Encrusting Cystitis Due to *Corynebacterium urealyticum* in a Patient with ANCA-Associated Vasculitis: Case Report and Review of the Literature

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Objectives: To report a patient with systemic ANCA-associated vasculitis, under maintenance treatment, who had persistent microscopic hematuria and developed recurrent pelvic pain due to *Corynebacterium urealyticum* encrusting cystitis. The relevant literature on this infection is reviewed.

Methods: Descriptive case report and a review of the literature (PubMed search).

Results: A 39-year-old woman on maintenance therapy for systemic ANCA-associated vasculitis, diagnosed 10 months earlier and with persistent microscopic hematuria, developed recurrent pelvic pain. She had received several immunosuppressants (including cyclophosphamide and rituximab) since the onset of her vasculitis, as well as cycles of broad-spectrum antibiotics during the acute initial phase of her disease. Computerized tomography of the pelvis and cystoscopy showed several encrusted calcifications in the bladder mucosa, and, finally, urine culture (selective media) led to the diagnosis of *C. urealyticum* infection. Most of the bladder-encrusted stones were removed during cystoscopy and daily intramuscular teicoplanin injections were given for 14 days. Her symptoms disappeared rapidly and completely. On reviewing the literature, immunosuppression, previous broad-spectrum antibiotics, urogenital alkaline pH, and prolonged bladder catheterization are predisposing factors for this rare infection. *C. urealyticum* encrusting cystitis has been reported in patients with systemic diseases but not yet in ANCA-associated vasculitis. Outcome is almost always good under adequate antibiotic therapy, mainly glycopeptides.

Conclusion: Physicians should be aware of this unusual but potentially emerging infectious complication that can be challenging in ANCA-associated vasculitis, because the urinary tract can be affected by the vasculitis or as a complication of previous cyclophosphamide therapy.
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ANCA-associated vasculitis (AAV) patients are at increased risk of infections, mainly because of longstanding therapy with corticosteroids (CS) and immunosuppressants, including cyclophosphamide (CYC). Several prophylactic measures have almost achieved the disappearance of some potential opportunistic infections, like pneumocystosis (1,2). However, during the course of their disease, 31 to 55% of the patients still develop major infections, including bronchopneumonias, herpes-zoster recurrences, candidiasis, cytomegalovirus infection, or bacterial septicemia (2). Some exceptional infections, like progressive multifocal leukoencephalopathy, have also been reported (3).

We describe herein the first case, to our knowledge, of *Corynebacterium urealyticum* encrusting cystitis due to AAV in a patient. This unusual complication can be challenging in AAV, because the urinary tract can be affected by the vasculitis or can appear as a complication of CYC therapy (4,5).

METHODS

In addition to the case presented, a literature search (PubMed) for articles published between 1956 and May 2010 was performed using the MedLine subheadings keywords "*Corynebacterium urealyticum*," "encrusting cystitis," and "encrusting pyelitis."

RESULTS

Case Report

A 39-year-old woman, a nonsmoker with no remarkable medical history, developed crusting rhinitis, sinusitis and otitis media, that persisted for a couple of months despite several oral antibiotics, then suffered of acute respiratory distress syndrome due to pulmonary-renal syndrome in July 2008. On examination, she also had purpuric leg lesions. Creatinine was 450 μmol/L (glomerular filtration rate (GFR), 10 mL/min). A computed tomography scan of the chest and sinuses revealed diffuse ground-glass opacities and pansinusitis. Initial bronchoalveolar lavage fluid revealed no infectious agent. Antineutrophil cytoplasm antibody (ANCA) testing was positive with a cytoplasmic immunofluorescence pattern (C-ANCA) and antiproteinase 3 specificity in enzyme-linked immunosorbent assay. Antiglomerular basement membrane antibodies were negative. Kidney biopsy revealed necrotizing pauci-immune glomerulonephritis. Biopsy of a leg skin lesion showed dermal and hypodermal necrotizing vasculitis.

The patient was diagnosed with AAV and received CS (1 daily methylprednisolone pulse for 3 days, then oral prednisone, initially at 1 mg/kg/d, then progressively tapered) and IV CYC pulses (500 mg/m^2 on D1, D14, and D28, then 600 mg/m^2 every 3 weeks), combined with 14 plasma exchanges and 6 hemodialyses within the first 2 weeks. She improved, but developed bacterial pneumonia and urinary tract infection, with wild-type *Pseudomonas aeruginosa* and extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*, requiring broad-spectrum IV antibiotics. She was extubated after 3 weeks and returned home after 2 months. She was considered in sustained remission after the 6th CYC pulse (creatinine 105 μmol/L; GFR 54 mL/min, but with persistent microscopic hematuria). ANCA became negative. She was switched to rituximab maintenance, after enrolling in an ongoing prospective trial (comparing rituximab, 500 mg on D1 and D15, then every 6 months for 18 months, vs conventional maintenance azathioprine; MAINRITSAN, ClinicalTrials.gov NCT00748644). She had been amenorrheic since AAV onset and stopped taking oral contraceptives 3 months after starting rituximab.

Two months after her 3rd rituximab maintenance infusion, she found out she was 20 weeks pregnant, as she complained of intermittent abdominal pain for several weeks and unrelenting gain weight (+20 kg since starting CS). She had mild chronic crusting rhinitis, but no other sign of active vasculitis. Prednisone (10 mg/d) was continued, but rituximab was stopped, and she received no other immunosuppressant until delivery. At 37 weeks, she developed infectious pneumonia, supposedly community-acquired, with acute respiratory distress syndrome but no microbial documentation, requiring mechanical ventilation, cesarean delivery, and then broad-spectrum antibiotics. She recovered rapidly and returned home 2 weeks after delivering her healthy newborn.

Three months later, she started to complain of pelvic pain, exacerbated after bowel movements and urinating. She had persistent rhinitis and intermittent low-grade fever but no other overt vasculitis symptoms. Creatinine was 65 μmol/L (GFR 94 mL/min), and C-reactive protein 25 mg/L. ANCA remained negative. Urine analysis revealed microscopic hematuria and persistent ESBL-producing *E. coli*. Oral ofloxacin and then nitrofuradantin and pipemidic acid were prescribed and her first cystoscopy revealed diffuse mucosal inflammation and some superficial ulcerations. Biopsy showed inflammatory mucosal necrosis, submucosal vessel microthrombi, and some interstitial calcifications. Colonoscopy found some diverticula, sigmoid inflammation, and superficial ulcerations, while histological examination detected mucosal and submucosal inflammation, and fibrinoid necrosis of some vessels. Azathioprine (2 mg/kg/d) was prescribed for maintenance, rather than for a suspected flare, and prednisone was continued.

Her pelvic pain and intermittent low-grade fever persisted. New blood work revealed increased C-reactive protein (250 mg/L). Microscopic hematuria persisted, but urine culture was negative. Computed tomography scan of the abdomen and pelvis showed several calcifications in the bladder (Fig. 1A) and inflamed colon diverticula. She improved after 3 days of IV ceftriaxone, metronidazole, and gentamicin for putative acute diverticulitis and was discharged with a prescription for amoxicillin–clavu-