**Case Report**

**An unusual case of dramatic acute bilateral pyelonephritis with systemic bacterial dissemination caused by uropathogenic *Escherichia coli***

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**Introduction**

Pyelonephritis is the most severe form of urinary tract infection (UTI) and occurs more frequently in women than in men [1]. *Escherichia coli* is the pathogen most often involved and causes >80% of community-acquired UTIs as well as ~50% of UTIs in hospital patients [2]. Although antibiotic treatment is effective in most cases, recurrent kidney infection may lead to chronic pyelonephritis in some patients. Here, we report a case of acute bilateral pyelonephritis due to an *E.coli* isolate which, despite antibiotic therapy, led to systemic bacterial dissemination and very rapid destruction of both kidneys. This infection was associated with prolonged septic shock that unavoidably led to bilateral nephrectomy. Host defences and pathogen virulence were studied.

**Case**

A 24-year-old French Caucasian woman was admitted to the hospital with clinical symptoms of pyelonephritis and renal failure. This young patient had no relevant medical history and, in particular, had no previous episodes of UTI. Six weeks before being admitted, the patient had presented with an initial episode of cystitis. This was treated by a single dose of fosfomycin (Monuril®), which led to regression of the clinical symptoms. One week before hospitalization, she had presented with headaches, vomiting and diarrhea, which called for prescription of gastrointestinal topicals and ibuprofen (Ketoprofen®), a non-steroidal anti-inflammatory drug (NSAID). Following the sudden onset of fever, chills, abdominal pain, oliguria and an unstable haemodynamic state, the patient was admitted to the Renal Intensive Care Unit. Pyuria and severe sepsis led to the diagnosis of acute pyelonephritis. Upon admission, physical examination revealed fever (39°C), mottling on the extremities, jaundice and lower back pain. Blood pressure was 100/70 mmHg and pulse rate was 120/min. A few hours after being admitted, the patient suffered seizures, but no cerebral lesions were visible on a computerized tomography scan.

Complete differential blood cell counts revealed the following values: white blood cells 7600/mm³ (with 6200/mm³ neutrophils), red blood cells 4.10⁶/mm³, haematocrit 31%, haemoglobin 10.8 g/dl and platelets 11 000/mm³. Other laboratory results included blood urea nitrogen 38 mmol/l, serum creatinine 864 μmol/l, plasma Na⁺ 128 mmol/l, Cl⁻ 93 mmol/l, K⁺ 4.2 mmol/l, protidaemia 56 g/l, total bilirubinaemia 155 μmol/l [most of it conjugated (154 μmol/l)], aspartate aminotransferase 81 IU/l, alanine aminotransferase 122 IU/l, lactate dehydrogenase 5080 IU/l, uric acid 691 μmol/l, fibrinogenemia 2.2 g/l and C-reactive protein 268 mg/l.

An *E.coli* strain (serotype O4:H51) was cultured from both urine and blood samples, which harboured an acquired, class A, beta-lactamase and which showed resistance to chloramphenicol, co-trimoxazole and tetracycline. Polymerase chain reaction analyses revealed that the *E.coli* strain isolated from the urine contained multiple virulence factors (VF) of extra-intestinal pathogenic *E.coli* [type 1, P and S fimbriae, type 2, S fimbriae, type 4, bundle forming pili (BFP), and type 52, P fimbriae].

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aerobactin, haemolysin and cytotoxic necrotizing factor type 1 (Cnf1) that belonged to group B2, suggesting that it was a member of a specific clone with established urovirulence [3]. Consistent with these data, there were no detected VF associated with the intestinal pathogenic *E. coli* strains in the studied isolate.

Ultrasound revealed normal-sized kidneys with one cyst-like lesion in the right kidney, suggesting an abscess, and no hydronephrosis. Abdominal magnetic resonance imaging revealed the presence of a large cystic lesion in the upper region of the right kidney and an area of bilateral cortical necrosis (Figure 1A) with numerous micro-abscesses in the cortical region of both kidneys (Figure 1B). An aspect of cholecystitis was also present (Figure 1B).

The patient received ceftriaxone and amikacin therapy, but showed no improvement. Her haemodynamic state deteriorated rapidly, in spite of antibiotics that included vancomycin and metronidazole. The patient developed disseminated intravascular coagulation (DIC), with persistent severe thrombopenia and elevated C-reactive protein (350 mg/l). She required mechanical ventilation as well as vasocative drugs (norepinephrine), platelets and plasma coagulation factors. Steroid supplementation was also initiated to deal with the septic shock and haemofiltration because of persistent anuria. Because of both the severity of the patient’s state and suspicion of an abscess in the right kidney, a laparotomy was performed 4 days after she had been admitted to remove the right kidney and to evaluate the gall bladder. The laparotomy revealed ascitis, acalculous cholecystitis (probably reactive) and an irregular aspect of both kidney capsules when palpated. A cholecystectomy and a right nephrectomy were performed.

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**Fig. 1.** (A, B) Coronal T1 weighted image on an early arterial phase (A) and axial T1 weighted image (B) after intravenous injection of chelates of gadolinium. (A) Typical aspect of cortical necrosis on the left kidney associated with a partial cortical necrosis of the lower pole of the right kidney with a cystic-like lesion localized in the upper medullary region of the right kidney. (B) Multiple small micro-abscesses (arrows) were observed in the cortical region of the left kidney, with enlargement and wall thickening of the gall bladder (*), suggesting cholecystitis. (C–I) Macroscopic and histological renal lesions. The right (C) and left (D) kidneys exhibited pale ischaemic areas with red congested rims in the superficial cortex. There was also a dilated calyx filled with pus (*) in the upper medullary region of the right kidney. (E) A small parenchymal abscess (arrowhead) close to the wall of the hydrocalyx. (F–H) The cortical micro-abscesses (F) were composed of a central ischaemic zone (G) surrounded by a congestive peripheral zone containing high levels of polymorphological cells (H). (I) Enlargement of a peritubular capillary filled with pathogens. Original magnifications: ×200 (G), ×400 (H and I).
and the administration of high doses of vasoactive drugs, the persistence of a very unstable haemodynamic state and prolonged septic shock complicated by DIC led to the decision to remove the left kidney 3 days later. Gross pathological examination of the kidneys revealed the presence of several white lesions (3–7 mm in diameter) with haemorrhagic rims located in the superficial cortex (Figures 1C and 1D). There was also a collection of pus in the upper lesion of the right kidney, corresponding to a hydrocalyx (25 mm in diameter) filled with yellowish pus (Figure 1C).

A small parenchymal abscess close to the wall of the hydrocalyx was also present (Figure 1E). Histological examination revealed that the white lesions had a target-like appearance (Figure 1F): the central area showed extensive ischemic necrosis of the glomeruli, tubule sections and arteries (Figure 1G), whereas the peripheral areas of the ischemic zones were filled with polymorphonuclear leukocytes and exhibited congested vessels (Figure 1H). Accumulations of pathogens were also detected in the glomerular and peritubular capillaries (Figure 1I). Very few or no inflammatory infiltrates were observed in the renal medulla (data not shown). Severe oedema and thickening of the gall-bladder wall were also observed.

Three days after removal of the infected left kidney, the haemodynamic state improved rapidly and the DIC resolved. The patient recovered quickly and a vascular access was created 1 month later.

In view of the gravity of the septic shock caused by uropathogenic *E. coli* and because polymorphonuclear neutrophils (PMNs) play a critical role in defending the host against invading microorganisms, PMN functions were tested in the absence of ongoing infection. The PMN oxidative burst was measured by the nitroblue tetrazolium reduction assay in the absence or presence of endotoxin [lipopolysaccharide (LPS)] from *E. coli* O55:B5, 10 µg/ml for 15 min or *Staphylococcus epidermidis* (10^7 PFU/ml for 15 min). PMNs primed with low doses of tumour necrosis factor (TNF)-α (100 U/ml) and LPS (10 ng/ml) were then stimulated with formyl-methionyl-leucyl-phenylalanine (fMLP) and the oxidative burst was measured using oxidizing hydroethidine [4]. The expression of adhesion molecules (β2-integrin, CD11b/CD18 and L-selectin CD62L) on the cell surface of resting PMNs was also analysed after stimulation with TNF-α and LPS. Findings from these assays revealed normal PMN responses to the various stimuli and normal oxidative burst responses.

The patient has undergone intermittent haemodialysis without any further infectious events for the past 2 years and has recently undergone a successful kidney transplant.

### Discussion

The present case demonstrates that a uropathogenic *E. coli* clone can cause rapid destruction of the kidneys, making bilateral nephrectomy unavoidable. During asymptomatic bacteriuria or acute cystitis, the bacteria remain in the urinary tract and the inflammatory response of the host remains restricted to this site. In patients that develop acute pyelonephritis, the infection causes a systemic host response, accompanied by an intense inflammatory reaction, with sustained high levels of C-reactive protein that are associated with severe kidney damage [5]. Toll-like receptors (TLRs) play a central role in innate immunity by mediating pathogen-associated molecular pattern recognition, as reflected by the increased susceptibility to such infections in children with deficient TLR transduction [6]. TLR4, which is highly expressed in monocytes/macrophages, PMNs and renal epithelial cells, plays a key role in initiating the inflammatory response by mediating the signaling pathway induced by LPS, the major virulent component of Gram-negative bacterial envelopes [7]. Mutations of the TLR4 receptor may predispose patients towards the development of septic shock in response to Gram-negative bacteria [8]. The finding of normal PMN responses to LPS and the fact that these responses did not differ from those observed with TNF-α enabled us to rule out the possibility of a defect in pattern recognition receptor signaling pathway(s). Although the *E. coli* isolate identified from the host clinical specimen exhibited features of uropathogenic *E. coli* clones, the identified VF could not fully account for the gravity of the pyelonephritis and we cannot rule out the possibility that this strain of *E. coli* may exhibit potent invasive capacities that could account for the particular severity of the septic shock.

The use of NSAIDs has been reported to increase the risk of necrotizing fasciitis caused by *Streptococcus A* infection in elderly patients [9] and to accelerate the onset of streptococcal toxic shock syndrome [10]. We cannot, therefore, rule out the possibility that NSAID administration may have contributed to the severity of the disease by masking the initial inflammatory symptoms caused by the uropathogenic *E. coli*, which may have promoted the systemic dissemination of bacteria initially collected in the benign hydrocalyx found in the right kidney.

In conclusion, we report here an unusual case of fulminating pyelonephritis with multiple intrarenal abscesses occurring in a young adult with no relevant previous history, which was caused by a particularly virulent strain of uropathogenic *E. coli*. The dramatic progress of septic shock was finally arrested by removing both kidneys. This case highlights the possibility that uropathogenic *E. coli* can be particularly virulent and, despite appropriate antibiotic therapy, can lead to the rapid destruction of the kidneys.

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### Conflict of interest statement

None declared.
References


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