Gemella species endocarditis in a child

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Organisms of the genus *Gemella* can, on occasion, cause serious systemic illness. The present paper reports a successfully treated case of endocarditis in a 12-year-old girl with congenital heart disease caused by species of *Gemella*. The child presented with cough, fatigue and decreased appetite without fever. Echocardiogram demonstrated marked mitral insufficiency with flail posterior mitral valve leaflet, mitral valve vegetations, and an enlarged left atrium and ventricle. While being treated with vancomycin, the child initially had persistent bacteremia, which resolved after the addition of gentamycin; the course of therapy was completed with penicillin G and gentamycin once antimicrobial susceptibilities were available. Attempts to identify the species of *Gemella* were unsuccessful in the local laboratory, and at reference laboratories in Canada and the United States. The isolate is undergoing further evaluation to determine its taxonomic status.

Key Words: *Endocarditis;* Gemella *species; Paediatrics*

Endocardite à *Gemella* chez une enfant

RÉSUMÉ : Les micro-organismes du genre *Gemella* peuvent causer parfois des maladies générales graves. Voici le cas d'une jeune fille de 12 ans, déjà porteuse d'une cardiopathie congénitale, souffrant d'une endocardite à *Gemella*; le traitement s'est avéré efficace. L'enfant se plaignait de toux, de fatigue et de perte d'appétit, mais elle ne présentait pas de fièvre. L'échocardiographie a révélé une insuffisance mitrale importante avec flottement du feuillet postérieur, la présence de végétations sur la valve mitrale ainsi qu'une dilatation du ventricule et de l'oreillette gauches. La fillette a d'abord été traitée à la vancomycine, mais la bactériémie persistait toujours; l'adjonction de gentamycine a résolu le problème. La pénicilline G et la gentamycine ont complété le traitement une fois qu'a été connue la sensibilité antimicrobienne. Les analyses faites tant au laboratoire local qu'aux laboratoires de référence au Canada et aux États-Unis n'ont pas permis d'identifier l'espèce de *Gemella* en cause. L'isolat fait l'objet d'évaluation plus poussée pour déterminer son appartenance taxonomique.

The genus *Gemella* has five known species: *Gemella haemolysans*, *Gemella morbillorum*, *Gemella bergeri*, *Gemella sanguinis* and *Gemella palaticanis* (1-4). All but the last are opportunistic human pathogens that may cause severe infections; *G palaticanis* has been identified only in dogs. These organisms have been implicated in serious systemic disease, including meningitis (5) and septic shock (6). In addition, several cases of endocarditis have been reported in the past 20 years, primarily in the adult population (4,7-9). The present article describes a case of endocarditis in a child caused by a species of *Gemella*.

CASE PRESENTATION

A 12-year-old girl with congenital heart disease (mitral stenosis, ventricular septal defect and patent ductus arteriosus) repaired at six months of age presented to her community paediatrician with a cough, decreased appetite and two-week history of fatigue. There was no history of fever, rash or symptoms of heart failure. There were no recent dental procedures. Several other members of her family had experienced a influenza-like illness with vomiting and diarrhea one week before the onset of her symptoms. A blood culture grew Gram-positive cocci in pairs within 24 h. The patient was given intra-

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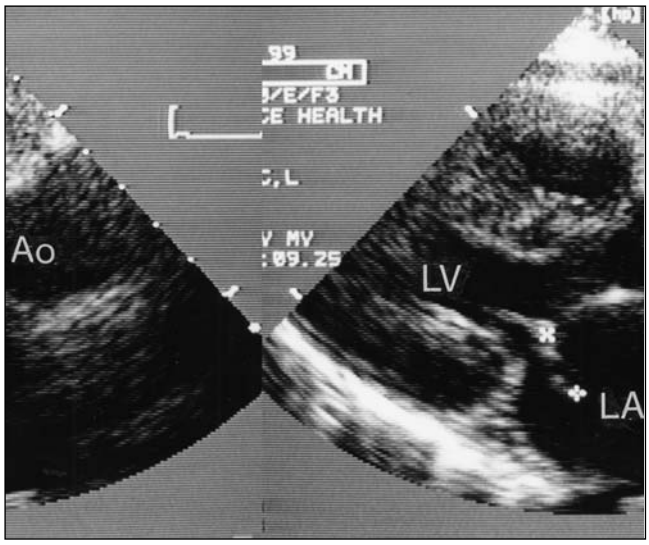

Figure 1) *Echocardiogram; parasternal long axis view of the heart showing flail mitral leaflet (between crosses) extending into left atrium (LA) and thickened. Ao Aorta; LV Left ventricle*

venous vancomycin 500 mg every 6 h and was referred to the cardiology service at the IWK Grace Health Centre (Halifax, Nova Scotia).

On physical examination, she was not toxic but appeared pale. She was afebrile but tachycardic with a resting heart rate of 100 beats/min. General examination was within normal limits. There was no evidence of infection, rash, lymphadenopathy, hepatosplenomegaly, splinter hemorrhages, Osler nodes, Janeway lesions or Roth's spots. There was no evidence of dental disease; however, there was granulation tissue around some loose primary teeth. Her cardiovascular examination revealed a grade 3/6 pansystolic murmur of mitral insufficiency at the apex and a grade 2/6 late diastolic murmur of mitral stenosis at the apex.

Investigations included a complete blood cell count that revealed anemia (hemoglobin 92 g/L) and a normal white blood cell count (6.6×10^9 cells/L with 62% neutrophils). She had an elevated erythrocyte sedimentation rate of 53 mm/L. Chest x-ray showed mild cardiomegaly with normal lungs. An echocardiogram revealed marked mitral insufficiency with flail posterior mitral leaflet, thickened mitral leaflets with vegetations, and an enlarged left atrium and ventricle (Figure 1). A diagnosis of infective endocarditis and ruptured chordae tendinae of the posterior mitral leaflet was made.

Gram stain of the positive blood cultures (Bactec 9240; Becton Dickinson Diagnostic Systems, Canada) revealed Gram-positive cocci in pairs. On subculture, the organism grew best at 35°C on chocolate agar incubated in an anaerobic jar using the BBL GasPak Anaerobic System (Becton Dickinson Diagnostic Systems, Canada); all cultures required 48 h of incubation before individual colonies could be seen. A slow growing *Streptococcus* species-like organism was recovered that was identified as *Gemella* species by the laboratory at the IWK Grace Health Centre. Identification was made using the MicroScan Walkaway 40 (Dade Behring, USA) with a Rapid Positive Combo 1 panel and a variety of conventional tests (Table 1). Susceptibility testing was performed on Mueller-Hinton agar with 5% defribrinated sheep blood and was incubated for 48 h in 5% to 10% carbon dioxide using the Kirby-Bauer method for streptococci. Susceptibility results took several days because of the slow growth of the organism.

The organism was referred to the National Centre for Streptococcus, Edmonton, Alberta for further investigation. Laboratory testing by classical methods indicated that the organism belonged to the *Gemella* genus (10), but the profile was not typical of any known *Gemella* species (1-4). Table 1 compares the reactions of this strain with those of the five currently recognized *Gemella* species. The isolate was forwarded to the Centers for Disease Control and Prevention (Atlanta, USA), where the genus was confirmed as *Gemella* without further speciation. Biochemical results obtained at the Centers for Disease Control and Prevention were consistent with those reported by the National Centre for

TABLE 1
Characteristics useful for *Gemella* speciation compared with the reactions of the case isolate

	*Gemella haemolysans**	*Gemella morbillorum*†	*Gemella bergeri*‡	*Gemella sanguinis*§	*Gemella palaticanis*¶	Case isolate
Beta-hemolysis	+ (rabbit blood)	– (rabbit blood)	V (horse blood)	V (horse blood)	– (sheep blood)	– (rabbit blood)
Voges-Proskauer	V	–	–	V	–	–
Nitrite reduction	+	–	NR	NR	NR	–
Lactose	–	–	–	V	+	–
Mannitol	–	+	V	+	–	–
Sorbitol	–	+	–	+	–	–
Sucrose	+	+	–	V	+ (weak)	+
Trehalose	+	+	–	–	+	+
Alkaline phosphatase**	+	–	–	+	–	–
Alanine phenylalanine-proline arylamidase**	–	V	–	V	+	+
Glycyl-tryptophane arylamidase**	V	V	–	–	+	+

**Reactions based on references 3 and 11, and Berger reference; †Reactions based on references 3 and 11, and Berger reference; ‡Reactions based on references 1 and 3; §Reactions based on references 2 and 3; ¶Reactions based on reference 3; **Determined by API rapid ID 32 Strep (bioMérieux, USA). NR Not reported; V Variable reaction.* + Positive for substance; – Negative for substance

Streptococcus. Molecular investigation of this isolate was not performed by either reference laboratory.

A total of three blood cultures were positive during the first week of antibiotic treatment. Gentamicin 70 mg given intravenously every 8 h was added on the third day for synergism after consultation with the infectious diseases service. Twelve days after the initial diagnosis, when the organism was identified as a *Gemella* species sensitive to penicillin, the vancomycin was discontinued, and penicillin 2,200,000 IU was given intravenously every 6 h. Blood cultures were negative after one week of antibiotic treatment.

The patient's hospital course was uneventful. She remained afebrile and her fatigue resolved. She was discharged home after two weeks in hospital on six weeks of penicillin (2,200,000 IU intravenously every 6 h) and gentamicin (70 mg intravenously every 8 h). At an eight-week follow-up visit with the IWK Grace Health Centre (Halifax, Nova Scotia), she was doing well with normal strength and activity levels. Cardiology follow-up is ongoing because of her underlying cardiac condition.

DISCUSSION

To our knowledge, this is only the third report of endocarditis in a child caused by *Gemella* species. In 1994, a six-year-old boy with congenital heart disease was diagnosed with endocarditis caused by *G haemolysans*, and was successfully treated with amoxicillin and gentamicin (7). In 1999, a nine-year-old girl with dental disease and recent dental procedures was diagnosed with endocarditis caused by *G morbillorum* (8). There are three reports of other serious infections caused by *Gemella* species in children, including two fatalities. A 15-year-old boy developed meningitis caused by *G morbillorum* and died within hours of admission to hospital (5). One other fatality resulted from septic shock in a two-year-old girl with Down's syndrome and complex cardiac disease (6). The child had undergone a Fontan procedure and died postoperatively after developing septic shock caused by *G morbillorum*. A second case of septic shock caused by *G morbillorum* occurred in an 11-year-old girl with nasopharyngeal Burkitt's lymphoma (6). These cases serve as a reminder that *Gemella* species can cause very serious infection and can be fatal, dispelling the common belief that it is a harmless commensal of the human pharynx.

Dental disease was often associated with previously reported cases of endocarditis caused by *Gemella* species (4,8,10). In other cases, there was an invasive procedure, concurrent infection or history of trauma that was the presumed portal of entry (6,10). In our patient, there was no identifiable source of infection. It is possible that the granulation tissue around her loose primary teeth may have been a site for bacterial invasion. She had pre-existing cardiac disease, a known risk factor for endocarditis that has been reported in other cases of *Gemella* species endocarditis (4,7-10).

Most cases of *Gemella* species endocarditis have been successfully treated with a combination of penicillin or vancomycin and an aminoglycoside two to four weeks (4,6-10). Our patient had an excellent response to vancomycin once gentamicin was added for synergism and responded well to penicillin when the organism was identified as penicillin-susceptible. She was treated for six weeks with both penicillin and gentamicin because of the difficulty in identifying the organism, the unusual nature of the organism and the persistently positive blood cultures for the first week of antibiotic therapy. Although there have been reports of resistance (6), it is still recommended that empirical therapy be started with penicillin or vancomycin and an aminoglycoside.

Gemella species are faculatively anaerobic, catalase-negative, Gram-positive cocci. These organisms often grow poorly on blood agar, and after 24 to 48 h of incubation, colonies are tiny and nonhemolytic or weakly alpha-hemolytic (11). Growth is enhanced by 5% carbon dioxide. *Gemella* species is easily overdecolourized in the Gram stain; cells are arranged in pairs, often with adjacent sides flattened, and short chains are observed (12). All *Gemella* species have a typical biochemical profile that includes positive leucine aminopeptidase and pyrrolidonylarylamidase reactions, and negative reactions for catalase, esculin, arginine, urease, hippurate and growth in 6.5% sodium chloride (11). The isolate from our patient was morphologically characteristic of *Gemella* species, and showed biochemical reactions that were consistent with this genus, but none of the three laboratories that examined this isolate were able to classify it further. This may indicate that this is a new species, not previously identified.

The colonial morphology of *Gemella* species resembles that of *Streptococcus* species. A positive pyrrolidonylarylamidase will rule out *Streptococcus* species, but the reaction for this test is typically weak and may be negative unless a heavy inoculum is used (11). Speciation presents a challenge for most routine clinical laboratories because only *G haemolysans* and *G morbillorum* are included in the databases of commercially available identification systems. Even when additional testing is performed, interpretation may be difficult, because comparisons of the published biochemical profiles are limited by the testing methodology that was used by the investigator. The three most recently described *Gemella* species (1-3) were characterized using API Rapid ID 32 Strep (bioMérieux, USA) and API ZYM (bioMérieux, USA) systems rather than by traditional methodologies that were used in the descriptions of the original two species, *G haemolysans* and *G morbillorum* (11-13). Table 1 summarizes the published phenotypic characteristics of *Gemella* species identified (1-3,12,13), but testing methodologies must be considered when interpreting these data, because there may be poor correlation between the use of dehydrated substrates and conventional media (11). Beta-hemolysis may also be useful for *Gemella* speciation, but the animal source of the blood will affect the demonstration of this characteristic (12). *G haemolysans*, the original *Gemella* species, was described as beta-hemolytic on Mueller-Hinton agar supplemented with rabbit blood, but showed "greening" on sheep blood agar plates (12). Beta-hemolysis has also been described as a variable characteristic for both *G bergeri*

and *G sanguinis*, but horse blood, rather than rabbit blood, was used (1,2).

Recognition of new bacterial species is facilitated by referral of unusual isolates to reference laboratories. Even with extensive testing, the reference laboratory may be unable to fully identify the organism, as we observed for this isolate. Typically molecular investigation of unidentified organisms is only initiated when a common pattern of biochemical reactions is observed for a number of clinical isolates. Both 16S ribosomal RNA gene sequencing and polyacrylamide gel electrophoresis analysis of whole cell proteins contribute to the verification of a unique new strain. The isolate recovered from our patient is currently being examined further to determine its taxonomic status.

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