ISSN 2607-9917 www.bdd.rdplf.org Volume 7, n° 3, Sept 2024 https://doi.org/10.25796/bdd.v7i3.84583

Bulletin de la Dialyse à Domicile

Home Dialysis Bulletin (BDD)

International bilingual journal for the exchange of knowledge and experience in home dialysis

(English edition) (version française disponible à la même adresse)

Renal graft intolerance syndrome in peritoneal dialysis: A report on three cases

(Le syndrome d'intolérance du greffon rénale en dialyse péritonéale: A propos de 3 cas)

Sara El Maakoul[1,2], Yassir Tahri[1,2], Naima Ouzeddoun[1,2], Loubna Benamar[1,2]

[1]Service de Néphrologie-Dialyse-transplantation rénale - CHU Ibn Sina - Rabat, Maroc
[2]Faculté de médecine et de pharmacie, Université Mohammed V – Rabat, Maroc

Pour citer : El Maakoul S, Tahri Y, Ouzeddoun N, Benamar L. Renal graft intolerance syndrome in peritoneal dialysis: A report on 3 cases. Bull Dial Domic [Internet];7(3). Available from DOI:https://doi.org/10.25796/bdd.v7i3.84583

Summary

Introduction:
Renal graft intolerance syndrome is a serious complication following return to dialysis, which may present as an atypical clinical picture. Transplantectomy is almost systematic. We report the observation of three renal transplant patients currently on peritoneal dialysis (PD) who underwent renal graft nephrectomy with maintenance of PD.
Observation:
The observation concerns three patients, two men and one woman, with an average age of 40 years. The average duration of renal transplantation was 11 years. The cause of the return to dialysis was chronic graft dysfunction. After an average delay in PD of 22 months, two patients presented asthenia and significant weight loss. One patient presented acute fever and severe graft pain. This was associated with chronic inflammatory syndrome. All patients underwent nephrectomy of the graft without interruption of the dialysis technique, with early resumption of exchanges. Pathological examination showed necrosis of the renal graft.
Conclusion:
Deterioration of the general condition associated with inflammatory syndrome and resistance to erythropoietin may reveal renal graft intolerance syndrome. Transplantectomy is indicated to improve survival in these patients without compromising the PD technique.
Keywords: graft intolerance syndrome, peritoneal dialysis, transplantectomy.

Résumé

Introduction :
Le syndrome d'intolérance du greffon rénale, est une complication redoutable après retour en dialyse, qui peut se manifester par un tableau clinique atypique. La transplantéctomie est quasi-sytématique.
Nous rapportons l'observation de trois anciens greffés, ayant bénéficié d'une tranplantéctomie avec maintien de la dialyse péritonéale.
Observation:
Il s'agit de 3 patients, 2 hommes et une femme avec un âge moyen de 40 ans. La durée moyenne en transplantation rénale est de 11 ans. La cause du retour en dialyse est un dysfonctionnement chronique du greffon. Après un délai moyen en DP de 22 mois, 2 patients ont présenté une asthénie, un amaigrissement important. Une patiente a présenté un tableau aigu fait d'une fièvre et douleur intense du greffon. Ceci associé à un syndrome inflammatoire chronique. Tous les patients ont bénéficié d'une transplantéctomie sans interruption de la technique de dialyse, avec une reprise précoce des échanges. L'examen anatomopathologique en faveur d'une nécrose du greffon rénal.
Conclusion :
L'altération de l'état général associée à un syndrome inflammatoire et une résistance à l'érythropoïétine peuvent révéler un syndrome d'intolérance du greffon rénal. La tranplantéctomie permet d'améliorer la survie de ces patients sans compromettre la technique de dialyse péritonéale.
Mots-clés : syndrome d'intolérance du greffon, Dialyse péritonéale, tranplantéctomie

Correspondance :
Sara El Maakoul
E-mail : saraelmkl@gmail.com
ORCID : Sara EL Maakoul :0009-0002-6071-928X
Tel :Sara EL Maakoul: +212 654541027

journal officiel du Registre de Dialyse Péritonéale de Langue Française **RDPLF** www.rdplf.org

www.bdd.rdplf.org Volume 7, n° 3, Sept 2024
https://doi.org/10.25796/bdd.v7i3.84583
ISSN 2607-9917

Introduction

As renal transplantation (RT) becomes more frequent, the number of patients with graft failure is also increasing. According to the REIN registry, 1,101 graft failures were recorded in 2021, compared with 988 graft failures in 2012. Returning to dialysis after RT is a difficult transition for patients and their treating physicians. The management of these patients during this period is complex, encompassing the treatment of complications due to chronic kidney disease, the initiation of dialysis, the management and cessation of immunosuppression, and transplantectomy [1-3].

However, the majority of patients with chronic graft dysfunction retain their graft in situ, with or without the use of low-dose immunosuppressive therapy [1,2]. Transplantation becomes necessary when space is needed for a new renal graft and in cases of vascular thrombosis, recurrent graft pyelonephritis, and graft intolerance syndrome (GIS) [1-4]. This reputedly difficult surgical procedure is fraught with significant morbidity and mortality and has a complication rate of 20-30% [5].

GIS is a dreaded complication after return to dialysis, with a clinical and paraclinical presentation that is sometimes atypical. The syndrome is reported in 30-50% of patients with graft failure and occurs mainly during the 1st year after the start of dialysis. It reflects a chronic inflammatory state induced by the graft in situ and generally occurs after immunosuppressive therapy has been discontinued [1,4].

We report the observation of three former transplant recipients currently on peritoneal dialysis (PD) with GIS who benefited from transplantectomy without interruption of the PD technique.

Observation

The observations concern three patients, two men and one woman, with an average age of 40 years, all of whom had received a kidney transplant from a living donor at low immunological risk in two cases and at high immunological risk in one case. The average duration of renal transplantation was 13 years.

The cause of return to dialysis was chronic allograft dysfunction in three patients. All our patients lost residual renal function within the 1st year of PD. After a mean delay in PD of 22 months, two patients presented an alteration in general condition (AEG) with asthenia and emaciation. Malignant hypertension was found in a single patient refractory to quadritherapy and optimal dialysis. At present, no patient is on immunosuppressive therapy.

One patient presented acute fever and severe graft pain with signs of graft necrosis on echo-Doppler. This clinical picture was associated with chronic inflammatory syndrome (CIS), consisting of hyperferritinemia, hyperfibrinogenemia, elevated C-reactive protein (CRP), and anemia resistant to erythropoiesis-stimulating agents (EPO). In view of this CIS, with a poor and atypical clinical presentation, additional investigations were carried out on two patients in search of a secondary cause. The infectious workup, including a blood quantiferon test, a GeneXpert test and mycobacteria in sputum, and a coproculture and parasitological examination of stools, was negative. Hepatitis B and C and HIV serologies came back unremarkable. Transthoracic

journal officiel du Registre de Dialyse Péritonéale de Langue Française RDPLF www.rdplf.org

www.bdd.rdplf.org Volume 7, n° 3, Sept 2024
https://doi.org/10.25796/bdd.v7i3.84583
ISSN 2607-9917

echocardiography revealed no evidence of infective endocarditis. Plasma protein electrophoresis and serum protein immunofixation returned normal. The angio scan showed no signs of aortitis or vasculitis. The oesogastroduodenal fibroscopy and cervicothoracoabdominopelvic CT scan did not reveal any lesions explaining the CIS. In view of the persistence of clinicobiological CIS, a PET scan was performed on a single patient, showing heterogeneous hypermetabolism of the graft. The diagnosis of GIS was accepted, and all patients underwent extraperitoneal transplantectomy by laparotomy, retaining the PD catheter. The postoperative course was simple and uncomplicated. Pathological examination of the surgical specimen revealed signs of graft necrosis but no histological evidence of malignancy.

The PD technique was maintained in all patients; 1 day after transplantation, a «washout» with a 1-L isotonic glucose bag was performed, immediately infusing and draining small volumes. This was done to test the catheter and ensure that there were no obvious leaks. Given the hydroelectrolytic disorders and anuria, we started dialysis early, before 15 days after transplante ctomy, in two patients, for purification and ultrafiltration. Continuous ambulatory peritoneal dialysis (CAPD) was resumed 15 days after surgery, with the infusion of small volumes (1.5 L) in only one patient (*Table I*).

Table I. Summary of the three cases

Case	Gender	Age	Cause of return to dialysis	Graft life	Start date of PD	Date of transplantectomy	Clinical history + paraclinical balance sheet	Anatomopathology	Management of PD
1	M	45 years	Chronic allograft dysfunction	16 years	19/2/2018	5 years after starting PD	- AEG + febrile spike of 38 °C - HTA resistant to quadritherapy - Inflammatory syndrome + anemia	Necrosis of the graft	Resumption of APD (700 cc) 3 days after surgery
2	F	44 years	Chronic allograft dysfunction	7 years	24/9/2014	1 year after starting PD	- Fever of 38 °C - Sudden FIG pain - Inflammatory syndrome + anemia	Necrosis of the graft	Resumption of CAPD (1.5 L) 2 weeks after surgery
3	M	56 years	Chronic allograft dysfunction	17 years	27/4/2020	2 years after starting PD	- Chronic inflammatory syndrome + anemia	Necrosis of the graft	Resumption of APD (1.5 L) the day after surgery

AEG: impaired general condition ;APD: automated peritoneal dialysis ; CAPD: continuous ambulatory peritoneal dialysis

No infectious complications were observed in our patients postoperatively; minimal dialysate leakage was reported in a single patient after resumption of PD, without compromising the technique.

The three patients are still on PD with a favorable evolution after transplantation, marked by weight gain, resumption of appetite, CRP negativation, and improvement of anemia with erythropoietin (EPO) dose reduction in three cases. We noted an improvement in blood pressure,

journal officiel du Registre de Dialyse Péritonéale de Langue Française RDPLF www.rdplf.org

www.bdd.rdplf.org Volume 7, n° 3, Sept 2024
https://doi.org/10.25796/bdd.v7i3.84583
ISSN 2607-9917

with discontinuation of treatment for arterial hypertension (AH) in one patient (*Tables I and II*).

Table II. Clinical and biological parameters after transplantation

	Before transplantectomy			1st month after surgery			3rd month after surgery			Currently		
	Case 1	Case 2	Case 3	Case 1	Case 2	Case 3	Case 1	Case 2	Case 3	Case 1	Case 2	Case 3
BP (cmHg)	18/11	10/6	11/8	12/8	12/6	10/7	12/8	12/8	13/8	12/6	11/7	13/8
CRP (mg/L)	198	108	118	13.4	17.5	64	3.5	9	8	<5	<5	<5
Hb (g/dL)	7.7	7.9	9.8	9.4	7.2	7.3	13.5	11.1	10.3	12	11	11
EPO dose (IU/kg/week)	250	250	185	234	230	176	156	153	117	70	74	120

BP: blood pressure ; CRP: C-reactive protein ; Hb: hemoglobin ; EPO: erythropoietin

Discussion

The number of kidney transplant patients returning to dialysis after transplant failure continues to rise. These patients represent a different group from non-transplanted chronic dialysis patients, with a much higher morbimortality rate, particularly cardiovascular and infectious, due to prolonged immunosuppressive therapy [1,3]. However, the major issue in these patients is whether or not to remove the non-functional renal graft.

In the absence of clearly defined guidelines, transplantectomy is performed according to the results of the clinical and paraclinical examination and the practice of each team. Some suggest systematic removal in order to unmask anti-HLA antibodies adsorbed by the graft and therefore undetectable in the blood, and also to avoid complications due to immunosuppression, while others propose this procedure only for non-functioning transplants causing GIS [3,4,6].

GIS is a chronic inflammatory condition related to the rejection of an allograft left in situ, with a variable clinical presentation in the form of unexplained fever, altered general condition, hematuria, and graft hypertrophy or tenderness. Biologically, GIS may reveal itself as CIS with anemic syndrome unresponsive to the usual doses of EPO. Infections or malignancies must be excluded before the diagnosis of GIS can be made. In a study by Woodside et al., 62% of patients had rejection as the source of fever with no identified source of infection [8,9].

In our work, only one patient presented acute CIS suggesting GIS, which was revealed by CIS only and resistance to EPO in two cases.

GIS is associated with high morbidity, and in most cases emergency transplantectomy is required. This procedure is not without risk: it is a laborious surgery with high morbidity and mortality [10,11]. Postoperative morbidity is greater the earlier the transplantectomy is performed, when immunosuppression is at its highest. Mortality due to general anesthesia appears to be exceptional [6]. However, the risks associated with transplantation include loss of residual renal function and HLA sensitization. This surgical procedure may also be complicated by rupture of the renal parenchyma, leading to hemorrhage. Loge hematomas are one of the most frequent complications, which may be complicated by abscesses requiring surgical drainage [6,12]. Potential advantages of transplantectomy include the prevention of GIS, the possibility of withdrawing immunosuppressive therapy, and the ability to make more room for a new graft

journal officiel du Registre de Dialyse Péritonéale de Langue Française RDPLF www.rdplf.org

https://doi.org/10.25796/bdd.v7i3.84583
ISSN 2607-9917

[1,3].

After open abdominal surgery, it is traditionally recommended to discontinue CAPD for at least 6 weeks to ensure complete healing and avoid complications, such as peritoneal fluid leakage, wound dehiscence, or abdominal hernia [13].

There are no reports in the literature of successful PD after transplantectomy secondary to GIS. In this article, we report three cases in which PD was successfully re-established after extraperitoneal transplantectomy. Exchanges were started early with small volumes of dialysate, which we gradually increased according to the patient's clinical condition. The evolution was favorable, marked by weight gain, resumption of appetite, correction of hypertension and anemia, and CRP negativation.

Keeping patients on PD after transplantectomy guarantees them greater autonomy and mobility, at a lower cost, than switching them to hemodialysis [14]. Renal artery embolization is an attractive alternative to transplantectomy that has been evaluated in the context of GIS. Data on the efficacy and safety of this procedure compared with transplantectomy are limited, but some studies have suggested that embolization can reduce morbidity and mortality, but at the cost of a 15.6% failure rate, with an equivalent length of hospital stay and rate of postoperative complications [2,15].
In the absence of established indications for transplantectomy, the option of percutaneous embolization should be considered, particularly for high-risk surgical and PD patients, to reduce the risk of peritoneal membrane injury [15].

Conclusion

Returning to dialysis after chronic renal graft dysfunction is always a difficult period for the patient, fraught with metabolic, infectious, and vascular complications.
Transplantation, reputedly morbid and difficult, is almost systematic. Although our study is limited by its small sample size and retrospective nature, we found that PD can be continued after extraperitoneal transplantectomy without major complications.

Conflicts of interest

The authors declare that they have no conflict of interest in connection with this article.

Authors' responsibilities

S.E wrote the article
Y.T provided editorial assistance
L.B and N.O provided constructive feedback

ORCID :
Sara EL Maakoul : https://orcid.org/0009-0002-6071-928X
Yassir Tahri
Naima Ouzeddoun : https://orcid.org/0000-0003-2358-4697
Loubna Benamar : https://orcid.org/0000-0003-1998-0320

journal officiel du Registre de Dialyse Péritonéale de Langue Française RDPLF www.rdplf.org

https://doi.org/10.25796/bdd.v7i3.84583
ISSN 2607-9917

References

1-Bunthof K, Saboerali K, Wetering JVD, Nurmohamed A, Bemelman F, Zuilen AV, Brand JVD, Baas M, Hilbrands L. Can we predict graft intolerance syndrome after kidney transplant failure? External validation of a previously developed model. Transpl. Int. 2023;36:11147. doi: 10.3389/ti.2023.11147.

2-Chowaniec Y, Luyckx F, Karam G, Glemain P, Dantal J, Rigaud J, Branchereau J. Transplant nephrectomy after graft failure: Is it so risky? Impact on morbidity, mortality and alloimmunization. Int. Urol. Nephrol. 2018;50(10):1787-1793. doi: 10.1007/s11255-018-1960-4.

3-Leal R, Pardinhas C, Martinho A, Sá HO, Figueiredo A, Alves R. Challenges in the management of the patient with a failing kidney graft: A narrative review. J. Clin. Med. 2022;11:6108. https://doi.org/10.3390/jcm11206108.

4-Bunthof KLW, Hazzan M, Hilbrands LB. Review: Management of patients with kidney allograft failure. Transpl. Rev. (Orlando) 2018;32(3):178-186. doi:10.1016/j.trre.2018.03.001.

5-Ghyselen L, Naesens M. Indications, risks and impact of failed allograft nephrectomy. Transplantation Reviews 2019;33(1):48-54.

6-Del Bello A, Rostaing L, Congy-Jolivet N, Sallusto F, Gamé X, Kamar N. Place of transplantectomy after failed renal transplantation. Nephrology and Therapeutics 2013;9(4):189-194.

7-Lubetzky M, Tantisattamo E, Molnar MZ, et al. The failing kidney allograft: A review and recommendations for the care and management of a complex group of patients. Am. J. Transplant. 2021;21(9):2937-2949. doi: 10.1111/ajt.16717.

8-Woodside KJ, Schirm ZW, Noon KA, et al. Fever, infection, and rejection after kidney transplant failure. Transplant. 2014;97(6):648-653.

9-Kainz A, Mayer B, Kramar R, Oberbauer R. Association of ESA hypo-responsiveness and haemoglobin variability with mortality in haemodialysis patients. Nephrol. Dial. Transplant. 2010;25(11):3701-3706.

10-Gómez-Dos-Santos V, Lorca-Álvaro J, Hevia-Palacios V, et al. The failing kidney transplant allograft. Transplant nephrectomy: Current state-of-the-art. Curr. Urol. Rep. 2020;21(1):4.

11-Alberts VP, Minnee RC, Bemelman FJ, van Donselaar-van der Pant KA, Idu MM. Transplant nephrectomy: What are the surgical risks? Ann. Transplant. 2013;18:174-181.

12-Mang J, Haag J, Liefeldt L, Budde K, Peters R, Hofbauer SL, Schulz M, Weinberger S, Dagnæs-Hansen J, Maxeiner A, Ralla B, Friedersdorff F. Transplant nephrectomy: Indication, surgical approach and complications-experiences from a single transplantation center. World J. Urol. 2024;42(1):120. doi: 10.1007/s00345-024-04884-8.

13-Del Peso G, Bajo MA, Costero O, Hevia C, Gil F, Díaz C, et al. Risk factors for abdominal wall complications in peritoneal dialysis patients. Perit. Dial. Int. 2003; 23:249-254.

14-Jwo SC, Chen KS, Lin YY. Video-assisted laparoscopic procedures in peritoneal dialysis. Surg. Endosc. 2003;17:1666-1670.

15-Pérez Martínez J, Gallego E, Juliá E, Llamas F, López A, Palao F, et al. Embolization of non-functioning renal allograft: Efficacy and control of systemic inflammation. Nefrologia 2005;25(4):422-427.

Submitted 2024-07-14 accepted after revision 2024-08-11 published 2024-09-09

journal officiel du Registre de Dialyse Péritonéale de Langue Française **RDPLF** www.rdplf.org