Successful Treatment of Sepsis Caused by *Staphylococcus lugdunensis* in an Adult with 22q11.2 Deletion Syndrome

Shoji Hirasaki¹,², Kazutoshi Murakami¹, Takaaki Mizushima¹, Kazuyoshi Ohmori¹, Seiko Fujita¹, Yoshihisa Hanayama¹, Tatsuya Kanamori¹, Ryo Yokota¹, Hirotaka Ebara¹, Nobuchika Kusano¹, Chieko Kudo³, Tomoko Yamaguchi¹, Teiji Akagi⁴ and Norio Koide¹,²

**Abstract**

A 27-year-old woman visited our hospital because of high fever. She had been diagnosed as 22q11.2 deletion syndrome (22q11.2DS) due to her cardiac history (tetralogy of Fallot), thymic hypoplasia and 22q11.2 deletion. She had a normal CD4/CD8 ratio, a slightly decreased lymphocyte count and normal serum immunoglobulin levels. Blood cultures were positive for *Staphylococcus lugdunensis* (*S. lugdunensis*). Infection route of *S. lugdunensis* in this case was unclear. The patient was successfully treated with several intravenous antibiotics. Infection should be considered when managing patients with 22q11.2DS, regardless of whether their immune system is impaired.

**Key words:** tetralogy of Fallot, staphylococcal infection, dental disease, blood culture


**Introduction**

Almost all cases of DiGeorge syndrome (DGS), which is also known as velocardiofacial syndrome, result from a common genetic defect, the 22q11.2 deletion, and various presentations of the syndrome have been described (1). This syndrome, which is now usually referred to as the 22q11.2 deletion syndrome (22q11.2DS), is becoming more common. Most patient with 22q11.2DS die early in life (2), and bacterial infection or sepsis is associated with a substantial mortality rate (3, 4). Herein, we describe an adult patient with 22q11.2DS who developed sepsis caused by *Staphylococcus lugdunensis* (*S. lugdunensis*), which was improved by treatment with intravenous antibiotics.

**Case Report**

The patient was a 27-year-old woman. She visited our hospital due to a high fever. She had no back pain, back tenderness or joint pain. She had a history of tetralogy of Fallot (TOF), partially repaired at 14 months of age (the details of the cardiac surgery that she underwent are not known). Thymic hypoplasia was noted during the surgery. She did not have any prosthetics, medical devices, or vascular grafts in her body. On a facial examination, it was found that she had single-fold swollen eyelids, and lateral displacement of the inner canthi and hypertelorism were recognized. Her nose was wide and flat, and her mouth was small (Fig. 1). A genetic examination demonstrated a hemizygous 22q11.2 deletion. The patient’s history of cardiac problems, thymic hypoplasia and 22q11.2 deletion led to a diagnosis of 22q11.2DS. One week prior to presentation, the patient developed recurrent high fevers and severe fatigue. On admission, her body temperature was 39.7°C, she suffered slight respiratory distress (respiration rate: 22-25/min) in room air, her blood pressure was 96/69 mmHg, and her radial pulse rate was 109 beats/min and regular. She had neither anemia nor jaundice. She did not display any joint swelling or abnormal neurological findings that were sug-
gestive of septic arthritis, osteomyelitis or discitis. Her abdomen was flat and soft. She had not undergone previous abdominal surgery. The patient had no gastrointestinal symptom and no symptoms of pelvic inflammatory disease. A chest examination revealed clear bilateral breath sounds, and a grade V holosystolic murmur. A neurological examination revealed no abnormal findings. She had poor speech and was mentally retarded. Her laboratory data on admission are shown in Table 1. Her serum calcium level was 7.8 mg/dL (normal range: 8.6-10.1), and her C reactive protein concentration was 9.5 mg/dL (normal<0.3 mg/dL). She had a fever and increased levels of serum CRP were observed during the dental caries therapy, resulting in long-term vancomycin administration. Her fever dissipated, and her general condition improved. We genotyped S. lugdunensis from her blood cultures and the coagulase-negative cocci from her dental plaques using random amplified polymorphic DNA (RAPD) analysis (6). The banding patterns generated by S. lugdunensis isolated from the blood cultures and the cocci isolated from the dental plaque cultures were different (data not shown). As a consequence, we could not prove that S. lugdunensis isolated from the patient’s blood and the cocci isolated from her dental plaque were related. She is currently undergoing therapy for dental plaque and dental caries.

**Discussion**

22q11.2DS is a relatively novel concept, and 22q11.2 deletion can be detected by fluorescence in-situ hybridization (FISH). Malformations of the cardiovascular system are frequently seen in 22q11.2 deletion syndrome, and abnormalities of the aortic arch are found in many patients (7, 8). The incidence of 22q11.2 chromosome deletion is unclear, but it is thought to be 1 in 4,000 live births in a preliminary report (2, 9). Thus, chromosome 22q11.2 deletion is not rare. van Engelen et al (10) reported that 6.5% (31/479) of TOF patients and 16.5% (13/79) of pulmonary atresia/ventricular septal defect patients displayed 22q11.2 deletion syndrome.

Many patients with this syndrome die early, and sepsis is a major cause of death in 22q11.2DS patients. Marmon et al (4) reported that 63% of 30 DGS patients with congenital heart disease (CHD) died due to infection with sepsis, regardless of whether they had undergone neonatal surgical treatment. Long-term survival in his series of DGS patients with CHD was 13% (4/30).

Patients with 22q11.2DS have underdeveloped thymi and hence display various degrees of immunodeficiency. However, the majority of patients only display a partial cellular defect involving reductions in their T cell numbers and mild to moderate immunodeficiency without a predisposition to opportunistic infections such as recurrent candidiasis and/or severe viral infections. In contrast, some patients with 22q11.2DS suffer from fatal infectious diseases such as candidiasis (11), *Pneumocystis jiroveci* (12) or Epstein-Barr vi-
subset (12, 13, 16). Gennery et al (17) described that housous immunologic abnormalities including elevated or dece-

teration.

ormal CD4/CD8 ratio and a slightly decreased lymphocyte
count, opportunistic infections should be taken into consid-

ernce or predisposition because CD4 cell counts are rarely

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tions that impair host defenses including being in an im-

munocompromised state. There might be many latent cases

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There are few reports describing the oral or dental find-

ings of patients with 22q11.2DS (18). However, some DGS

patients with abnormal dental findings have been re-

ported (18, 19). Fukui et al (18) described that the charac-

teristic oral or dental findings of DGS patients were 1) en-

amel hypoplasia of the permanent teeth relating to hy-

pocalcemia, 2) delayed tooth germ development and erup-

tion of the permanent teeth, and 3) hypoplasia of the naso-

pharynx. The abnormal dental findings of the present case

were compatible with those mentioned by Fukui et al (18).

In the present case, since the patient underwent therapy for

depression, and dental caries, long-term vancomycin therapy was

ferred although endocarditis was clinically less likely. We

speculated that the peroral route might have been a causa-

ptive path of the *staphylococcal* sepsis observed in this case.

However, we could not prove that *S. lugdunensis* isolated

from the blood and the cocci isolated from the dental plaque

were related using the RAPD method.

In the present case, *S. lugdunensis* caused sepsis. *S. lug-

dunensis*, which was first described in 1988, is a coagulase-

negative species of the genus *Staphylococcus*, and the iso-

lation rates of *S. lugdunensis* are about 10% for non-*S. epider-

midis* coagulase negative isolates (20). *S. lugdunensis* is

associated with several infections, mainly skin/soft tissues

fection and serious infections such as endocarditis or sep-

sis, and is known to behave similarly to *S. aureus* (21, 22).

*S. lugdunensis* is susceptible to a wide array of antimicrobial

agents. It has been suggested that penicillin resistance is rare in

*S. lugdunensis*; however, Mateo et al (23) reported that

11.8% of strains were penicillin resistant in their series. *S.

lugdunensis* of the present case was susceptible to oxacillin

and ampicillin/sulbactam. Choi et al (22) evaluated the inci-

dence, characteristics, and outcomes of *S. lugdunensis* bac-

teremia (SLB). They reported that the incidence of SLB was

1.3 cases per 100,000 admissions. Moreover, 23.8% (15/63)

of their SLB series had clinically significant bacteremia, 3

cases had endocarditis, and the mortality rate was 6.7% (1/15).

They concluded that SLB was associated with a low risk of

bacteremia-related mortality, but death in patients with signifi-

cant SLB might be due to the presence of serious underly-

ing diseases such as endocarditis. In the present case, the risk of serious infection such as endocarditis or rec-

current sepsis should continue to be considered as her car-

diac shunt still persists. Since she had no skin lesions and

Table 1. Laboratory Data on Admission

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Chemistry</th>
<th>Immunology</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 5300 /μL</td>
<td>AST 37 IU/L</td>
<td>CD4 44% (NR:25-60)</td>
</tr>
<tr>
<td>Seg 83.5%</td>
<td>ALT 25 IU/L</td>
<td>CD8 35% (NR:12-36)</td>
</tr>
<tr>
<td>Mono 5.8%</td>
<td>LDH 343 IU/L</td>
<td>CD4/CD8 1.3 (NR:0.9-3.2)</td>
</tr>
<tr>
<td>Eo 0.6%</td>
<td>γGTP 55 IU/L</td>
<td>IgG 1456 mg/dL</td>
</tr>
<tr>
<td>Ba 0.3%</td>
<td>ChE 169 IU/L</td>
<td>IgM 290 mg/dL</td>
</tr>
<tr>
<td>Lymph 9.8%</td>
<td>ALP 195 IU/L</td>
<td>IgA 114 mg/dL</td>
</tr>
<tr>
<td>RBC 662 × 10⁵ /μL</td>
<td>T.Bil 1.0 mg/dL</td>
<td>Urinalysis</td>
</tr>
<tr>
<td>Hb 19.7 g/dL</td>
<td>T.Chol 156 mg/dL</td>
<td>Protein (-)</td>
</tr>
<tr>
<td>Ht 58.3%</td>
<td>CRP 95 mg/dL</td>
<td>Sugar (-)</td>
</tr>
<tr>
<td>MCV 88.1 fL</td>
<td>TP 6.5 g/dL</td>
<td>Occult blood (-)</td>
</tr>
<tr>
<td>Plt 52.0 × 10⁹ /μL</td>
<td>Cr 0.7 mg/dL</td>
<td></td>
</tr>
<tr>
<td>ESR 28 min/h</td>
<td>BUN 5.2 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Na 139 mm/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K 3.3 mmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cl 104 mmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ca 7.8 mg/dL</td>
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</tr>
</tbody>
</table>

![Figure 2](image_url)  

**Figure 2.** Dental findings in this case. An open bite, insufficient eruption of the permanent teeth, slight enamel hypoplasia with plaque, gingivitis and dental caries were seen.

rus infection (13). The occurrence of opportunistic infections is more common among patients with predisposing conditions that impair host defenses including being in an immunocompromised state. There might be many latent cases of 22q11.2DS patients who have potential immunodeficiency or predisposition because CD4 cell counts are rarely determined in patients without human immunodeficiency virus infection (14, 15). Although the present patient showed a normal CD4/CD8 ratio and a slightly decreased lymphocyte count, opportunistic infections should be taken into consideration.

Patients with 22q11.2DS, might be associated with various immunologic abnormalities including elevated or decreased IgG levels, IgA deficiency, and a decreased B cell subset (12, 13, 16). Gennery et al (17) described that hormonal immunodeficiency is more common than previously recognized in patients with 22q11.2DS, and 26 (81%) of their 32 22q11.2DS patients had severe or recurrent sinusopulmonary infection. Moreover, 13 (50%) of 26 patients had abnormal serum immunoglobulin measurements (17). Infections should be considered when managing patients with 22q11.2DS.

There are few reports describing the oral or dental findings of patients with 22q11.2DS (18). However, some DGS patients with abnormal dental findings have been re-
did not undergo a catheter examination or catheter therapy (22, 24), the infectious route of *S. lugdunensis* that induced sepsis in this case was unclear. In a literature review, Seenivasan and Yu (25) described that perineal skin flora appeared to be the source of the organism in patients with *S. lugdunensis* endocarditis. Moreover, the aggressive nature of *S. lugdunensis* resembles *S. aureus* (24). Thus, we speculated that the mode of transmission of *S. lugdunensis* infection observed in the present case was from the skin, although there was no direct evidence to support this.

In conclusion, we reported a case of sepsis caused by *S. lugdunensis* in an adult 22q11.2DS patient that was successfully managed with several intravenous antibiotics. Infections such as endocarditis or recurrent sepsis should be considered when managing patients with 22q11.2DS.

The authors state that they have no Conflict of Interest (COI).

**References**


