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Treatment of Mycobacterium abscessus-Related Peritoneal Dialysis-Associated Peritonitis with Clofazimine and Omadacycline

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Abstract: *Mycobacterium abscessus* is a rare cause of peritoneal dialysis-associated peritonitis for which standard therapy has not been defined. Moreover, therapy can often pose a challenge to practitioners due to variable resistance patterns and adverse effects related to standard antimycobacterial therapy.

Keywords: mycobacterium; peritoneal; dialysis; omadacycline; clofazimine; end-stage renal disease; hemodialysis

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Introduction

Treatment of *Mycobacterium abscessus*-related peritoneal dialysis (PD)-associated peritonitis can be difficult due to the lack of supporting data outlining the standard of care, high levels of antibiotic resistance, and adverse effects related to therapy. Here, we present a case of *M abscessus* PD-associated peritonitis treated successfully with clofazimine and omadacycline.

Case Report

A 75-year-old female with a history of end-stage renal disease on PD presented with abdominal pain that had been ongoing for several weeks. The catheter site appeared erythematous, and she was treated empirically with antibiotics and had no clinical response. This led to the removal of the

catheter and its immediate replacement with a new catheter in the contralateral site. Three months later, she presented again with purulent drainage from the new catheter. After removal of the catheter, she was started on hemodialysis. Upon presentation, PD fluid analysis revealed 11 WBC with 44% lymphocytes and 51% monocytes. Cultures from PD fluid and the catheter tip ultimately returned positive results for *M abscessus*. The PD catheter was removed and the patient's treatment course was converted to hemodialysis. She was treated with imipenem, amikacin, and clarithromycin and discharged to a skilled nursing facility.

The patient returned to the hospital one month later with worsening abdominal pain and hearing loss. Upon examination, it was also discovered that she had developed skin and subcutaneous nodules on her abdominal wall, consistent with *M abscessus* infection. A computed tomography scan of her abdomen showed free fluid, which was not sampled. Results of the final PD fluid culture from the previous admission were reviewed, and *M abscessus* demonstrated susceptibility to amikacin (minimum inhibitory concentration [MIC] 4.0 μg/mL), resistance to clarithromycin (MIC > 16 μg/mL), and intermediate susceptibility to imipenem (MIC 8.0 μg/mL). Susceptibility to both clofazimine (MIC 0.25 μg/mL) and tigecycline (MIC 0.12 μg/mL) was also noted. The amikacin course was stopped due to hearing loss, and the patient's therapy was consolidated into clofazimine and omadacycline.

The patient tolerated the treatment, with no significant adverse events. She did not develop skin discoloration. Although the nodules on her abdomen had persisted following the removal of the PD catheter, they resolved by the fourth month of antimicrobial therapy.

She was treated for a total of 8 months and tolerated both medications well. Her abdominal pain abated and the subcutaneous nodules resolved. Her hearing had not returned but had stabilized after the amikacin course was stopped. In a 2-month follow-up after completing an antibiotic treatment, she continued to be pain-free. Her abdomen had no residual nodularity. She remained on hemodialysis.

Discussion

Mycobacterium abscessus remains a rare cause of PD-catheter-related peritonitis, with fewer than 30 case reports published to date [1]. Most cases are preceded by an exit-site infection or a tunnel infection, which are often culture-negative [1]. *M abscessus* has a predisposition to produce biofilms, making the eradication of catheter infections difficult without removal of the catheter. All previously published reports on *M abscessus*-related PD-catheter-associated peritonitis required a combination of catheter removal and prolonged antimicrobial therapy [1].

The optimal type and duration of antimicrobial therapy have not been defined. Susceptibility patterns of *M abscessus* with respect to typical antimycobacterial agents vary, with higher resistance rates seen with doxycycline, quinolones, and imipenem, and lower rates of resistance to amikacin. Variable resistance rates have been reported with clarithromycin, ranging from 0% to 38% [2]. Treatment regimens must be individualized based on given susceptibility patterns and, as in the case of our patient, can occasionally require alteration based on adverse effects. Duration of therapy for nonpulmonary *M abscessus* infections has been recommended to be between 4 and 6 months, but there is no consensus on the duration of therapy for peritonitis related to *M abscessus* in particular [3]. In previously reported cases, duration of therapy ranged from 4 to 34 weeks and always involved combination therapy [4].

Given variable resistance to common antimycobacterial agents, newer therapies, including with clofazimine and omadacycline, have been used successfully, particularly in pulmonary and skin/soft tissue infections related to *M abscessus* [5]. The use of clofazimine for *M abscessus*-related peritonitis has only been reported once previously [6], and omadacycline as a treatment for peritonitis has never been described prior to our case. Both of these agents offer a relatively favorable side-effect profile. Occasionally, skin discoloration and darkening of sweat, urine, and tears occur while on clofazimine but typically resolve within 6 months of stopping therapy. Both can cause mild gastrointestinal upset that can be treated symptomatically. One main benefit of their use is that both clofazimine

and omadacycline are available orally, which presumably should increase compliance, especially in prolonged treatment courses.

Mycobacterium abscessus is a rare cause of PD-catheter-associated peritonitis but should be considered in cases of culture negativity. Although catheter removal is universally recommended in the acute phase of treatment, the optimal type and duration of antimycobacterial therapy has not yet been defined. Given the toxicities associated with common agents and variable resistance patterns, more data are needed to support the utilization of newer agents in treating PD-catheter-associated *M abscessus* peritonitis.

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