Rapidly progressive kidney failure induced by fungal mycelia obstructing indwelling ureteral stents

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SUMMARY

Antibiotics reduce the commensal flora in the gut, thereby facilitating the overgrowth of undesirable microorganisms such as *Candida albicans*. Here, we report the case of a 48-year-old woman with a history of obstructive uropathy consecutive to a radiation therapy, in whom both indwelling ureteral stents were rapidly occluded by fungal mycelia, resulting in a rapidly progressive kidney failure. Ascendant infection by *C albicans* had occurred after a 2-week course of antibiotics, prescribed for a perforative peritonitis also due to radiation-induced colitis. As shown by iterative CT scans made before (at the time of the diagnosis of peritonitis) and after the antibiotic course, kidney failure was explained by a sudden and bilateral pyelocaliceal dilation, due to the obstruction of the ureteral stents. Fungal mycelia were objectivised during the replacement procedure. Intravenous fluconazole was started, and renal function recovered ad integrum with the relief of the obstruction.

creatinine 71 µmol/l) and urinalysis was normal (ie, no pyuria and no bacteriuria). Surgery consisted in a sigmoid resection with closure of the rectal stump (Hartmann's procedure). Peritoneal fluid culture yielded three bacteria: *Streptococcus constellatus*, *Escherichia coli* and *Pseudomonas aeruginosa*. The mycological examination was negative, though. The patient was successfully treated with ceftriaxone and gentamycin for a total period of 15 and 3 days, respectively.

At day 14, she developed fever (39.3°C), oliguria and bilateral iliac fossa tenderness (without abdominal guarding). Blood pressure was preserved. Incidentally, she also presented vaginal burns and redness with leucorrhoea. Acute kidney failure rapidly developed (serum creatine increased to 507 µmol/l). The abdominal CT scan showed a bilateral pyelocaliceal dilation, effusion of peritoneal liquid and raised doubts about a peritoneal abscess, which an exploratory laparotomy eventually ruled out (and no visceral perforation was found; cf figure 1).

BACKGROUND

- More than 10¹⁴ bacteria occupy the gut, the cutaneous and vaginal mucous membranes in a human being. Some situations, such as a stress, an infection or the intake of antibiotics, may dysregulate the commensal flora up to the point that the overgrowth of other pathogens like *Candida albicans* is facilitated. Although the intake of probiotics can reduce their emergence, they are rarely considered in the clinic.
- The case presented here shows that an infection by *C albicans* may rapidly arise after an antibiotic course, and induce life-threatening complications in patients with a permanent need for ureteral catheterisation.
- The occlusion of ureteral stents by fungal mycelia is rare, and the diagnostic procedure is complex in the setting of a bacterial sepsis.

CASE PRESENTATION

A 45-year-old woman was admitted to our hospital because of abdominal pain, fever and nausea. Her medical history was a uterus cervical cancer 1 year before, which had been treated by chemotherapy and radiotherapy. She developed radiation-induced ureteral obstruction requiring bilateral ureteral stents that were periodically replaced (the current stents had been placed 4 months ago).

She complained about a diffuse abdominal pain, with nausea and fever (38.7°C). There was no haemodynamic failure. A CT scan of the abdomen showed a stercoral peritonitis caused by a colic perforation, complicating a radiation-induced colitis. Renal function was normal at that time (serum

INVESTIGATIONS

Peripheral white blood cell (WBC) count was 35×10⁹/l including 30.8×10⁹/l polymorphonuclear neutrophils; serum C reactive protein was 35 mg/l. Urinalysis showed pyuria with fungal filaments. Fungus mycelia were found to obstruct both double J catheters on the ureteroscopy, explaining the bilateral dilation of the urinary tract. Subsequently, pyelic urine, blood cultures and a sample of vaginal discharge were positive for *C albicans*. Culture of peritoneal fluid was negative, including for *C albicans*.

DIFFERENTIAL DIAGNOSIS

- The presence of a bilateral dilation of the pyelocaliceal cavities on the CT scan reasonably ruled out an acute kidney injury due to a recurring sepsis (acute tubular necrosis, unlikely in the absence of a shock), a renal toxicity of gentamycin (for which she was never found to have high trough levels), as well as an immunoallergic nephritis due to one of the drugs that the patient had received at the hospital (she had no hypereosinophilia, and no skin rash).
- In this particular case of infection with *C albicans*, ureteral obstruction could have been the consequence of so-called 'fungus balls' (also known as fungus bezoards), which may also cause a pyelocaliceal dilation, unless a papillary necrosis is associated.¹ Instead of fungal mycelia, ureteroscopy would then have shown a brown-coloured material, as described in a previous study.² The typical radiological feature is a non-opaque intraluminal filling defect.³

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Figure 1 Abdominal CT scan performed at the time of the peritonitis, before acute kidney failure (A), and after a 2-week course of antibiotics (B). Arrows point to the massive and bilateral dilation of the pyelocaliceal system.

TREATMENT

Double J catheters were transiently replaced by ureteral catheters attached to a Foley catheter, and fluconazole was given both intravenously and directly into the ureteral catheters to eradicate *C albicans*, for a total period of 2 weeks.

OUTCOME AND FOLLOW-UP

Fever and abdominal pain disappeared within 24 h. At day 7, the WBC count was 17 000/mm³, serum creatine had decreased from 507 to 130 µmol/l and both urine and blood cultures were sterile. At 1 month, serum creatine was 73 µmol/l.

DISCUSSION

The patient presented an obstructive acute kidney failure caused by fungus mycelia obstructing double J catheters. The diagnosis of fungus mycelia may be difficult. Differential diagnosis includes radiolucent urinary calculi, blood clots or a transitional cell carcinoma.

The major risk factors for funguria include diabetes mellitus, urinary tract abnormalities, steroid intake, solid organ transplantation, malignancy, immunosuppression and the presence of foreign materials.⁴ There are two different modalities of renal infections by *Candida* species: haematogenous dissemination⁵ or, more frequently, retrograde contamination via a vaginal or rectal infection. Urinary infection or colonisation by fungi is important to recognise prior to ureteral stenting, since cases of *Candida* urosepsis have been reported following the procedure.^{6–8} *C albicans* is the most frequent microorganism^{3 9} but infections by *Candida tropicalis*^{10 11} or *Torulopsis glabrata* have also been reported.¹²

Here, our patient had a history of cancer, and a vaginal mycosis triggered by a 2-week antibiotic treatment, to treat a peritonitis. Although it is well known that fungal infections may be precipitated by antibiotics, the pathophysiology is complex.

The human commensal flora is made of a million different types of microorganisms including bacteria and fungi. Their status of commensal versus harmful is constantly changing. This fragile state is a fine balance between proinflammatory and anti-inflammatory signals. Dysregulation of this balance can lead to pathological situations. Pro-inflammatory signals lead to fungal and bacterial proliferation. Pathogen-associated molecular patterns, such as the lipopolysaccharide or peptidoglycans, are recognised by pattern recognition receptors (such as the Toll-like receptors, the C-type lectine receptors or the galectin family proteins) which, upon stimulation, mediate an intracellular signal promoting the activation of nuclear factor-κB, nucleotide-binding oligomerization domain (NOD), leucine-rich repeats (LRR) and Nod-like receptor pyrin-domain containing 3 (NLRP3), which subsequently lead to the production of defensins, cytokines and chemokines with an antifungal action.¹³

Some of these pathogen-associated signals are even produced by the commensal bacteria themselves, for example, by lactobacillus.¹⁴

Since antibiotics eradicate commensal bacteria, they also induce a decrease in pro-inflammatory signals against fungi. The largest their spectrum is, the highest the probability to develop fungal infections. Furthermore, the eradication of millions of commensal bacteria in the gut increases the availability of nutrients for fungi to grow faster. These are the two main reasons accounting for proliferation of fungi during or after antibiotherapy.

While probiotics (commensal bacteria orally available) are rarely prescribed in the clinic, they could help to restore pro-inflammatory signals in the digestive tract, and prevent the occurrence of severe fungal infections in patients at high risk.¹⁵ In patients with recurrent candidal vulvovaginitis, the prophylactic or therapeutic use of lactobacillus was found to be of some efficacy.^{16 17} However, large studies are needed to recommend the systematic use of probiotics. As for antifungal agents themselves, their prophylactic use is not recommended in patients receiving antibiotics for a long period of time.¹⁸

To cure an infection by *C albicans*, topical irrigation with antifungal drugs albicans is widely recommended but does not seem to be sufficient.¹² A systemic chemotherapy, usually fluconazole or echinocandine, is thus required, especially in a situation of disseminated infection.¹⁹ If fungus balls have arisen, a percutaneous extraction is another option.^{3 12}

There are less than 10 cases of acute renal failure caused by fungus balls or fungus mycelia in the literature. To our knowledge, we report here the first case of fungus mycelia obstructing indwelling catheters and causing renal failure.

Learning points

- ▶ Antibiotics dramatically reduce the commensal flora, compromising the physiological balance that prevents the outgrowth of fungi.
- ▶ Probiotics should be considered to prevent this complication, which can be severe and life threatening in immunocompromised patients.
- ▶ Obstruction of indwelling ureteral catheters by fungal mycelia is rare, but it can lead to a rapidly progressive kidney failure, the diagnosis of which, in the setting of a bacterial sepsis and antibiotics intake, can be misleading.

Competing interests None.

Patient consent Obtained.

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