Case Report

A deep sternal wound infection caused by *Ureaplasma urealyticum*

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Introduction

*Ureaplasma* spp. belong to the class *Mollicutes*, which are characterized by the lack of a cell wall. To date there are eight known species. Two of them were found in humans: *Ureaplasma urealyticum* and *Ureaplasma parvum* (Robertson et al., 2002). *Ureaplasma* spp. are usually associated with infections of the urogenital tract. We report a case of a deep sternal wound infection (DSWI) caused by the atypical organism *U. urealyticum*.

Case report

A 41-year-old male was hospitalized (at the University Hospital of Zurich, Zurich, Switzerland) for scheduled aortic valve replacement. His medical history showed severe aortic valve regurgitation due to native aortic valve endocarditis with *Staphylococcus epidermidis*, followed by a 6 week course of directed antibiotic therapy. In addition, the patient was a multiple-drug user and suffered from chronic hepatitis C.

After completion of the antibiotic therapy, bioprosthetic aortic valve replacement and closure of a persistent foramen ovale were performed. On the same day, sternal revision surgery followed due to postoperative bleeding.

On postoperative day 13, the patient developed upper venous stasis, systemic inflammatory response syndrome and progressive acute renal failure. He was somnolent, febrile, and suffered from non-specific thoracic and pelvic pain. Laboratory results revealed leukocytosis with a left shift, as well as an increased level of C-reactive protein. No pulmonary infiltrates could be detected on a chest X-ray. However, echocardiography showed evidence of pericardial effusion, which was drained on the subsequent day.

Dressler’s syndrome was initially ranked highest in the differential diagnosis. Blood cultures remained negative for growth after prolonged incubation, whereas a urine culture was positive, containing >10^5 c.f.u. *Escherichia coli* ml^-1_. Meanwhile, a fluctuating swelling was detected at the cranial end of the sternotomy wound. Empiric antibiotic therapy with piperacillin–tazobactam was started after incision and microbiological sampling of the fluid that had collected. No organisms were observed on Gram stain, and bacterial growth was not observed under standard aerobic and anaerobic culture conditions. Over the next few days, the patient’s condition improved, the upper venous stasis disappeared and the signs of inflammation decreased slightly.

On postoperative day 17, a DSWI was suspected because of persistent purulent wound secretion. Subsequently, operative wound revision was performed, followed by vacuum-assisted wound closure. Daptomycin was added to the antibiotic regimen after surgery. Routine microbiological procedures were performed on three perioperative samples. No micro-organisms could be detected using Gram staining or in cultures on conventional media.

Since routine culturing did not reveal bacterial growth from the first sampling, as well as from second sampling, specimens were analysed with a broad-range bacterial PCR on postoperative day 21. DNA was extracted from the clinical specimens and subjected to amplification of the 5' end part of the 16S rRNA gene using universal bacterial 16S rRNA gene primers as described elsewhere (Bosshard et al., 2003). PCR products were detected, sequenced (±500 bp) and homology analysis was performed using IDNS software (SmartGene). A homology of >99%, with a minimal of 0.5% difference with the second homologous species, allows for identification at the species level. The sequences of the PCR products (ranging between 486 and 491 bp) showed 100% identity to the 16S rRNA gene of *U. urealyticum* in all three tissue specimens from the operative

Abbreviation: DSWI, deep sternal wound infection.

The GenBank/EMBL/DBJ accession number for the 16S rRNA sequence of the *U. urealyticum* isolate is GU272020.
wound revision. The second homologous species was *U. parvum* with an identity of 98.2\%, allowing the identification of *U. urealyticum* present in the specimens. The longest sequence (491 bp) was submitted to GenBank under accession no. GU272020.

Retrospectively, two stored specimens taken after secondary wound closure were cultured on A7 agar (bioMérieux) and enrichment broth (arginine LYO 2; bioMérieux) used as selective media for *Mycoplasma* sp. After 2 days of incubation, tiny, brownish cotton-wool-like colonies typical for *Ureaplasma* sp. were observed under the plate microscope, confirming the molecular diagnosis of *U. urealyticum*. In addition, we successfully cultured *Ureaplasma* sp. from the clinical samples using a commercial Mycoplasma IST 2 kit (bioMérieux), which showed urealytic activity enabling the differentiation between *Ureaplasma* sp. and *Mycoplasma hominis*. Culturing allowed us to perform susceptibility testing using the IST 2 kit, which contained nine antibiotics (doxycycline, tetracycline, josamycin, erythromycin, azithromycin, clarithromycin, pristinamycin, ofloxacin and ciprofloxacin). The antibiotic strip was incubated with the inoculated broth for 48 h and the results were interpreted according to the manufacturer’s recommendations. To date there are no standardized guidelines for *U. urealyticum* susceptibility interpretation provided by the Clinical and Laboratory Standard Institute or the European Committee on Antimicrobial Susceptibility Testing. Our *U. urealyticum* strain was susceptible to tetracycline (MIC <4 mg l\(^{-1}\)), doxycycline (MIC <4 mg l\(^{-1}\)), josamycin (MIC <2 mg l\(^{-1}\)), erythromycin (MIC <1 mg l\(^{-1}\)), azithromycin (MIC <0.12 mg l\(^{-1}\)), clarithromycin (MIC <1 mg l\(^{-1}\)) and pristinamycin (MIC <2 mg l\(^{-1}\)). Quinolones were interpreted as intermediately susceptible to ofloxacin (1 mg l\(^{-1}\) <MIC ≤4 mg l\(^{-1}\)) and resistant to ciprofloxacin (MIC >2 mg l\(^{-1}\)).

After obtaining the molecular identification, antibiotic therapy with clarithromycin (500 mg every 12 h), which had already been started empirically, was continued, resulting in clinical improvement of the sternal wound. The patient remained free from further complications following completion of a 6 week antibiotic course.

**Discussion**

DSWI is an uncommon but serious complication of median sternotomy in cardiac surgery, associated with increased resource utilization due to the frequently required follow-up surgery (Mauermann *et al.*, 2008). Re-exploration for a bleeding complication, as occurred with this patient, has been shown to be associated with DSWI and is regarded as a risk factor for the development of DSWI. In addition, there is a higher risk for iatrogenic wound infection due to a second operative exposure, where blood loss may lead to inadequate tissue perfusion and a retrosternal haematoma can serve as an ideal medium for bacterial growth (Mauermann *et al.*, 2008). It has been reported that more than 70% of isolated organisms from DSWIs in the USA and Western Europe are *Staphylococcus aureus* and coagulase-negative staphylococci (Mauermann *et al.*, 2008). However, there are very few reports in the literature that describe the isolation of *Ureaplasma* sp. from sternal wounds: two cases from Spain described a post-operative mediastinitis and a sternal infection caused by *M. hominis* and *U. urealyticum* as mixed infections (Garcia-de-la-Fuente *et al.*, 2008; Pigrau *et al.*, 1995). In our case, a polymicrobial infection was not identified. In addition, a case from Canada reported a sternal wound infection caused by *U. parvum* (Walkty *et al.*, 2009).

*Ureaplasma* sp. are usually associated with infections of the urogenital tract. *Ureaplasma* sp. colonize the lower genitourinary tract in up to 80% of sexually active women and 25–40% of sexually active men, and may cause genital infection (Cordtz & Jensen, 2006). Infections outside of the urinary tract are unusual and are associated with chorioamnionitis, septic arthritis, bacteraemia, hypogammaglobulinaemia, meningitis and wound infections (Cordtz & Jensen, 2006; Geissdorfer *et al.*, 2008; Waites & Taylor-Robinson, 2007). Haematogenous spread from the genitourinary tract has been discussed, as well as direct inoculation of the wound (Pigrau *et al.*, 1995). The presence of *U. urealyticum* in the genitourinary tract of our patient as a potential source for wound infection was not determined due to the initiated antibiotic therapy.

Culturing can be used to identify *Ureaplasma* sp. However, non-selective culture conditions and the inability to demonstrate the organisms by Gram staining can lead to the delayed or failed diagnoses of *Mycoplasma* sp. infections. Identification at the species level can only be achieved through molecular methods. In recent years, DNA amplification techniques have been used to distinguish between *U. parvum* and *U. urealyticum* (Robertson *et al.*, 2002). In our case, *U. urealyticum* was initially not identified by culture, since selective culturing for *Mycoplasma* sp. was not performed in our routine diagnostic program.

Retrospective selective culturing of *U. urealyticum* enabled us to perform susceptibility testing. Tetracycline, macrolides and fluoroquinolones are considered effective for the treatment of *U. urealyticum*. It is important to differentiate between *Ureaplasma* sp. and *M. hominis* for empirical antibiotic therapy. *M. hominis* is naturally resistant to macrolides (except josamycin), while *Ureaplasma* sp. are intrinsically resistant to lincomides, like clindamycin (Kenny & Cartwright, 2001; Pereyre *et al.*, 2002; Waites *et al.*, 2005). However, using the IST 2 kit the isolate showed resistance to ciprofloxacin (MIC ≥2 mg l\(^{-1}\)) and intermediate susceptibility to ofloxacin (1 mg l\(^{-1}\) <MIC ≤4 mg l\(^{-1}\)) (according to the guidelines of the IST 2 kit). Previously, quinolone resistance was reported as being determined by acquired mutations in gyrase and topoisomerase in *U. urealyticum* (Geissdorfer *et al.*, 2008; Xie & Zhang, 2006). A study from Germany showed a significant increase of the MIC for ciprofloxacin over a period of 20 years (Krause & Schubert, 2010). Of *Ureaplasma* strains (n=144) isolated in hospitals from central Switzerland...
during 2005 and 2006 88% showed resistance against ciprofloxacin (personal communication Dr H. Hächer, Institute of Food Safety, University of Zurich, Zurich, Switzerland), possibly as a result of the extensive use of quinolones for treatment. Prior exposure to quinolones in our patient as a reason for quinolone resistance could not be confirmed.

In summary, we have described an unusual case of DSWI caused by *U. urealyticum*. When routine cultures from a sternal wound infection fail to yield a pathogen, diagnostic testing for *Mycoplastataceae* should be considered. Molecular techniques could accelerate the identification of *Ureaplasma* infections. The widespread use of fluoroquinolones has led to the emergence of quinolone resistance in various bacterial species (Wilcox, 2009). Susceptibility testing is recommended if the clinical condition warrants antibiotic therapy.

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**References**


