Title

Kidney transplantation after peritoneal dialysis-associated peritonitis and abdominal abscesses caused by *Mycobacterium massiliense*: Lessons for the clinical nephrologist

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Keywords

abscess; kidney transplantation; non-tuberculous mycobacteria; peritoneal dialysis

Case

A 3-year-old girl with Finnish-type congenital nephrotic syndrome, who had been on peritoneal dialysis (PD) for a year, presented with swelling at the PD catheter tunnel (day 1). Tunnel infection was diagnosed, and cefaclor was prescribed (Fig. 1). Cefaclor was replaced with trimethoprim-sulfamethoxazole because pus was observed at the exit site on day 14. The PD catheter was removed on day 20, because pus cultures grew *Mycobacterium massiliense* on day 18 (the *hsp65* gene was sequenced for mycobacterial species identification; *erm*(41) gene deletion was confirmed on polymerase chain reaction), and a new one inserted on day 27. On day 33, she developed peritonitis; therefore, clarithromycin, intraperitoneal amikacin, and intravenous meropenem were initiated. The catheter was removed on day 40 because culture of the PD effluent grew *M. massiliense*. Moreover, *M. massiliense* was resistant to trimethoprim-sulfamethoxazole and susceptible to clarithromycin and amikacin; it had intermediate susceptibility to imipenem and cefoxitin by susceptibility testing. After catheter removal, meropenem was replaced with imipenem, and amikacin was administered intravenously. Thereafter, her condition improved. Owing to eosinophilia, imipenem and amikacin were discontinued after 5 and 7 weeks of administration, respectively. Prednisolone (1.4 mg/kg/day) was administered to treat eosinophilia and tapered in over 5 weeks. Hemodialysis was initiated on day 92, as she became anuric.

On day 67, computed tomography revealed an intra-abdominal abscess (Fig. 2a, b). Percutaneous drainage of the abscess was performed on day 119. Pus cultures grew no organism;

however, fluorescent staining showed acid-fast bacilli; therefore, amikacin was reinitiated. She underwent surgical drainage of the intra-abdominal abscess on day 161 because the abscess had grown. Although acid-fast bacilli were not detected in surgical specimens, histopathological examination of the abscess capsule revealed granulomatous inflammation. Tigecycline and clofazimine were initiated postoperatively. New abscesses around the spleen required additional surgical drainage on day 208. Tigecycline was discontinued on day 238 because pancytopenia, hypoproteinemia, hyperkalemia, hyperphosphatemia, and hypoglycemia developed. Owing to hearing loss, amikacin was discontinued on day 249. On day 306, she underwent surgical drainage for multiple abdominal wall abscesses (Fig. 2c). Cefmetazole was added on day 316, and tigecycline was restarted on day 347 but discontinued again due to similar abnormal laboratory findings.

Thereafter, no new abdominal lesions were detected on serial imaging. On day 449, all antibiotics were discontinued, and on day 524, computed tomography revealed no abdominal abscesses. On day 545, ABO-compatible living-donor kidney transplantation (KT) was performed. The immunosuppression regimen comprised methylprednisolone, tacrolimus, mycophenolate mofetil, and basiliximab. Her postoperative course was uneventful. One year after KT, computed tomography revealed no abscess recurrence. Her graft is functioning well on follow-up.

Lessons for the clinical nephrologist

This case proved that when planning an organ transplantation after controlling a refractory infection caused by a rare pathogen and there are no appropriate guidelines nor sufficient evidence on optimal management for transplantation, physicians may consider setting an observation period without treatment, at least for several months. This period will help in confirming infection recurrence before introducing the immunosuppressants for transplantation. Details are described below.

Which strategy is better to stop or continue antibiotics before KT?

The present case suggests that in PD-associated infections caused by treatment-resistant pathogens, such as non-tuberculous mycobacteria in KT recipient candidates, physicians may consider performing KT after confirming the absence of recurrence after discontinuation of antibiotics. *M. massiliense* belongs to the non-tuberculous mycobacteria group, which are resistant to various antibiotics and difficult to treat [1]. Although PD-associated infections caused by non-tuberculous mycobacteria are relatively rare, they are often associated with poor outcomes, such as PD catheter loss and death [2]. KT after infection with the non-tuberculous mycobacteria, is a concern because introduction of the immunosuppressants associated with transplantation can trigger the recurrence of infection. There is no consensus regarding the appropriate management for KT after PD-associated infection caused by the non-tuberculous mycobacteria.

In planning transplantation after treating intractable infection, it is difficult to determine which strategy is

better between the following: discontinue antibiotics before transplantation and confirm the absence of recurrence of infection or perform transplantation while still administering antibiotics. The strategy of discontinuing antibiotics before KT involves the risk of recurrence of infection during the observation period without antibiotics. However, if pathogens could be eradicated by aggressive treatment including long-term multidrug antibiotics and surgical interventions, this strategy may be ideal in establishing the absence of infection before transplantation, although it may be difficult to judge “eradication.” To our knowledge, there is only one reported case of a successful living-donor KT after PD-associated infection caused by non-tuberculous mycobacteria in a boy with bilateral hypoplastic kidneys [3]. In that case, KT was performed 8 months after discontinuation of antimycobacterial treatment for PD-associated peritonitis caused by *Mycobacterium avium* complex. However, it should be noted that these successful cases including ours may not be extrapolated to all patients. Although not in the field of PD-associated infection, there is a case report of recurrence of genitourinary tract infection caused by *Mycobacterium avium* complex after KT [4]. In that case, liver and KT was performed 3 months after discontinuation of 17-month antimycobacterial treatment for genitourinary tract infection caused by *Mycobacterium avium* complex; however, genitourinary tract infection by the same organism relapsed a year after the transplantation. In contrast, performing KT under administration of antibiotics seems like the safer strategy at first glance. In lung transplantation, antimycobacterial treatment is often continued until after transplantation in recipients who had non-tuberculous mycobacterial infections prior to transplantation [5,

6]. However, there is a risk of introducing immunosuppressants in those with latent non-tuberculous mycobacteria. In addition, there is paucity of evidence on the appropriate length of antimycobacterial treatment following KT. Further studies are needed to determine the best strategy.

After discontinuation of antibiotics, how long should we observe until transplantation?

After discontinuation of treatment for intractable infection, several months may be required until transplantation to see if infection recurs. Careful follow-up including imaging studies is required for signs of recurrence depending on the pathogen type and the site of infection to determine the optimal timing for transplantation. As for the present case, where abdominal abscesses were difficult to treat, long-term multidrug antimycobacterial treatment and repetitive surgical interventions led to a stable state where no recurrence of abscesses was confirmed on serial imaging studies. We decided to perform living-donor KT if no new abdominal abscesses developed 3 months after discontinuing antibiotics, because hemodialysis had lasted for more than a year and KT was considered necessary as soon as possible. Regarding KT and non-tuberculous mycobacterial infection, as previously described, some cases may be successful by 8-month observation period after discontinuation of antibiotics [3], whereas others may be unsuccessful by 3-month observation period [4]. Owing to lack of evidence, it is unclear whether the 3-month observation period we set was appropriate. The accumulation of evidence on similar cases is awaited.

Can non-tuberculous mycobacteria manifest as intra-abdominal abscesses?

The present case suggests that PD-associated infection caused by the non-tuberculous mycobacteria can manifest as intra-abdominal abscesses. Although non-tuberculous mycobacteria can cause skin and soft tissue infections [7], intra-abdominal abscesses due to non-tuberculous mycobacteria are rarely reported. It is unclear why intra-abdominal abscesses developed in the present case; immunocompromise by glucocorticoid administration for eosinophilia, nephrotic state, or kidney failure may have contributed to the abscess formation. Since the abscess specimen obtained during surgical drainage grew no organisms and no acid-fast bacilli were observed on fluorescent staining in the present case, it was imperative to rule out other differential diagnoses such as aseptic abscess syndrome or paradoxical reaction in tuberculous infection [8, 9]. However, the granulomatous inflammation found in the abscess capsule is consistent with non-tuberculous mycobacterial infection. Considering the refractory nature of non-tuberculous mycobacteria, long-term multidrug therapy and surgical interventions would be necessary for suspected abscesses.

Statements and Declarations

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The authors did not receive support from any organization for the submitted work.

Conflicts of Interest

The authors have no relevant financial or non-financial interests to disclose.

Research involving Human Participants and/or Animals

This study was performed in line with the principles of the 1964 Helsinki Declaration and its later amendments.

Ethics approval

The local Ethics Committee of Hokkaido University Hospital has confirmed that no ethical approval is required for this study.

Consent to participate

Informed consent was obtained from the parents of the patient.

Consent for publication

The parents of the patient consented to the submission of the case report to the journal

Data availability

Data sharing is not applicable to this article as no datasets were generated or analyzed in this study.

Authors' contribution

Conceptualization: Takayuki Okamoto, Yasuyuki Sato, Asako Hayashi, Toshiyuki Takahashi, Keisuke Kamada, Shohei Honda, Kiyohiko Hotta; Writing – original draft preparation: Yasuhiro Ueda; Writing – review and editing: Takayuki Okamoto.

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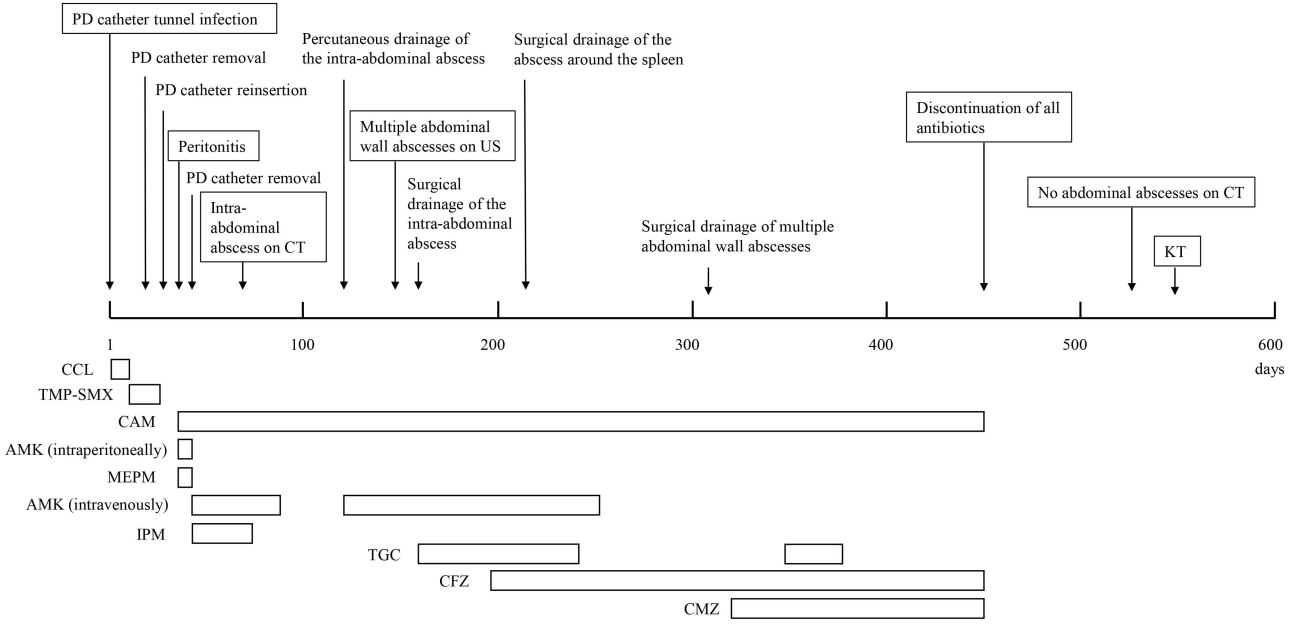
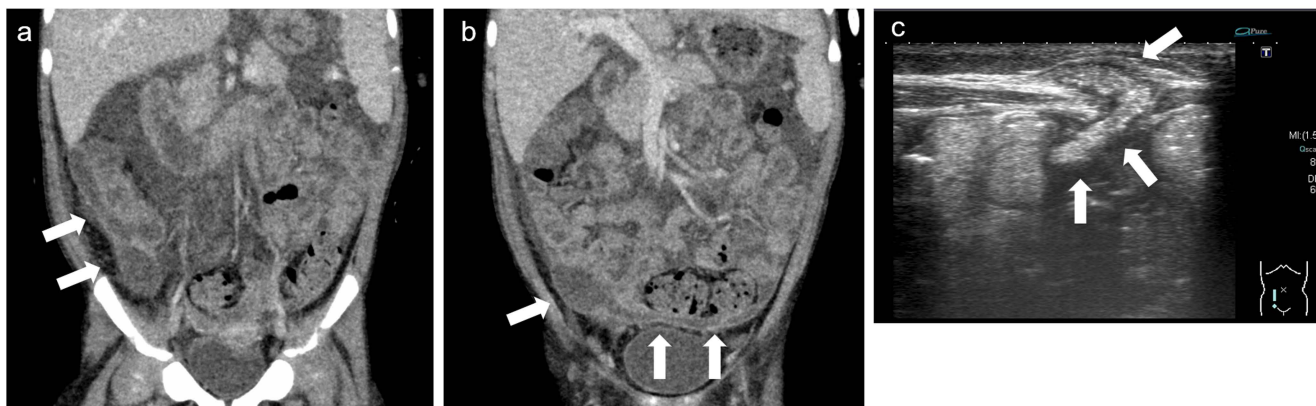
Figure Captions

Fig. 1 Clinical course with administration of antibiotics. Abbreviations: AMK, amikacin; CAM, clarithromycin; CCL, cefaclor; CFZ, clofazimine; CMZ, cefmetazole; CT, computed tomography; IPM, imipenem; KT, kidney transplantation; MEPM, meropenem; PD, peritoneal dialysis; TGC, tigecycline; TMP-SMX, trimethoprim-sulfamethoxazole; US, ultrasonography

Fig. 2 Imaging findings in the patient. **a, b** Contrast-enhanced computed tomography on the coronal plane of the abdomen. An abscess is visible (arrows) in the right paracolic gutter and extends to the left side of the abdomen along the peritoneum. **c** Ultrasonography of the abdominal wall at the right lower quadrant. A hyperechoic abscess (arrows) is seen in the subcutaneous tissue extending into the abdominal cavity


PD catheter tunnel infection
PD catheter removal
PD catheter reinsertion
Peritonitis
PD catheter removal
Intra-abdominal abscess on CT
Percutaneous drainage of the intra-abdominal abscess
Multiple abdominal wall abscesses on US
Surgical drainage of the intra-abdominal abscess
Surgical drainage of the abscess around the spleen
Surgical drainage of multiple abdominal wall abscesses
Discontinuation of all antibiotics
No abdominal abscesses on CT
KT
1
100
200
300
400
500
600
days
CCL
TMP-SMX
CAM
AMK (intraperitoneally)
MEPM
AMK (intravenously)
IPM
TGC
CFZ
CMZ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