Case Report

Xanthogranulomatous pyelonephritis with nephrocutaneous fistula due to Providencia rettgeri infection

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We describe what is to our knowledge the first case of xanthogranulomatous pyelonephritis combined with nephrocutaneous fistula caused by Providencia rettgeri. Surgical extirpation including nephrectomy and fistulectomy was successfully performed. The strain was identified by 16S rRNA gene sequencing in both renal tissue and pus culture from the fistula.

Introduction

Xanthogranulomatous pyelonephritis (XGP) is an atypical, chronic inflammatory disease of the kidney. Although the pathogenesis of XGP is still unclear, the primary factors are urolithiasis, urinary tract obstruction and infection (Gregg et al., 1999). Although the inflammatory process is usually diffuse and can extend beyond the kidney, nephrocutaneous fistula formation is a very rare presenting sign (Loffroy et al., 2007). Proteus species and Escherichia coli are the organisms most commonly isolated in XGP (Korkes et al., 2008). Even though Providencia rettgeri has been isolated from nosocomial urinary tract infection (O’Hara et al., 2000) and was found to form crystalline bacterial biofilms on urinary catheters (Broomfield et al., 2009), it has not been reported in XGP cases. Herein, we report an unusual case of XGP with nephrocutaneous fistula due to Providencia rettgeri infection that was genetically confirmed by 16S rRNA gene sequencing in both renal tissue and culture from fistulous discharge.

Case report

A 37-year-old man presented with purulent discharge and a palpable mass on the right lumbar area. Intermittent purulent pus-like drainage had persisted for the previous 1 year. Although he had general malaise and febrile sensation during that time, proper management had not been applied. Twenty years previously, he had developed a traumatic brain injury from an external vehicle accident. He had remained in a bedridden state due to cognitive deficits and physical disabilities. There was no notable medical history including diabetes mellitus, urolithiasis and other comorbidities. His guardian denied any history of indwelling urinary catheter or of the patient undergoing a urinary tract procedure with instrumentation.

Laboratory investigation revealed a normal leukocyte count (8890 mm$^{-3}$), anaemia (haemoglobin of 8.3 g dl$^{-1}$) and increased C-reactive protein level of 6.41 mg dl$^{-1}$. Urinalysis showed the presence of more than 100 leukocytes per high-power microscopic field, but no bacterial growth was observed. Culture from the fistulous discharge grew Gram-negative bacilli which appeared as sticky grey–white colonies on agar plates after incubation for 48 h at 37 °C. However, an accurate identification of the micro-organism was difficult by morphological characteristics alone. Providencia rettgeri was tentatively identified by the VITEK 2 automated microbiology system (bioMérieux). A computed tomography scan of the abdomen revealed a diffusely enlarged right kidney with a staghorn stone and nephrocutaneous fistula which was surrounded by massive retroperitoneal lipomatosis (Fig. 1). Total nephrectomy and fistulectomy was successfully performed through a conventional laparotomy. On histopathological examination, chronic granulomatous inflammation with diffuse infiltration of lipid-laden histiocytes was noted. The patient was clinically asymptomatic at 12 months of follow-up period.

Several bacterial species have been reported to be associated with XGP including E. coli, Proteus mirabilis, Klebsiella species, Enterobacter species and Serratia species. Providencia rettgeri was isolated from our patient; to our knowledge, this organism has not been previously described as causing XGP. Not all of the commercial biochemical systems identify isolates correctly to the species level. To confirm the result of the VITEK 2 system, 16S rRNA gene sequence analysis was performed. Genomic DNA was extracted from a small grey–white colony from the overnight pus culture on LB (Luria–Bertani) broth using a Wizard Genomic DNA Purification kit (Promega). We also homogenized the renal tissue samples taken from the necrotic area, which is away from the fistulous tract in the nephrectomy specimen, and extracted genomic DNA using the MagneSil Genomic, Fixed Tissue System (Promega). To identify the bacterial species, we amplified the extracted DNA from both samples using universal 16S
rRNA gene primer sets. A trace sequence was obtained and compared to those in GenBank using the BLAST search engine. The best match was a *Providencia* species (GenBank accession nos AM040492 and GQ416220). Again, we used primer sets specific for the *Providencia* 16S rRNA gene and amplified the templates. Finally, the specific sequences for *Providencia rettgeri* were equally identified in both renal tissue and pus culture (Fig. 2).

**Discussion**

The organisms most commonly isolated in XGP are known to be *Proteus* species and *E. coli* (Gregg et al., 1999; Korkes et al., 2008). Although many XGP patients have shown pyuria, bacterial growth in their urine has only been demonstrated for two-thirds probably because urinary obstruction blocks contaminated urine from reaching the bladder. Rather, the unidentified organism could be revealed by renal tissue cultures taken during surgery (Malek & Elder, 1978).

The identification of Gram-negative organisms in the clinical laboratory mainly relies on colony morphology and biochemical characteristics. However, identification of many organisms can often be inconclusive by morphological characteristics alone. Moreover, biochemical reactions by the VITEK 2 system might misidentify the organisms (Zbinden et al., 2007). Sequence analysis of the 16S rRNA gene has become the gold standard for identification of bacteria (Clarridge, 2004).

*Providencia rettgeri* is a Gram-negative, urea-splitting organism which has been known to cause urinary tract infections and bacteraemia, especially in immunosuppressed patients (O’Hara et al., 2000). Residents of long-term care

**Fig. 1.** Enhanced computed tomography showing large staghorn calculi and hydronephrosis. Multiple cortical, low-density, fluid-filled areas represent either dilated calyces or abscess cavities filled with pus or debris. A fistulous tract (white arrows) which extends to the right lumbar area was noted.

**Fig. 2.** Analysis of the 16S rRNA gene sequences. The electropherograms revealed variations in the 16S rRNA gene sequence between *Providencia rettgeri* DSM 4542 (GenBank accession no. AM040492) and an uncultured *Providencia* sp. (accession no. GQ416220) and of our isolate.
facilities, particularly those with indwelling urinary devices, are at high risk of Providencia urinary tract infection. In our patient, although there was no history of long-term indwelling urinary catheter, Providencia rettgeri was isolated from the pus culture and identified by the commercial VITEK 2 system. To the best of our knowledge, this microorganism has never previously been implicated in patients with XGP. Therefore, we attempted to confirm the result of the VITEK 2 system using 16S rRNA gene sequence analysis. Consequently, the specific sequence of Providencia rettgeri was identified in both homogenized renal tissue and pus culture from the fistula. Because the 16S rRNA gene sequences were identical in both samples, it seems reasonable to assume that Providencia rettgeri was the causative organism. The 16S rRNA gene sequence of our isolate matched well with that of Providencia rettgeri strain DSM 4542 (AM040492), revealing only two variations at 235 (G→A) and 761 (A→C) among 1295 bp. When compared with that of an uncultured Providencia sp. (GQ416220), one addition of cytosine at 776 and a variation at 1264 (A→G) among 1290 bp were observed (Fig. 2). Further studies will be needed to clarify the relationship between genetic variations and phenotype differences among Providencia species.

Providencia has undergone many taxonomic changes with frequent confusion and overlap between organisms of the closely related genera Providencia, Proteus and Morganella. This XGP case caused by Providencia rettgeri is the first one reported in the literature to our knowledge, as evidenced by a MEDLINE database search. Our finding was verified by 16S rRNA gene sequencing in the necrotic renal tissue culture taken during surgery. Because Providencia species are rarely found in uncomplicated urinary tract infection, physicians should be aware of the possibility of underlying urological abnormalities even if there is no history of urinary catheterization. Providencia infection may recur or progress after empirical treatment with antibiotics, particularly if an infection source remains in place. Therefore, surgical correction of underlying genitourinary pathology may help assist with total eradication of this infection. Based on the clinical and bacteriological identification findings, Providencia rettgeri urinary tract infection and obstructive staghorn calculi are underlying risk factors for the development of XGP with nephrocutaneous fistula.

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References