Acute peritonitis and salpingitis associated with streptococcal toxic shock syndrome caused by Lancefield group G α-haemolytic \textit{Streptococcus dysgalactiae} subsp. \textit{equisimilis}

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The authors treated a patient for what appears to be the first reported occurrence of acute peritonitis and salpingitis associated with streptococcal toxic shock syndrome (STSS). This was caused by Lancefield group G \textit{S. dysgalactiae} subsp. \textit{equisimilis} (TKCH2004-001). The isolate showed M protein type stc36 and carried the spegg gene. To the best of the authors' knowledge, the present report represents the first case of STSS complicating acute peritonitis and salpingitis caused by Lancefield group G \textit{S. dysgalactiae} subsp. \textit{equisimilis}.

Introduction

\textit{Streptococcus dysgalactiae} subsp. \textit{equisimilis} can be classified by a combination of phenotypic and genotypic characterization into various groups: Lancefield group C \textit{α}-haemolytic, Lancefield group C \textit{β}-haemolytic, Lancefield group G \textit{β}-haemolytic and Lancefield group L \textit{β}-haemolytic \textit{S. dysgalactiae} subsp. \textit{equisimilis} (Vieira et al., 1998). Lancefield group C and G \textit{S. dysgalactiae} subsp. \textit{equisimilis} (GCS and GGS, respectively) account for 5–8 % of human streptococcal infections, including bacteraemia, wound infections, otitis media, purulent pharyngitis and streptococcal toxic shock syndrome (STSS) (Bisno et al., 1996; Hashikawa et al., 2004; Keiser & Campbell, 1992; Lopardo et al., 2005; Natoli et al., 1996; Roth et al., 1999; Turner et al., 1993; Wagner et al., 1996; Woo et al., 2001). Streptococci are a rare cause of peritonitis and salpingitis (Berenguer et al., 1992; Stevens et al., 1989; Vuilleumier & Halkic, 2001). Recently, several cases of STSS caused by GGS have been described (Hashikawa et al., 2004; Woo et al., 2003). Underlying diseases in most patients with GCS- and GGS-related STSS have included diabetes mellitus, malignant neoplasms, cirrhosis and burns (Hashikawa et al., 2004; Lopardo et al., 2005; Wagner et al., 1996; Woo et al., 2003). In the present study, we characterized a clinical isolate of GGS that caused acute peritonitis and salpingitis, with progression to STSS in a patient with a history of endometriosis and resection of an endometriotic ovarian cyst.

Case report

A 43-year-old woman with a history of endometriosis and resection of an endometriotic ovarian cyst was admitted to the Toyokawa City Hospital in July 2004 because of abdominal pain with a sudden mid-menstrual onset. Laboratory results included a white blood cell (WBC) count of 11,600 mm\(^{-3}\), a platelet count of 402 \(\times\) 10\(^9\) l\(^{-1}\) and a C-reactive protein (CRP) concentration of 6–6 mg l\(^{-1}\). On hospital day 2, shock developed, with hypotension, hypothermia, clouding of consciousness and progressive ascites. In an emergency adnexectomy, the left fallopian tube and ovary were resected. \textit{α}-Haemolytic \textit{S. dysgalactiae} subsp.
equisimilis TKCH2004-001 was isolated from ascitic fluid. After initiation of treatment with a carbapenem, panipenem (0.5 g intravenously twice daily; Sankyo), three sets of blood samples were collected for aerobic and anaerobic cultures; no isolate was recovered. Pathologic examination of the resection specimen disclosed a ruptured endometriotic cyst of the left ovary. Pus consisting of coccoid organisms, inflammation, and fibrin were present both in the ruptured ovary and the left tube (Fig. 1). The pathologic diagnosis was acute inflammation of the left tube and ovary with exudative serositis and infections with cocci. On hospital day 3, the patient developed acute respiratory distress syndrome (ARDS) and disseminated intravascular coagulation, dying of septic shock on day 5.

S. dysgalactiae subsp. equisimilis TKCH2004-001 was identified on the basis of phenotypic analysis (API 20 Strep, bioMérieux Vitek). Lancefield serologic testing (Seroiden Strepto kit; Eiken Chemical) assigned the isolate to group G. The isolate was stored at -70°C in heart infusion broth (Nissui Pharmaceutical) containing 2% Supplement F (Nissui Pharmaceutical) and 20% (v/v) glycerol. Before further testing, the bacteria were inoculated on trypticase soy agar II with 5% sheep blood (TSA II, Nippon Becton Dickinson) and incubated at 37°C overnight. Phylogenetic analysis was performed by 16S rRNA gene (rDNA) sequencing, as described elsewhere (Hashikawa et al., 2004). A 1272 bp sequence was amplified by PCR, corresponding to positions 49–1380 of the 16S rDNA sequences of clinical isolates of S. dysgalactiae subsp. equisimilis. The 16S rRNA gene sequence was deposited in DDBJ/EMBL/GenBank with accession number AB498561.

Fig. 1. Histopathologic appearance of cocci (b, arrow) in a meshlike fibrin network in the lumen of the fallopian tube. Panel (b) is a higher-power view (×1700) of the area delineated by a broken square in (a) (×425). Haematoxylin and eosin staining. Bar, 100 μm.
isolates of *S. dysgalactiae* subsp. *equisimilis*, including Hiroshima, Fukuoka, A-22-84, A-ka and A-sa strains (Hashikawa et al., 2004). Small-restricted fragment patterns of chromosomal DNA from the present *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 and Hiroshima, Fukuoka, A-22-84, A-ka and A-sa were compared by PFGE. The restriction patterns of *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 and A-22-84 were indistinguishable from each other (data not shown).

MICs were determined by an Etest method (AB Biodisk) in accordance with the manufacturer’s instructions. MICs of β-lactams, macrolides and fluoroquinolones for *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 were as follows: 0·016 μg ml⁻¹ for penicillin G, 0·125 μg ml⁻¹ for oxacillin, 0·19 μg ml⁻¹ for ceftazidime, 0·016 μg ml⁻¹ for cephirome, 0·032 μg ml⁻¹ for cefepime, <0·016 μg ml⁻¹ for imipenem, 0·064 μg ml⁻¹ for clarithromycin, 0·5 μg ml⁻¹ for azithromycin, 0·064 μg ml⁻¹ for clindamycin and 0·38 μg ml⁻¹ for levofloxacin. The M protein type was determined as stc36 according to an M protein gene (*emm*) typing protocol by the sequencing of the *emm* gene (http://www.cdc.gov/ncidod/biotech/strep/strepindex.html). Detection of superantigenic genes was performed by PCR; primers for the *speA*, *speB*, *speC*, *speG* and *speF* genes were designed as described elsewhere (Hashikawa et al., 2004). The *speG* gene, but none of the other superantigenic genes, was detected in *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001.

**Discussion**

The presently reported patient developed acute peritonitis and salpingitis caused by GGS, with progression to septic shock, ARDS and multiple organ failure. This is compatible with the well-recognized syndrome of STSS (Alouf & Müller-Alouf, 2003; The Working Group on Severe Streptococcal Infections, 1993). *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 was isolated from ascitic fluid, while three sets of blood cultures following initiation of panipenem administration failed to recover an organism. Underlying diseases included endometriosis with previous resection of an ovarian cyst, an unusual setting for GCS and GGS (Hashikawa et al., 2004). In the present study, the PFGE genotypes of *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 and A-22-84 were indistinguishable from one another. Our results suggest that it is important to monitor genetically clonal dissemination involving certain GGS among STSS patients.

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**References**


Both z-haemolytic and haemolysin-deficient isolates of *S. dysgalactiae* subsp. *equisimilis* have been identified phenotypically by the API 20 Strept system as well as genotypically by 16S rDNA sequencing (Dierk森 & Tagg, 2000; Woo et al., 2003). Our z-haemolytic isolate, TKCH2004-001, was identified by both methods as *S. dysgalactiae* subsp. *equisimilis*. An earlier study proposed that streptococcal superantigens may be responsible for development of STSS caused by GCS and GGS (Hashikawa et al., 2004). In the present case, *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 carried the *speG* gene, which is a homologue of the *S. pyogenes* superantigenic gene *speG*, although involvement of SpeG in the pathogenesis of GGS-related STSS remains unclear. It would be advisable to determine if the superantigenic genes are actually expressed, since superantigenic genes such as *speG* are found in a number of *S. pyogenes* isolates, although the degree of expression of the genes varies from strain to strain (Nagamune et al., 2005). M protein, known to be a major virulence factor of *S. pyogenes*, inhibits activation of the alternative complement pathway and impedes phagocytosis by polymorphonuclear leukocytes (Campos et al., 1995). Although an earlier study found the M proteins of GCS and GGS isolated from STSS patients to be highly variable (Hashikawa et al., 2004), the M protein type identified in our TKCH2004-001 isolate was stc36, which had also been identified in GGS A-22-84, isolated as a causative pathogen from an STSS patient at a location in Japan far from Toyokawa City (Hashikawa et al., 2004). In the present study, the PFGE genotypes of *S. dysgalactiae* subsp. *equisimilis* TKCH2004-001 and A-22-84 were indistinguishable from one another. Our results suggest that it is important to monitor genetically clonal dissemination involving certain GGS among STSS patients.

**References**


