producing *E. coli*) simultaneously was observed in the two sets of blood culture bottles. *G. sanguinis* and ESBL-producing *E.coli* in her urine culture were also identified. She was diagnosed with bacteremia due to UTI caused by both of the organisms. The antimicrobial treatment was altered to meropenem 0.5 g every 12 h, for a 14-day course, considering

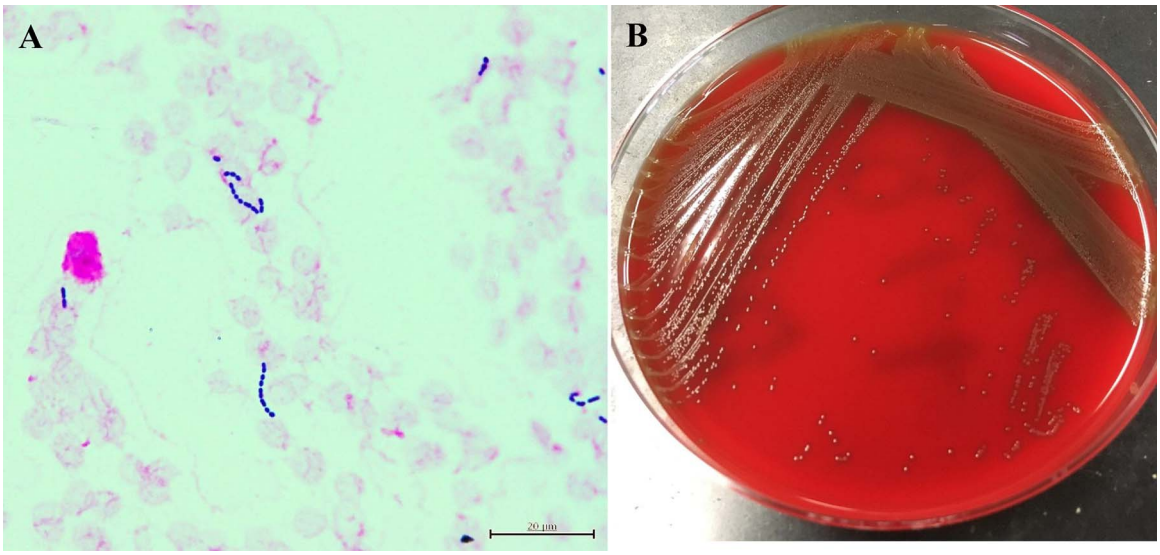

Fig. 1. (A) Microscopic appearance of the isolates from her blood after Gram staining (×1000). (B) morphology of colonies on sheep blood agar.

Table 2
Susceptibility Testing Results of *G. sanguinis*.

	MIC mg/mL	Interpretation
AMPC/CVA	< = 0.25	*
ABPC	< = 0.06	S
AZM	< = 0.25	S
CDTR-PI	1	*
CFPM	1	S
CTX	2	I
CTM	> 4	*
CTRX	2	I
CZOP	1	S
CP	< = 4	S
CLDM	< = 0.12	S
EM	< = 0.12	S
LVFX	8	R
MEPM	0.25	S
MINO	< = 0.5	S
PCG	0.06	S
ST	> 4	*
VCM	0.25	S

antimicrobial susceptibility testing results (Table 2) by WalkAway 40 SI system (Beckman Coulter, California, USA) and her renal function test results. Urine culture obtained before treating with meropenem showed the growth of *G. sanguinis* again, but her repeated blood and urine cultures after treatment were negative.

On day 6 of the treatment with meropenem, transthoracic echocardiography revealed a 3 mm (in diameter) vegetation (Fig. 2A) on the mitral valve besides mild aortic, mitral and tricuspid regurgitation. Meeting with Duke's criteria (1 major and 3 minor criteria), she was eventually diagnosed with IE due to UTI-associated bacteremia. Her CT scans showed there was no abscess formation on the entire body. On day 10 of meropenem, a 2 mm vegetation on left coronary cusp of aortic valve was discovered by transesophageal echocardiography (TEE) (Fig. 2B). We presumed that *G. sanguinis* caused the endocarditis and administered her a 2 week of ampicillin 2 g every 8 h intravenously after completion of the meropenem treatment. After the 2 weeks of ampicillin, no vegetation was detected on TEE. She showed improvement and was discharged from the hospital to a nursing facility. She was in the hospital for 40 days.

Discussion

We believe that this is the first case of having IE followed with UTI caused *G. sanguinis* complicated with ESBL-producing *E.coli* infection. *G. sanguinis* looks like viridans streptococci in Gram-stain morphology and colonial morphology including hemolysis pattern on sheep blood agar but has difference in not producing leucine aminopeptidase (LAP) and growth in the presence of 6.5% NaCl. Susceptibility to the third-generation cephalosporins is also different: *G. sanguinis* is resistant while a-streptococcus is susceptible [3]. Although we successfully identified *G. sanguinis* by rapid ID32 Strep with a high certainty (98.8%), there are some past cases that failed *G. sanguinis* identification by the same methods [4]. There may be two reasons; one is that *G. sanguinis* shows various biochemical reaction depending on strain [5] and the other is that the data of *G. sanguinis* had not been collected on the database of the rapid ID32 Strep system until 2006. If rapid ID32 Strep fails to identify *G. sanguinis,* 16S rRNA sequencing is required. We additionally attempted Bruker matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, Bremen, Germany) with MBT Compass software using MALDI Biotyper library version 5.0. The identification process suggested not *G. sanguinis* but *G. sulfidifaciens* with cutoff score of 1.97 (Table 3). *G. sulfidifaciens,* first described in 2001 isolated only from animals, has 99.2% similarity in 16S rRNA gene sequencing to *G. sanguinis* [6] but is different in biochemical reaction. Although, Miller et al. succeeded to identify *G. sanguinis* with Bruker MALDI-TOF MS with MBT 6903 MSP library database [7], MALDI-TOF MS is not so useful to identify the organism because there are only 3 *G. sanguinis* strains appeared in the database. An update of the database is needed.

In our case, both *G. sanguinis* and *E. coli* were found in blood culture when the patient was admitted. IE caused by *E. coli* is rare (< 1%) and *G. sanguinis* has been reported to be an opportunistic pathogen [8–10]. Patients diagnosed with E.colli IE are reported to be often diabetic with

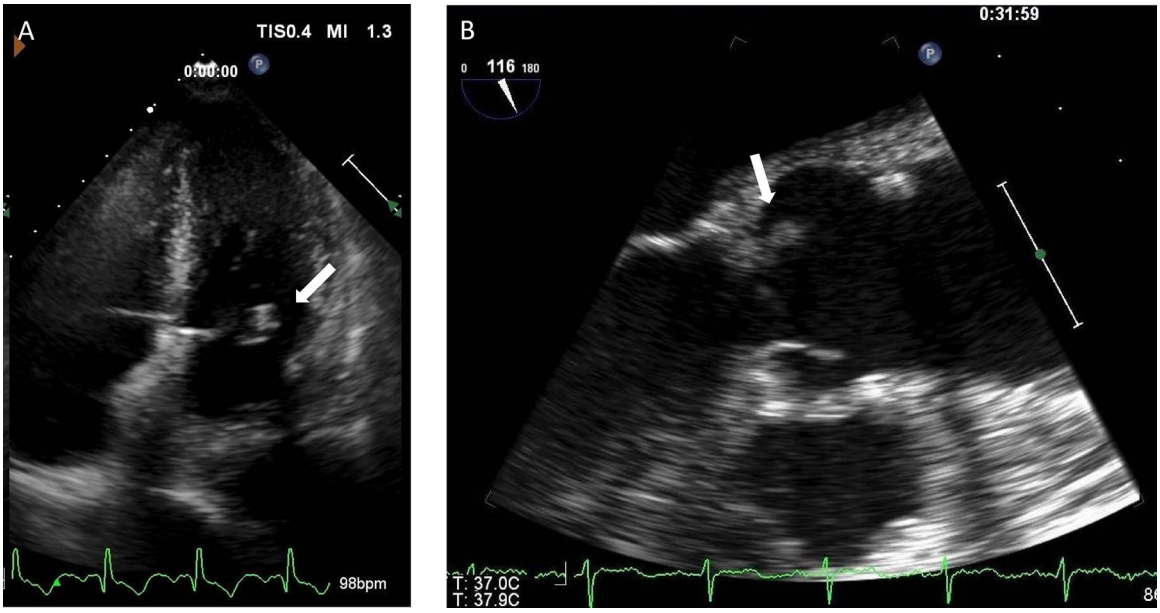

Fig. 2. (A) Parasternal long axis view on transthoracic echocardiogram shows a vegetation on posterior leaflet of mitral valve (arrow). (B) Parasternal long axis view on transesophageal echocardiogram shows a vegetation on left coronary cusp of aortic valve (arrow).

Table 3
Results of Bruker MALDI-TOF MS analysis.

Rank (Quality)	Matched Pattern	Score value
1 (+)	Globicatella sulfidifaciens 11_ 0100356_001_01 LGL	1.97
2 (-)	Stenotrophomonas maltophilia 10942 CHB	1.44
3 (-)	Pseudomonas boreopolis LMG 979T HAM	1.39
4 (-)	Stenotrophomonas sp 109_Neb28 NFI	1.37
5 (-)	Lactobacillus pentosus DSM 16366 DSM	1.33

underlying heart disease or have prosthetic valves. Surgery is often necessary and the mortality rate is high (17%) [11]. Therefore, we speculated that IE caused by *G. sanguinis* followed a subacute clinical course, similar to viridans streptococcus, and her IE was caused by *G. sanguinis*. In order to verify our speculation, identifying *G. sanguinis* IE correctly with Rapid ID 32 Strep, collecting more cases of *G. sanguinis* IE, and then revealing clinical feature of *G. sanguinis* IE are required.

Ethics statement

Written informed consent to publish clinical details was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Conflict of interest

We have no conflict of interest to disclose.

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