Rapid Diagnosis of Pneumococcal Infection in PD Patients by Detection of the *Streptococcus pneumoniae* Antigen in the Peritoneal Effluent

CASE PRESENTATION

A 64-year-old peritoneal dialysis (PD) patient with diabetic end-stage renal disease was admitted for fever, shivering, and back pain during the previous 3 days. She had been on automated PD for the previous 7 years, with 2.27% glucose-based dialysate on the cycler and 7.5% icodextrin for the long daytime dwells. During the course of PD, she had developed 3 episodes of PD-related peritonitis. The last 4-hour 3.86% peritoneal equilibration test 6 months before admission showed a fast transport status and preserved ultrafiltration capacity. Current medications included levothyroxine, omeprazole, acetylsalicylic acid, folic acid, sevelamer, and barnidipine.

On physical examination, blood pressure was 100/60 mmHg, heart rate 100 bpm, oxygen saturation 90% at room air and temperature 39°C; chest examination revealed crackles in the inferior area of the left lung; there was no neck rigidity. Blood tests showed an acute phase response with C-reactive protein level of 156 mg/L (normal < 10). Chest X-ray confirmed the diagnosis of pneumonia, and magnetic resonance imaging of the spine showed an osteomyelitis of the sixth thoracic vertebrae. Given the recent onset of anuria, *Streptococcus pneumoniae* antigen was tested on the peritoneal effluent instead of urine, for which the test was initially developed. Peritoneal dialysate was obtained from the icodextrin long dwell (~12 hours) (clear macroscopic appearance and white

blood cell count 45 cells/mL, 30% neutrophils), and assessed using the NOW *Streptococcus pneumoniae* urinary antigen test (Binax, Portland, OR, USA), which was positive within 15 minutes. The patient was rapidly started on intravenous ampicillin. Thirty-six hours after admission, all blood cultures were positive for *Streptococcus pneumoniae*. The pneumococcal antigen was also detected in the plasma at presentation. The NOW *Streptococcus pneumoniae* urinary antigen test was still positive on the peritoneal dialysate at 5 days but returned negative 3 months later.

DISCUSSION

Streptococcus pneumoniae is the most common cause of community-acquired pneumonia, and can also be responsible for meningitis, sinusitis and otitis media, and osteomyelitis (1). Early bacterial diagnosis and targeted antibiotherapy is a key prognostic factor (1), both for community-acquired pneumonia and invasive pneumococcal disease (2). A rapid immunochromatographic test for detection of *Streptococcus pneumoniae* antigen in urine samples has been developed to provide diagnosis of pneumococcal infection within 15 minutes (3). Sensitivity of the test has been shown to be ~80% in patients with septicemia (considered as the gold-standard), and specificity is high (> 90%) (3). The technique is based on the detection in urine of the C-polysaccharide present on the cell wall of all pneumococcal strains, and the antigen can be detected not only in the urine but also in pleural and cerebrospinal fluids (4). Given its molecular weight of 20 – 30 kDa (3) (less than half that of albumin, 64 kDa), it is not surprising that *Streptococcus pneumoniae* antigen can also pass through the peritoneal membrane and be retrieved in the peritoneal effluent in case of pneumococcal infection, as in our patient. Specificity of the technique should be high, as for the urine, and we found no positive test in the peritoneal effluent (icodextrin, long dwell) from 2 control PD patients without pneumococcal infection, suggesting a good specificity, similarly to what has been observed for urine samples.

In our patient, antibiotherapy against *Streptococcus pneumoniae* allowed the rapid control of septicemia. Transesophageal heart echography ruled out endocarditis. Treatment was prolonged for a total duration of 3 months because of bone involvement.

The *Streptococcus pneumoniae* antigen was detected in the plasma of our patient, as previously reported (5). However, the superiority of urine versus plasma as an antigen detection sample has been previously documented and attributed — at least partially — to the lack of confounding antibodies in the urine (6). Although the superiority of testing peritoneal effluent versus plasma remains to be demonstrated, it is well established that peritoneal transport of macromolecules, such as immunoglobulins (e.g. IgG, 150 kDa), occurs from the circulation to the peritoneal cavity at a much lower rate than low- and middle-molecular-weight solutes, and is size-selectively restricted (7). One can therefore postulate that the lower immunoglobulin concentration as compared with

Streptococcus pneumoniae antigen (20 – 30 kDa) will contribute to an increase in the superiority of testing the peritoneal effluent rather than the plasma.

Persistent positivity (8) and potential cross-reactivity with other microorganisms species (i.e. *Streptococcus* and *Enterococcus* species) (9) have been reported as potential pitfalls of the test. In our patient, the last peritonitis episode occurred 19 months before current admission, and *Enterobacter cloacae* was then identified as the cause of the infection. To formally rule out any interference of this last episode of peritoneal infection with the NOW Binax test, we tested frozen (-80°C) peritoneal effluent obtained 9 months after the peritonitis episode (10 months before the recent *Streptococcus pneumoniae* infection). This test returned a negative result, definitively ruling out any influence of the last peritonitis episode. Regarding the duration of test positivity, previous data have determined the half-life of pneumococcal antigen to be 1 – 3 weeks in the urine and serum (5).

Here we demonstrate the possibility of detecting *Streptococcus pneumoniae* antigen in the peritoneal effluent, which could lead to the rapid identification of pneumococcal infections among anuric PD patients in daily clinical practice. Future studies will need to assess the sensitivity and potential pitfalls of this new application of a well-established and useful test when used on urine samples.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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