

## Pneumococcal peritonitis in peritoneal dialysis – three case reports and literature review

### Peritonite pneumocócica em diálise peritoneal – três casos clínicos e revisão da literatura

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Received for publication: 30/08/2015

Accepted in revised form: 01/11/2015

#### ■ ABSTRACT

Peritonitis and catheter-related infections are a frequent complication in peritoneal dialysis, usually driven by commensal microorganisms. They carry a significant morbidity and mortality burden and have known consequences on viability of peritoneal dialysis and patient survival.

This article describes three clinical cases, in which three different peritoneal dialysis patients presented pneumococcal peritonitis, two of which were related with obvious previous or concomitant respiratory symptoms suggesting respiratory infection.

There is scarce literature reporting pneumococcal peritonitis; only four cases are described and, excepting one, with identified primary foci of infection other than respiratory tract. The authors reinforce the probable haematogenous route of infection by a probable respiratory primary point. Although no direct or contiguous relation is evident, peritoneal patients present a higher risk of peritonitis during extra-peritoneal infections, likewise invasive pneumococcal disease, and appropriate antimicrobial approach and pro-active prophylaxis, when applicable, is necessary (e.g., vaccination).

**Key-Words:** Invasive pneumococcal disease; peritoneal dialysis; pneumococcal peritonitis.

#### ■ RESUMO

As peritonites e infeções associadas ao catéter de diálise peritoneal constituem uma complicação frequente na diálise peritoneal. Os microrganismos responsáveis mais comuns são os constituintes da flora comensal. Estes quadros infecciosos comportam um elevado risco de morbi-mortalidade e de sobrevivência da técnica dialítica.

O presente artigo reporta três casos clínicos de peritonite pneumocócica em diferentes doentes em diálise peritoneal. Em dois destes casos, a instalação do quadro clínico foi precedida ou simultaneamente acompanhada de sintomatologia infecciosa respiratória.

Apenas quatro casos clínicos de peritonite pneumocócica em diálise peritoneal foram descritos na literatura – destes, só num foi reportada relação causal e/ou temporal com quadro infeccioso respiratório.

Os autores consideram que os casos clínicos descritos neste artigo são sugestivos de disseminação hematogénica com ponto de partida respiratório. Assim, concluiu-se por doença pneumocócica invasiva que nos doentes em diálise peritoneal pode complicar-se de peritonite.

Assim, reconhecendo este risco, embora pouco frequente, as infeções “extra-peritoneais” devem ser abordadas adequadamente. Em particular, o risco de doença pneumocócica invasiva pode levar ao reforço de medidas profiláticas (por exemplo, a vacinação).

**Palavras-Chave:** Diálise peritoneal; doença pneumocócica invasiva; peritonite pneumocócica.

## ■ INTRODUCTION

Peritonitis remains one of the main complications and clinical causes of failure and dropout of peritoneal dialysis (PD), a worldwide implemented renal replacement treatment. Still, peritonitis remains an important cause of morbidity, namely through hospitalization, and mortality<sup>1,2</sup>.

The most frequent aetiological microorganisms are skin commensal gram-positive bacteria, as *Staphylococcus aureus* and coagulase-negative species, followed by another pathogens and negative culture peritonitis. Beyond more frequent per luminal or intraluminal contamination, trans-visceral, haematogenous and trans-vaginal pathways are recognized<sup>1,2</sup>. *Streptococcus pneumoniae* is a common pathogen, gram-positive diplococci, which constitutes part of the oropharynx resident flora. It is frequently involved in respiratory tract infections, from non-invasive to life-threatening invasive disease. Invasive pneumococcal disease (meningitis, bacteraemia and endocarditis) is a serious medical complication associated with certain clinical conditions, such as immunodeficiency (HIV infection, splenectomy and alcoholism) and chronic heart, kidney or lung disease<sup>3,4</sup>.

Pneumococcal peritonitis in patients not treated with PD has been reported, as primary peritonitis in patients with cirrhosis and secondary peritonitis from the gastrointestinal tract or, in females, after upper genital tract infection, recent delivery or intrauterine contraceptive devices. Haematogenous spread of *S. pneumoniae* from a respiratory tract infection was considered the most probable origin of pneumococcal peritonitis in cirrhotic patients by Capdevilla *et al.* In addition, gastro-intestinal endoscopic procedures have been also related with pneumococcal peritonitis<sup>5,6</sup>.

To the extent of our knowledge, only four cases of pneumococcal peritonitis in PD have been reported to date. Instead of a local/regional infection, here we report three cases of probable systemic involvement, this is, secondary peritonitis following haematogenous dissemination.

## ■ CASE REPORTS

### ■ Case 1

A 58-year-old man who had been treated with automated PD due to hypertensive nephrosclerosis for 90 months started an upper respiratory tract infection, characterized by mild cough, mucous expectoration and nasal discharge, without fever. Symptomatic approach was adopted, with favourable response.

One week later, already without respiratory symptoms, patient presented with abdominal pain, vomits, fever and cloudy peritoneal effluent. On physical examination, his abdomen was mildly tender and there were no inflammatory changes of the catheter exit site or respiratory and oropharyngeal signs. The patient's laboratorial findings included haemoglobin 8.9 g/dL peripheral white blood cell count (WBCC) 5.200/mm<sup>3</sup> with 64% neutrophils, C-reactive protein (CRP) 8.3 mg/dL and peritoneal cell count (PCC) 4.500 cells/mm<sup>3</sup> with more than 95% of neutrophils. Chest and abdominal radiographies were normal.

Pending culture results, empirical antibiotic treatment comprising intraperitoneal (IP) cefazolin and ceftazidime was instituted, with clinical and laboratorial response.

The peritoneal effluent microscopic observation revealed many gram-positive *coccus* bacteria, however blood and peritoneal cultures were negative. Empirical therapy was pursued, with initial favourable clinical and laboratorial evolution.

However, at the 14<sup>th</sup> day a clinical relapse emerged with increased inflammatory parameters. Antibiotic therapy was switched to IP vancomycin and gentamicin. The new peritoneal fluid cultures were also sterile. Molecular identification of the first sample was prosecuted and *S. pneumoniae* was identified. Vancomycin was maintained for 21 days, with cure.

## ■ Case 2

A 41-year-old man with vesico-ureteral reflux kidney disease, smoker, receiving CAPD for two months presented with productive cough, without fever. Empirical therapy included macrolide and symptomatic medication. After two weeks, there was an unfavourable evolution, including fever, pleuritic chest pain, dyspnoea, bloody sputum, abdominal pain and cloudy peritoneal effluent. Abdominal tenderness was detected and lung auscultation revealed crackles and diminished vesicular murmur in the intermediate region of the right lung.

Blood work revealed haemoglobin 7.4 g/dL, 18.000 WBC/mm<sup>3</sup> with neutrophilia, CRP 29.6 mg/dL and PCC 32.620/mm<sup>3</sup> with 93% neutrophils. Chest radiography showed a homogeneous consolidation involving the entire right middle lung lobe compatible with lobar pneumonia (Fig. 1).

The patient was admitted and intravenous levofloxacin was instituted due to pneumonia, and IP cefazolin and ceftazidime due to peritonitis. Besides negative blood and sputum cultures, peritoneal culture was positive to *S. pneumoniae*, with sensitivity to penicillin.

Levofloxacin was maintained for 14 days, and cefazolin and ceftazidime switched to IP ampicillin for 14 days. The infection resolved and there were no further complications.

## ■ Case 3

A 62-year-old man with hypertensive nephrosclerosis, smoker with chronic lung disease, who started on automated PD 43 months ago, presented with

**Figure 1**

Case 2 chest radiography – right middle lobar pneumonia



generalized myalgia, abdominal pain and cloudy effluent. No fever, haemodynamic instability or respiratory symptoms were noted. Laboratory investigations revealed haemoglobin 12.1 g/dL, 10.400 peripheral WBC/mm<sup>3</sup> (72% neutrophils), CRP 2 mg/dL and PCC 8.654/mm<sup>3</sup> with 97% neutrophils. After collection of peritoneal fluid to be cultured, empirical IP cefazolin and gentamicin were initiated.

After 48 hours, there was no clinical and laboratorial response and the patient evolved with chills, and was admitted to our department. Cefazolin was changed to Vancomycin and peritoneal cultures showed *S. pneumoniae*, with sensitivity to penicillin. No blood cultures were collected and thoracic radiography did not show remarkable lesions. Antibiotics were changed to IP ampicillin and oral levofloxacin.

The patient recovered without complications, after 1 week of Levofloxacin and 2 weeks of IP ampicillin.

## ■ DISCUSSION

*Streptococcus pneumoniae* peritonitis is associated, in general, with predisposing conditions, like immunodeficiency, cirrhosis or gynaecologic complications<sup>6,7</sup>. In PD, only one case of pneumococcal peritonitis secondary to respiratory infection was described to date to our knowledge<sup>8</sup>. Three other cases were reported, one associated with mild

vaginitis and two others with intrauterine contraceptive devices<sup>9-11</sup>.

We report three cases of pneumococcal peritonitis in PD, two of which share the same infectious source (respiratory tract) but with some clinical differences (Table I). Besides chronic kidney disease in all, smoking in two patients (one with chronic pulmonary disease), the patients had no history of encapsulated bacterial strains infections, gastrointestinal diseases or recent procedures, and presented normal liver and spleen function and anatomy. It is noteworthy that they have not been vaccinated against pneumococcal disease.

In cases 1 and 2, once started in respiratory tract, the infection seemed to spread haematologically, with transdiaphragmatic route less plausible in these cases, given the location of infection and absence of diaphragmatic-localized symptoms or pleural disease evidence. The third case did not present specific respiratory symptoms, which makes peritonitis secondary to respiratory airway entry and subjacent bacteraemia implausible. An alternative hypothesis is that whilst in incubation time, secondary peritonitis and subsequent clinical manifestations occurred before respiratory emerged. In this case, blood cultures (not collected) would be essential to document bacteraemia, as chills occurrence seems to indicate.

Diagnosis was possible in case 1 only by molecular techniques, whereas in cases 2 and 3 a peritoneal culture was positive. Although haematogenous spread was suspected, blood cultures were negative. Urinary pneumococcal antigens were not pursued, however it could be collected since patients had renal residual function.

Regarding antibiotic susceptibility, only in case 1 there was probable methicillin-resistance to cefazolin and ceftazidime and susceptibility to vancomycin, given the clinical course. In the other patients, antibiotic susceptibility was evaluated *in vitro* and confirmed clinically.

Penicillin pneumococcal resistance has met a world-wide rising prevalence that varies between regions and populations, as well a greater macrolide resistance. Vancomycin has been recognized as one alternative antibiotic against *S. pneumoniae* resistant to penicillin and other classes in pneumococcal disease<sup>12</sup>.

Chronic kidney disease is considered a high risk factor of invasive pneumococcal disease, probably due to reduced antibody response to bacterial polysaccharide antigens. Prevention of high-risk groups, targeting a minor incidence and severity of infection, has been advocated and concretized since the 1980s, by vaccination with polysaccharide and/or conjugate vaccine<sup>13</sup>.

**Table I**

Characteristics of patients and peritonitis (CKD – chronic kidney disease)

Characteristics	Case 1	Case 2	Case 3
Age	58	41	61
CKD aetiology	Hypertensive nephrosclerosis	Vesico-ureteral reflux	Hypertensive nephrosclerosis
PD time	90 months	2 months	43 months
Specific risk factors	None	Smoking	Smoking
Anti-pneumococcal vaccination status	Non-vaccinated	Non-vaccinated	Non-vaccinated
Month	April	December	November
Time from respiratory symptoms to peritonitis symptoms	1 week	2 weeks	Not applied
Initial peritoneal cell count/mm <sup>3</sup>	4.500 cells (95% neutrophils)	32.620 cells (93% neutrophils)	8.654 cells (93% neutrophils)
Systemic toxicity (fever, chills)	Yes	Yes	Yes
Peritonitis recurrence	Yes (14 days)	No	No
Technique failure or drop-out	No	No	No
Organism identification	<ul style="list-style-type: none"> <li>• Molecular techniques</li> <li>• Peritoneal liquid culture NEGATIVE</li> <li>• Blood culture NEGATIVE</li> </ul>	<ul style="list-style-type: none"> <li>• Peritoneal liquid culture POSITIVE</li> <li>• Blood culture NEGATIVE</li> </ul>	<ul style="list-style-type: none"> <li>• Peritoneal liquid culture POSITIVE</li> <li>• No blood culture collected</li> </ul>
Antibiotic sensitivity	<ul style="list-style-type: none"> <li>• Clinical failure to cefazolin and ceftazidime</li> <li>• Clinical response to Vancomycin</li> </ul>	Sensitivity to Penicillin	Sensitivity to Penicillin, Clarithromycin and Levofloxacin

Different medical organizations recommend pneumococcal vaccination for patients with chronic renal failure, but with discrepant recommendations (between single-time vaccinations to a 5-year interval vaccination schedule). Like other vaccinations response, the pneumococcal seems to lack a full serum response, supporting a more frequent revaccination plan<sup>13,14</sup>. An observational study by Gilbertson *et al.* evaluated pneumococcal vaccination in haemodialysis patients, revealing a significant association between vaccination and lower mortality, accounting some poorer prognosis factors associated with the vaccination group. The authors argued in favour of this vaccination in haemodialysis patients, even with reinforced vaccination schedules<sup>15</sup>. These results were further supported by a retrospective study where influenza and pneumococcal vaccination were independently associated with improved survival in this population<sup>16</sup>.

In Portugal, pneumococcal vaccination has been available since 2001, however it was not included in the National Immunization Plan (free of charge and universal) and was only granted to children pertaining to high-risk groups. Since July 2015, a new public clinical directive resulted in a universal and free vaccination in all children and adult high-risk groups for invasive pneumococcal disease. For this last group, which includes chronic kidney disease patients, it is recommended a sequential vaccination with 13-valent conjugate vaccines and 23-valent polysaccharide vaccines, in order to promote a broader protection against pneumococcal serotypes. The expected consequences are direct protection from the main pneumococcal serotypes and indirect protection by group immunization<sup>17</sup>.

These three cases reinforce the need of concretizing anti-pneumococcal vaccination in chronic kidney disease patients, as well as early diagnosis and timely approach of respiratory infectious illnesses in order to prevent invasive or systemic repercussion.

Although a rare cause of peritonitis in PD, pneumococcal infection should be included in the differential diagnoses in the setting of suspicious peritonitis simultaneously or shortly after respiratory tract infection, considered the potential invasive nature of this disease.

**Conflict of interest statement:** None declared.

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