**Nocardia asteroides** peritoneal dialysis-related peritonitis: First case in pediatrics, treated with protracted linezolid

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**KEYWORDS**
Continuous ambulatory peritoneal dialysis; Peritoneal dialysis; Intra-abdominal abscess; *Nocardia asteroides*; Peritonitis; Oman

**Summary** *Nocardia asteroides* is a rare pathogen in peritoneal dialysis-related peritonitis. We report on a 13-year-old female with *Nocardia asteroides* peritonitis complicated by an intra-abdominal abscess. Linezolid was administered intravenously for 3 months and followed by oral therapy for an additional 5 months with close monitoring for adverse effects. The patient was discharged after 3 months of hospitalization on hemodialysis. The diagnosis and management of such cases can be problematic due to the slow growth and difficulty of identifying Nocardia species. The optimal duration of treatment for Nocardia peritonitis is not known. Linezolid can be used for prolonged periods in cases of trimethoprim/sulfamethoxazole-resistant cases with close monitoring for adverse effects.

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**Introduction**

Peritoneal dialysis (PD) is a widely used modality for renal replacement therapy. Peritonitis is a common problem in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) and represents the most frequent cause of hospitalization...
Peritoneal catheter loss, technique failure, discontinuation of CAPD, and mortality are exhibited by these patients. *Staphylococcus* species are usually implicated in infectious cases of peritonitis in patients undergoing CAPD. Fungi and higher bacteria such as *Nocardia asteroides* are less frequent causative agents [1].

Nocardiosis was named after the French veterinarian Edmond Nocard in the late 1800s and is an infection caused by gram-positive aerobic bacteria of the genus *Nocardia* [2]. Despite its universal presence in soil, organic matter and water, *Nocardia* is a rare pathogen of PD-related peritonitis [2]. Human infections are primarily observed in immunocompromised hosts and typically originate in the lungs and then spread to other organ systems, including the brain, skin and kidney [4].

Linezolid is a synthetic oxazolidinone, which is a novel class of antibiotics with clinical utility in the treatment of infections caused by gram-positive aerobic bacteria. Linezolid binds to a site on the bacterial 23S ribosomal RNA of the 50S subunit to prevent the formation of a functional 70S initiation complex, which is an essential component of the bacterial translation process. Linezolid is primarily indicated for the treatment of infections caused by resistant gram-positive organisms particularly methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* species. Linezolid also exhibits *in vitro* activities against some gram-negative anaerobes and mycobacterial species, including *Mycobacterium tuberculosis* and *Nocardia* spp. [5–7]. Here, we report the first case of *Nocardia asteroides* peritonitis in a pediatric patient who was treated with a protracted course of linezolid.

**Case report**

A 13-year-old female had been receiving CAPD for 3 years due to diffuse global sclerosis complicated by end-stage renal failure. She also had familial leukodystrophy with cerebellar ataxia and pyramidal features. She presented with high-grade fever, leakage from the exit site of the peritoneal catheter, and diffuse abdominal pain for 7 days. She was admitted with a suspected catheter exit-site or tunnel infection complicated by peritonitis.

On presentation, she was lethargic, tachypneic (40–45 breaths/min) with no respiratory distress, tachycardic (heart rate 125–135 beats/min), with a temperature of 40.2°C. Her weight was 18 kg (below the 3rd percentile for age and sex). Physical examinations were all within normal limits except for generalized, mild abdominal tenderness and neurological findings consistent with the primary disease. The exit site exhibited no inflammation, but there was marked dialysate leakage. The laboratory data revealed the following: white cell count 10,300/mm³, hemoglobin 5.9 g/dL, platelets 505,000/mm³, C-reactive protein 146 mg/L, albumin 24 g/L, ALT 15 U/L, AST 24 U/L, Na 125 mmol/L, K 3.6 mmol/L, bicarbonate 17 mmol/L, creatinine 847 μmol/L, and urea 20.9 mmol/L. The dialysate was turbid with white sediment, and the leukocyte count 300/mm³ (neutrophils 90% and lymphocytes 10%). Gram-stain of the dialysate revealed gram-positive bacilli, and a modified Kinyoun stain revealed partially acid-fast branching bacilli. In blood agar, the colonies exhibited a chalky white, cotton candy appearance with reductus on the surface, which denoted *Nocardia* species. The isolate was ultimately identified as *Nocardia* species after 2 weeks of incubation.

The running peritoneal dialysis prescription was for Bicavera peritoneal fluid at a 1000-ml volume, 10-min input, indwelling time of 4 hr and an output of 20 min. We used an alternating cycle of 1.5% and 2.3% for a total of 5 cycles. We used rapid cycles in and out with no rest indwelling time until the fluid was clear because the fluid was still turbid and full of sediment. Next, we initiated a 1.5-h cycle (10 min input with an indwelling time 1 hr and out at 20 min) with a small volume of 600 ml 1.5% glucose. A short-cycle regimen and small fill volume were used for more efficient dialysis and to decrease the dialysate leakage. The patient was initiated on intraperitoneal vancomycin, ciprofloxacin and intravenous (IV) cloxacinilin. Amphoteracin-B was added after 4 days due to suspected fungal peritonitis. Because no clinical improvement was observed, ciprofloxacin was replaced with intraperitoneal cefazidine, the IV cloxacinilin was stopped, and IV meropenen and amikacin were added. The child went into cardiac arrest and septic shock after 10 days of conservative management with the different antibiotic regimens. A peritoneal culture grew *Nocardia asteroides* after 2 weeks that exhibited sensitivity to linezolid, imipenem and amikacin and resistance to trimethoprim-sulfamethoxazole. Repeated blood cultures revealed no growth with no isolation of organisms even after a prolonged incubation period.

The catheter was removed, and the child was managed in the pediatric intensive care unit with continuous venovenous hemofiltration (CVVH), mechanical ventilation and inotropic support. CVVH was performed because the child was very sick, and conventional pediatric hemodialysis is not available in our institute. The case was complicated.
Abdominal U/S revealing an abscess in lower abdomen in the left iliac fossa.

CT-ABD: sagittal section revealing a lower left iliac abscess.

CT-ABD: cross-section revealing a lower left iliac abscess with free intra-abdominal collection.

Discussion

Nocardia is an uncommon cause of PD-related peritonitis. The species of the genus Nocardia are gram-positive branching bacteria that belong to the order Actinomycetales. These bacteria are ubiquitous in the environment and are found in the soil, in fresh and salt water, and in decaying vegetation. Most Nocardia infections in humans are caused by a peritoneal abscess following the removal of the catheter. Abdominal ultrasound revealed an intraabdominally localized collection that was evacuated by ultrasound-guided aspiration (Fig. 1). Jejunal adhesions with some feeding intolerance were treated conservatively (Figs. 2 and 3).

Linezolid was commenced based on drug sensitivity findings and the critical clinical situation of the child despite the cost, the paucity of literature on linezolid in other Nocardia infections, and the fact that it had never been used for Nocardia peritonitis. The guardian consented to the use of linezolid after counseling regarding these issues. Linezolid was intravenously administered (10 mg/kg BID) for 3 months in the hospital. Good clinical improvement was observed, and weaning and extubation were successfully performed. The patient was closely monitored for treatment-related adverse effects, including myelosuppression. Hematological abnormalities in the forms of anemia, thrombocytopenia and leucopenia are early side effects that have been reported with linezolid therapy. Serial full blood counts were performed and found to be normal. The patient was discharged from hospital after 3 months of hospitalization and rehabilitation on hemodialysis and tolerated oral and small bowel feeding. Linezolid oral therapy (10 mg/kg BID) was continued for 5 months, and no side effects were reported. A prolonged duration of treatment with linezolid was anticipated given that Nocardia infection has a high incidence of recurrence.
Table 1  Summary of previous reports of Nocardia CAPD peritonitis.

<table>
<thead>
<tr>
<th>Author (year) (Ref.)</th>
<th>Age</th>
<th>Sex</th>
<th>Cause of ESRD</th>
<th>Organism</th>
<th>Incubation period</th>
<th>CAPD duration (years)</th>
<th>Previous peritonitis event(s)</th>
<th>Medical treatment</th>
<th>Catheter removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arfania et al. [3]</td>
<td>70</td>
<td>M</td>
<td>CIN</td>
<td>N. asteroides</td>
<td>—</td>
<td>1</td>
<td>1</td>
<td>IP sulfisoxazole 6 weeks</td>
<td>No</td>
</tr>
<tr>
<td>Chan et al. [10]</td>
<td>60</td>
<td>M</td>
<td>PCKD</td>
<td>Nocardia spp.</td>
<td>5 Weeks</td>
<td>5</td>
<td>2</td>
<td>IP/TMP-SMX 3 weeks</td>
<td>No</td>
</tr>
<tr>
<td>Kaczmarski et al.</td>
<td>58</td>
<td>F</td>
<td>NA</td>
<td>N. asteroides</td>
<td>6 days</td>
<td>2</td>
<td>10</td>
<td>IP/IV ceftazidime + netilmicin 2 weeks</td>
<td>Yes</td>
</tr>
<tr>
<td>Lopes et al. [12]</td>
<td>38</td>
<td>M</td>
<td>SLE</td>
<td>N. asteroides</td>
<td>7 days</td>
<td>6</td>
<td>2</td>
<td>IP/TMP-SMX 4 weeks</td>
<td>No</td>
</tr>
<tr>
<td>Recule et al. [13]</td>
<td>80</td>
<td>M</td>
<td>NA</td>
<td>Nocardia nova</td>
<td>4 days</td>
<td>1.5</td>
<td>3</td>
<td>After removal of catheter, oral TMP-SMX 3 weeks</td>
<td>Yes</td>
</tr>
<tr>
<td>Dwyer et al. [14]</td>
<td>32</td>
<td>M</td>
<td>Type 1 DM</td>
<td>Nocardia nova</td>
<td>1 week</td>
<td>6</td>
<td>6</td>
<td>1 week antibiotic</td>
<td>Yes&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chu et al. [15]</td>
<td>68</td>
<td>F</td>
<td>NA</td>
<td>Nocardia spp.</td>
<td>4 days</td>
<td>4</td>
<td>0</td>
<td>IP/TMP-SMX + IV ceftriaxone 2 weeks</td>
<td>No&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ortiz et al. [16]</td>
<td>35</td>
<td>M</td>
<td>CBUS</td>
<td>N. asteroides</td>
<td>—</td>
<td>2.5</td>
<td>0</td>
<td>IV/TMP-SMX + IP Amikacin 5 weeks, Oral Ceftriaxone + IP Amikacin 12 weeks,</td>
<td>No</td>
</tr>
<tr>
<td>Li et al. [17]</td>
<td>75</td>
<td>M</td>
<td>Type 2 DM</td>
<td>Nocardia spp.</td>
<td>2 weeks</td>
<td>1</td>
<td>0</td>
<td>Oral/TMP-SMX 4 weeks, IP T Amp SMX 3 weeks,</td>
<td>Yes</td>
</tr>
<tr>
<td>Jones et al. [18]</td>
<td>66</td>
<td>M</td>
<td>Type 2 DM</td>
<td>N. asteroides</td>
<td>3 weeks</td>
<td>3</td>
<td>1</td>
<td>IP cephalcin and gentamicin, Oral T Amp SMX</td>
<td>Yes</td>
</tr>
<tr>
<td>Prasad et al. [19]</td>
<td>52</td>
<td>M</td>
<td>Type 2 DM</td>
<td>N. asteroides</td>
<td>—</td>
<td>1.5</td>
<td>2</td>
<td>IP/TMP-SMX 4 Days, IV Ceftriaxone + Ciprofloxin 2 weeks</td>
<td>Yes&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Current case</td>
<td>12</td>
<td>F</td>
<td>DGS</td>
<td>N. asteroides</td>
<td>2 weeks</td>
<td>3</td>
<td>1</td>
<td>IP vancomycin + cipro/ceftazidime 2 wk, IV linezolid 3 M, oral 5 M</td>
<td>Yes&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

CAPD = continuous ambulatory peritoneal dialysis; ESRD = end-stage renal disease; CIN = chronic interstitial nephropathy; PCKD = polycystic kidney disease; NA = not available; SLE = systemic lupus erythematosus; DM = diabetes mellitus; Rx = prescription; IP = intraperitoneal; TMP-SMX = trimethoprim-sulphamethoxazole; IV = intravenous; CBUS = congenital bilateral ureteral stenosis; DGS = diffuse global sclerosis.

<sup>a</sup> Intra-abdominal abscess occurred 10 days after catheter removal, requiring surgical drainage and 4 months of IV imipenem treatment.

<sup>b</sup> Died of myocardial infarction before IP antibiotic treatment was complete.

<sup>c</sup> Died of relapsing peritonitis after 2 weeks of admission, associated with Nocardia pneumonia.

<sup>d</sup> Complicated with intra-abdominal abscess that need drainage.

<sup>*</sup> APD = Automated Peritoneal Dialysis.

Rubin et al. [20] reported one case of Nocardia peritonitis in CAPD patient.
by *N. asteroides*, *N. nova*, *N. farcinica*, and *N. brasiliensis*. The majority of patients with clinically recognized disease have underlying predisposing factors [4]. Our patient had potential environmental exposure through her rural lifestyle, and we speculate that contaminated soil or water containing *Nocardia* was introduced into the peritoneum via her PD catheter or she had a tunnel infection due to touch contamination. Unusual organisms must be considered when PD peritonitis is culture-negative or refractory to standard antibiotic treatment.

To the best of our knowledge, there are 10 case reports of *Nocardia* CAPD peritonitis and only one case report of a patient on automated PD in the literature (Table 1). Decisions regarding catheter removal appear to be crucial in the management of peritonitis. Successful treatment of *Nocardia* peritonitis has been reported with and without PD catheter removal. The catheters have been removed in five of the 11 patient cases reported thus far.

Moylett et al. [5] reported six cases of *Nocardia* treated with linezolid, and all of these cases were cured. Linezolid was used as monotherapy in four of these cases. Two pediatric cases at ages of 6 and 9 years were diagnosed as chronic granulomatous disease with pneumonia and disseminated *Nocardia*, respectively. Linezolid was used for 24 months in the first and 12 months in the second case with complete cure and no reported adverse effects. Therefore, linezolid therefore appears to be an effective alternative for the treatment of nocardiosis. Shen et al. [7] reported 14 cases of *Nocardia* that were treated with linezolid, and 13 cases were confirmed to have achieved clinical cure.

In an evaluation of linezolid treatment in 447 children, Chiappini et al. [8] reported variable clinical cure rates ranging from 77.5% to 90.0% in children with bacteremia or pneumonia. The most frequently reported adverse events were diarrhea (incidence 3.1–16.8%), nausea and/or vomiting (2.9–11.9%), and thrombocytopenia (1.9–4.7%). To date, three cases of neuropathy have been described in children.

Garazzino et al. [9] studied the clinical experience of linezolid use in infants and children (611 children in four clinical trials and 206 children in case reports and case series aged up to 17 years). Thrombocytopenia occurred in 1.9% of the patients, anemia in 1.4% of the patients, and neutropenia in none of the patients. Four cases of peripheral and optic neuropathy in children have been reported thus far. *Nocardia* infection generally presents as an infection that is unresponsive to empirical treatment and initially appears as ‘culture-negative’ peritonitis. The diagnosis and management of *Nocardia* infection can be problematic due to the slow growth and difficult identification of *Nocardia* species. The choice of therapy should be determined based on local sensitivity patterns. Linezolid was used in this study because there was no alternative agent; linezolid can be used in the pediatric age group over the long-term without side effects if monitoring is performed. Additionally, long-term treatment with linezolid requires at least one year if no complications are observed.

**Conclusion**

We report the first case of *Nocardia asteroides* peritonitis in a pediatric subject who was successfully treated with the administration of linezolid for eight months under monitoring without any side effects. Catheter removal and shifting to hemodialysis should be considered for patients who do not respond to intraperitoneal antibiotics.

The optimal duration of treatment for *Nocardia* peritonitis is not known; however, a prolonged treatment course is necessary due to the occurrence of a considerable number of relapses following shorter courses of therapy. Linezolid can be used in pediatric patients for prolonged periods in trimethoprim/sulfamethoxazole-resistant cases with close monitoring for adverse effects.

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**Competing interests**

None declared.

**Ethical approval**

Not required.

**References**


Nocardia asteroides peritoneal dialysis-related peritonitis


