

## Incisional Hernia After Peritoneal Dialysis Catheter Placement in a Patient on Sirolimus

Simratdeep Sandhu,<sup>1</sup> Richard Dickerman,<sup>2</sup> Bruce Smith,<sup>3</sup> Anupkumar Shetty<sup>1,2</sup>

---

*Hernias and peritoneal dialysis (PD) catheter leaks are frequent complications in patients on PD. Transplant recipients have multiple risk factors for delayed wound healing, such as use of corticosteroids and sirolimus, and the presence of uremia and diabetes mellitus. We report a rare occurrence of incisional hernia attributable to internal wound dehiscence after PD catheter placement in a patient on sirolimus.*

*A 34-year-old Latino American man was started on PD training 4 weeks after placement of a PD catheter. Soon after completing training, he developed a large soft bulge close to the PD catheter, with expansile cough impulse suggestive of an incisional hernia filled with peritoneal dialysate. The size of the bulge would decrease after the dialysate was drained. No external leak of dialysate was evident along the exit site.*

*Because of the size of the hernia and the history of it filling soon after dialysis exchange, the feeling was that wound dehiscence had occurred from the peritoneal side, resulting in a large incisional hernia. Because of the large size of the hernia within few weeks of starting PD, sirolimus was suspected to have induced poor wound healing, contributing to formation of the hernia.*

*Sirolimus was stopped, and the patient underwent PD catheter removal and repair of the hernia. A new PD catheter was placed on the opposite side of the abdomen 10 days later. After another 6 weeks, the patient was started on PD. He has been doing well for the 15 months since then, with no recurrence of the hernia. Because he still had residual renal function, he continued to receive low-dose prednisone and mycophenolate sodium. At 10 months after PD start, he*

*stopped the mycophenolate sodium on his own, and we did not resume it. He is still on low-dose prednisone.*

*In end-stage renal disease resulting from failing renal transplantation or from calcineurin inhibitor nephropathy in solid-organ transplantation, sirolimus is a risk factor for wound dehiscence, development of incisional hernia, and peritoneal dialysate leak.*

*Practical tips: Sirolimus should be stopped several days before PD catheter placement. Sirolimus should also be stopped if a PD catheter leak is detected or if incisional hernia develops soon after initiation of PD. Sirolimus should be held till surgical repair of the hernia and removal and replacement of the catheter.*

### Key words

Hernia, herniorrhaphy, end-stage renal disease, sirolimus

### Introduction

Techniques for lowering the rate of peritonitis have been extremely successful in patients on peritoneal dialysis (PD), making noninfectious complications relatively more frequent. Prevention, early recognition, and appropriate management of such complications is important because of the morbidity and technique failure that can follow (1–3). Use of sirolimus in patients after renal transplantation increases the risk of wound dehiscence and incisional hernia because of inhibition of fibroblast activity through the inhibition of mTOR (the mammalian target of rapamycin) (4–8).

Even though incisional hernia is common after renal transplantation, no reports have been published of incisional hernia attributable to sirolimus in patients on PD. Here, we report the first such patient in the literature. In our patient, we believe that continuous use of sirolimus and initiation of PD after peritoneal catheter placement resulted in the formation of a large incisional hernia. Early recognition of causative factors and discontinuation of specific

---

From: <sup>1</sup>Dallas Nephrology Associates, <sup>2</sup>Methodist Dallas Medical Center, and <sup>3</sup>Baylor University Medical Center, Dallas, Texas, U.S.A.

immunosuppressant drugs known to delay wound healing can diminish the risk of dialysate leaks and incisional hernias in PD patients.

Incisional hernias and PD catheter leaks are frequent complications in patients on PD. The risk is further increased in patients who undergo renal transplantation or experience allograft failure. Renal transplantation patients often have multiple risk factors for delayed wound healing, such as use of corticosteroids and mTOR inhibitors such as sirolimus, and the presence of uremia, obesity, and diabetes mellitus. The rare occurrence of incisional hernia because of fascial wound dehiscence after PD catheter implantation that we report here occurred in a patient on sirolimus.

Dialysate leak because of poor wound healing is a largely preventable complication of PD. Withholding sirolimus for several weeks and minimizing corticosteroids before PD catheter implantation can help to avoid the delayed healing that results in incisional hernia and dialysate leak.

### Case presentation

A 34-year-old Mexican American man, born in Mexico, had end-stage renal disease secondary to lupus nephritis and uremic pericarditis requiring pericardial window and initiation of hemodialysis. He had undergone related living-donor transplantation in Mexico in 2008.

This patient's history included embolic stroke in 2008, with good recovery and ongoing use of anticoagulation; pulmonary hypertension of unknown source diagnosed in 2009; and non-ischemic dilated cardiomyopathy diagnosed in January 2015, followed by placement of an automated implantable cardioverter and defibrillator in February 2015. His immunosuppression included prednisone, mycophenolate sodium, and tacrolimus. As his renal function deteriorated, tacrolimus was replaced with sirolimus.

In August 2015, the patient underwent laparoscopic PD catheter placement, with successful PD training 6 weeks later. Soon after completing PD training, he reported a large bulge around the PD catheter after the abdomen had been filled with fluid; the bulge would disappear after the dialysate was drained.

On examination, an expansile cough impulse around the surgical scar was observed, suggestive of a large hernia. No external leak of the fluid around the PD catheter was evident. Referral to a transplantation surgeon who also performs PD catheter placements

helped us to suspect sirolimus as the cause of such a large early postoperative incisional hernia.

Subsequently, the patient was referred to a surgeon with expertise in repairing large hernias. He underwent open herniorrhaphy 2 weeks after sirolimus was stopped. The PD catheter was wrapped with omentum and was removed. A fascial defect measuring 8×6 cm was found.

A 10×16 cm piece of semi-absorbable mesh was placed into the preperitoneal space after 1.25 cm had been trimmed at the lateral side in the short dimension. Corner sutures were placed in the inferior medial corner, through all fascial layers, with the fascial layers retracted in appropriate tension, through the mesh, and then back up to the fascial layers about 2 cm off the initial suture placement. This suturing was used in 2 corners and then snugged down so that a little bit of tension would be exerted on the closure (enough to reapproximate the muscle fascial layers). Inferior and superior midpoints were identified, with similar placement of sutures and then intervening stitches, 2 in each of the four quadrants. Once all sutures were in place in the fascia, the layers were closed with a running suture, being sure to incorporate the transversalis and internal oblique portions of the fascia to bring them back to the midpoint of the wound.

A 15×15 cm piece of a non-absorbable mesh was then placed between the fascia and the subcutaneous fat. The mesh was turned on the diagonal to create a longer elliptical piece. The 2 corner sutures were again passed through the mesh and tied down. They were then snugged down to hold them in place. All the sutures were then threaded through the mesh and tied down. Once the mesh was nicely snugged down to the fascia, excess mesh was trimmed such that at least 4 cm overlay from the fascial incision was achieved in all directions.

The patient underwent laparoscopic PD catheter placement on the other side of the abdomen 10 days later, and he resumed low-volume PD 6 weeks later, gradually increasing to his optimum volume. He has been doing well since then. Because the patient had residual kidney function, mycophenolate sodium was continued for 10 more months. For the same reason, the patient is still taking low-dose prednisone. He developed 1 episode of culture-negative peritonitis that was treated with antibiotics, achieving prompt resolution. We suspect that this episode was a non-infective peritonitis from an unclear cause.

## Discussion

The unique features of this case are the patient's very early development of incisional hernia (a possible fascial wound dehiscence without PD fluid leak), the medical challenges of immunosuppression when a patient is on dialysis, and the surgical challenges in a patient on immunosuppression. Moreover, this case is the first to be published of a PD-related incisional hernia attributed to sirolimus.

### *Timing of incisional hernia development*

It is unusual to see incisional hernia in the first month after PD start. Almost all forms of hernias have been reported in patients on PD. Umbilical, inguinal, and femoral hernias typically develop soon after PD start, but incisional hernias develop from months to years later. If an incisional hernia develops soon after PD start, fascial dehiscence because of poor wound healing should be suspected. Even though uremic patients with failing renal or non-renal allografts have multiple causes of poor wound healing, no reports have been published of a higher prevalence of wound complications after PD catheter placement in such patients. In our experience, wound complications in such patients have not been highly prevalent (unpublished and unanalyzed opinion). Given that a higher prevalence of wound complications is well known in patients on sirolimus, we feel that sirolimus contributed to poor wound healing in our patient, causing early development of incisional hernia. No edema of the abdominal wall was evident beyond the area in which an expansile cough impulse was detected, suggesting that no extravasation of peritoneal fluid into the abdominal wall had occurred.

### *Immunosuppression in patients on PD*

The practice of immunosuppression in patients with a failed renal allograft after dialysis start is variable. No published evidence-based guidelines with respect to the management of immunosuppression in such patients are available. The advantages of continuing some immunosuppression include preserving residual renal function for longer time; preventing acute rejection of a poorly functioning allograft, which might require transplant nephrectomy; and possibly preventing the development of antibodies against human leukocyte antigens. Preserving residual renal function helps to achieve better urea clearance, better control of fluid balance, better control of phosphorus,

and possibly better quality of life because of a lesser need for fluid restriction, among other considerations. The disadvantages of continuing immunosuppression are the standard risks of infections and malignancies that are associated with an increase in lifetime immunosuppression. The risks specific to the PD population are the potential risks of peritonitis and calcineurin-induced peritoneal toxicity. In addition, measures have to be taken to avoid or minimize sirolimus-induced wound complications.

Jayasena *et al.* (9) in their cohort of 17 heart transplant and heart and lung transplant recipients observed rates of peritonitis similar to those seen in patients immunosuppressed for other indications ( $n = 19$ ), but the peritonitis rate in their immunosuppressed patients was higher (1 episode every 15 months) than the rate in patients not on immunosuppressants (1 episode every 29 months in 135 patients). However, no mortality related to peritonitis was observed in the immunosuppressed group. Peritoneal toxicity from calcineurin inhibitors has been demonstrated in animals, but it is not proved in human beings, although case reports of encapsulating peritoneal sclerosis in recipients of solid-organ transplants who are on PD have been published. The role of calcineurin inhibition in causing encapsulating peritoneal sclerosis in human beings is not established. But calcineurin inhibitor-induced chronic kidney disease is an emerging cause of end-stage renal disease in recipients of non-renal solid-organ transplants, given the increasing longevity of such patients. It contributes 3%–5% to the hemodialysis population in the United States. Peritoneal dialysis is thought to be underutilized in this population.

### *Hernia surgery and PD*

Hernia surgery in patients on PD is somewhat different than typical hernia surgery, in that resuming PD will increase intra-abdominal pressure, which can increase the risk of hernia recurrence. For that reason, measures have to be taken to reduce that risk, including using a patch much larger than the neck of the hernia so as to distribute the pressure over a larger area; using 2 patches, 1 between the subcutaneous fat and fascia, and 1 between the parietal peritoneum and the muscle layer or the posterior rectus sheath, depending upon the location of the hernia; using a transverse incision rather than vertical incision of the hernia sac; using a lower volume of peritoneal dialysate for as long a

period as possible after the surgery; keeping the abdomen dry during the day, if that is feasible without compromising the quality of dialysis; avoiding constipation by using prophylactic laxatives; and reducing the use of narcotics. In patients on PD, the practice of placing a patch on the inner surface of the parietal peritoneum has to be avoided to prevent the risk of bacterial colonization of the patch.

#### *PD after hernia repair*

In most situations, it is not necessary to switch patients to hemodialysis unless they have a functioning arteriovenous access. We follow the protocol suggested by Crabtree *et al.* (10) with some modifications (Table I). For obvious reasons, patients should go to surgery after the dialysate has been drained. After surgery, we avoid dialysis for 1 – 2 days, if possible in patients with residual kidney function. After that, we prescribe about six 1 L exchanges at night over 10 hours in patients receiving automated PD, keeping the abdomen dry during the day. During week 2, we increase the volume to 1.5 L at night and keep the abdomen dry

during the day. During week 3, we increase the volume further to 2 L at night, with either 1.5 L – 2 L during the day or remaining dry, if that is possible. We avoid the use of 10 exchanges over 10 hours because of the short dwell time. In patients who are not trained for automated PD, the options are intermittent PD using similar volumes in the PD clinic for about 8 hours, 4 days per week for 2 weeks after surgery. We have also used low-volume manual exchanges during the evening and night, while keeping the abdomen dry during most of the day when patients are ambulatory.

#### *Mechanism of poor wound healing with sirolimus*

The antifungal, antiproliferative, and immunosuppressive activities of sirolimus all have the same underlying molecular mechanism. Sirolimus forms an immunosuppressive complex with intracellular protein FKBP12. That complex blocks activation of the cell cycle-specific kinase mTOR. The downstream events that follow from the inactivation of mTOR result in cell-cycle progression being blocked at the juncture of the G1 and S phases (4). Results of an

TABLE I Suggested management protocol for postoperative peritoneal dialysis (PD)<sup>a</sup>

#### *For patients who can perform automated PD*

Week 1	Six 1 L exchanges over 10 hours at night, with the abdomen dry during the rest of the day while ambulant.
Week 2	Six 1.5 L exchanges over 10 hours at night, with the abdomen dry during the rest of the day while ambulant.
Week 3	Six 2 L exchanges over 10 hours at night, with a last fill of 1.5 L, drain after 6 hours, and keep the abdomen dry during the rest of the day.
Weeks 4–6	Four to six 2 L exchanges over 10 hours at night, with a last fill of 2 L or original prescription without exceeding a 2 L fill volume.
Week 7	Resume original prescription.

#### *For patients who are not trained to perform automated PD*

##### Option 1

##### Automated PD in the PD clinic, 4 days per week

Week 1	Six 1 L exchanges over 8 hours, with the abdomen dry the rest of the time.
Week 2	Six 1.5 L exchanges over 8 hours, with the abdomen dry the rest of the time.
Week 3–6	Resume original prescription without exceeding 2 L fill volume.
Week 7	Resume original prescription.

##### Option 2

Week 1	Four 1 L exchanges during the evening and night, with the abdomen dry while ambulant during the day.
Week 2	Four 1.5 L exchanges during the evening and night, with the abdomen dry while ambulant during the day.
Week 3–6	Resume original prescription without exceeding a 2 L fill volume.
Week 7	Resume original prescription.

<sup>a</sup> Modified from Crabtree *et al.* (10).

animal study showed that sirolimus led to a significant decrease in splenic lymphocyte proliferative activity ( $p < 0.05$ ). Sirolimus levels were found to be higher in wound fluid than in blood by a factor of 2–5 ( $p < 0.01$ ). Sirolimus reduced wound breaking strength ( $p < 0.01$ ) and wound collagen deposition ( $p < 0.05$ ). Those effects were paralleled by decreased expression of vascular endothelial growth factor and nitric oxide in wounds (6).

#### *Clinical studies correlating sirolimus and wound healing*

Wound-healing complications after kidney transplantation are well known. In a prospective randomized comparison, Dean *et al.* (11) found wound-healing complications (perigraft fluid collections, superficial wound infections, and incisional hernia) in 30 of 64 patients (47%) receiving a sirolimus-based regimen (sirolimus–mycophenolate mofetil–prednisone) and in 5 of 59 patients (8%) receiving a tacrolimus-based regimen (tacrolimus–mycophenolate mofetil–prednisone). That difference was statistically significant ( $p < 0.0001$ ). They also found that lowering the sirolimus dose reduced the risk of wound-related complications.

#### *Sirolimus and PD*

Perl *et al.* (12) reported a patient on sirolimus who developed a significant PD catheter exit-site leak that delayed the initiation of dialysis. No cases of incisional hernia attributed to the use of sirolimus in patients on PD have been published, making the present case the first to be reported, to the best of our knowledge.

#### **Summary and suggestions**

- The present case is the first to be reported of incisional hernia attributable to sirolimus after PD catheter placement.
- Sirolimus should be stopped several (preferably 6) weeks before elective PD catheter placement.
- Sirolimus should be suspected as the cause of early development of incisional hernia or pericatheter dialysate leak.
- A surgeon with expertise in specialized hernia surgery should be consulted when such patients have large hernias.
- Uninterrupted PD is possible after hernia surgery, especially if the patient has some residual kidney function.

#### **Disclosures**

We understand that *Advances in Peritoneal Dialysis* requires disclosure of any conflicts of interest, and we declare that we have no conflicts to disclose.

#### **References**

- 1 McCormick BB, Bargman JM. Noninfectious complications of peritoneal dialysis: implications for patient and technique survival. *J Am Soc Nephrol* 2007;18:3023–5.
- 2 Leblanc M, Ouimet D, Pichette V. Dialysate leaks in peritoneal dialysis. *Semin Dial* 2001;14:50–4.
- 3 Tzamaloukas AH, Gibel LJ, Eisenberg B, *et al.* Early and late peritoneal dialysate leaks in patients on CAPD. *Adv Perit Dial* 1990;6:64–71.
- 4 Sehgal SN. Sirolimus: its discovery, biological properties, and mechanism of action. *Transplant Proc* 2003;35(suppl):7S–14S.
- 5 Merkel S, Mogilevska N, Mengel M, Haller H, Schwarz A. Side effects of sirolimus. *Transplant Proc* 2006;38:714–15.
- 6 Schäffer M, Schier R, Napirei M, Michalski S, Traska T, Viebahn R. Sirolimus impairs wound healing. *Langenbecks Arch Surg* 2007;392:297–303.
- 7 Roine E, Björk IT, Oyen O. Targeting risk factors for impaired wound healing and wound complications after kidney transplantation. *Transplant Proc* 2010;42:2542–6.
- 8 Del Peso G, Bajo MA, Costero O, *et al.* Risk factors for abdominal wall complications in peritoneal dialysis patients. *Perit Dial Int* 2003;23:249–54.
- 9 Jayasena SD, Riaz A, Lewis CM, Neild GH, Thompson FD, Woolfson RG. Outcome in patients with end-stage renal disease following heart or heart–lung transplantation receiving peritoneal dialysis. *Nephrol Dial Transplant* 2001;16:1681–5.
- 10 Crabtree JH. Hernia repair without delay in initiating or continuing peritoneal dialysis. *Perit Dial Int* 2006;26:178–82.
- 11 Dean PG, Lund WJ, Larson TS, *et al.* Wound-healing complications after kidney transplantation: a prospective, randomized comparison of sirolimus and tacrolimus. *Transplantation* 2004;77:1555–61.
- 12 Perl J, Jassal SV, Bargman JM. Persistent peritoneal dialysis catheter exit-site leak in a patient receiving maintenance immunosuppression with sirolimus. *Clin Transplant* 2008;22:672–3.

#### *Corresponding author:*

Anupkumar Shetty, MD, 1150 N Bishop Avenue, Dallas, Texas 75208 U.S.A.

#### *E-mail:*

shettya@dneph.com