



Case Report

Nephrotic Syndrome due to Nodular Glomerulosclerosis in a Non-Diabetic Lung Transplant Recipient with Cystic Fibrosis

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Abstract

Background: Nephrotic syndrome due to severe nodular glomerulosclerosis in a non-diabetic cystic fibrosis (CF) patient is uncommon and is rarely discovered after lung transplantation (LTx).

Case: A 34-year-old non-smoker Caucasian woman with a history of CF end-stage lung disease underwent LTx in 2013. Five years later, she developed nephrotic syndrome. The renal biopsy revealed nodular glomerulosclerosis, very similar to diabetic glomerulosclerosis. However the patient did not show any abnormality in blood glucose regulation.

Conclusion: Kidney diseases other than calcineurin-inhibitor nephrotoxicity can develop in CF LTx patients. A thorough clinico-pathological assessment is essential to guide the diagnosis and an early treatment in a patient with multiple risk factors for kidney diseases

Keywords: Cystic fibrosis; Cystic Fibrosis kidney disease; Lung transplantation; Nodular glomerulosclerosis

Introduction

Kidney disease is a serious complication after (remove lung) LTx: it may lead to renal function loss and increases the risk of death [1]. Severe kidney dysfunction (non dialysis or dialysis dependant, or treated with kidney transplantation) has been reported in up to 41% of the recipients, ten years after LTx [2]. So regular monitoring of kidney function is essential in this transplanted population. Renal complications are often attributed to the use of calcineurin inhibitors, however other renal disorders related to the cause of end stage lung disease may be implicated. CF which is a common indication of LTx [3] can result in a large spectrum of kidney injuries which may appear after lung transplant [4,5]. We report a case of nephrotic syndrome in a non-diabetic lung transplant CF recipient with severe nodular glomerulosclerosis.

A 34-year-old non-smoker Caucasian woman with a history of CF end-stage lung disease underwent LTx in 2013. Maintenance immunosuppression consisted of tacrolimus, mycophenolic acid and prednisone. The post-transplant course was complicated by acute renal failure episodes associated to pulmonary infections and gastro-enteritis. At the end of 2018, serum creatinine was 115 $\mu\text{mol/l}$ and proteinuria (1g/l) appeared. After a respiratory tract infection in March 2019, she presented with edema (weight 63,1kg, height 159 cm). Blood pressure was 146-88 mmHg. Laboratory results showed: serum albumin: 26 g/l proteinuria: > 5 g/l; urine protein/creatinine ratio 0,606 g/mmol; serum creatinine: 154 $\mu\text{mol/l}$. C3 and C4 levels, autoimmunity tests, serologies for hepatitis C and hepatitis B and HIV virus, serum protein electrophoresis were unremarkable. Urine culture was negative. Renal ultrasound revealed no abnormalities. The kidney biopsy demonstrated features consistent with the diagnosis of nodular glomerulosclerosis (Figure 1), very similar to diabetic glomerulosclerosis.

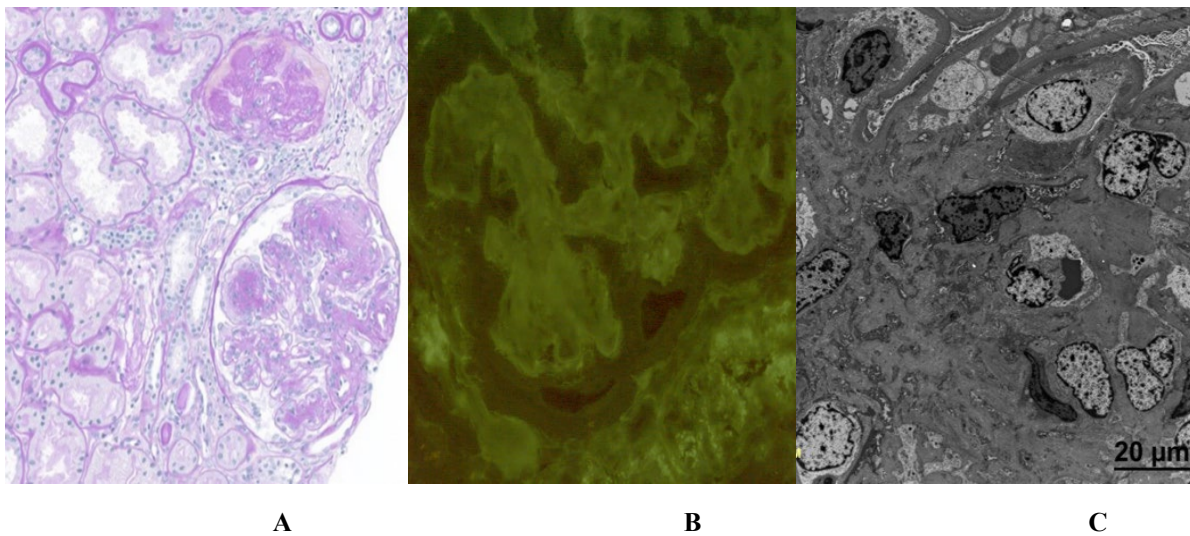


Figure 1: **A:** Glomerulus showing nodular mesangial expansion with foci of mesangiolysis and thickened glomerular basement membranes. Periodic Acid Schiff, original magnification 200x **B:** Direct immunofluorescence shows mild linear accentuation along the glomerular membrane basement (GBM) with IgG, without any granular staining in the glomeruli. Other stains (IgA, IgM, C3, C1q, Kappa and Lambda) did not show significant staining. Original magnification 600x **C:** Electron microscopy showed mesangial matrix expansion with variably thickened GBM. No electron dense deposits were identified. Original magnification 2500x.

Fasting glucose, the oral glucose tolerance test and HbA1c were normal. Screening for diabetic retinopathy was negative. Diuretics and candesartan were added to the treatment. One year later, serum albumin is 23 g/l with serum creatinine 236 µmol/l and urine protein/creatinine ratio 1,075 g/mmol.

As LTx improves survival in CF [3] without curing this multi-system disease, CF-related comorbidities increase after transplantation. Among the wide spectrum of renal manifestations described in CF [5], nephrotic syndrome is uncommon and usually related to secondary amyloidosis or diabetic nephropathy. Nodular glomerulopathy without diabetes has rarely been described in CF patients [5-8]. The reported patient did not show any abnormality in blood glucose regulation using conventional OGTT criteria although she was at high risk of diabetes. Pancreatic destruction occurs during childhood of CF patients and may contribute to the insidious development of diabetes. Early glucose abnormalities in CF subjects may be difficult to detect and very little is known about their clinical impact [9]. Nevertheless diabetes is present in more than 30% of CF adults by the age of 40 and with LTx, corticosteroids and tacrolimus increase the prevalence of diabetes which develops in 20 to 60% of CF patients posttransplant [10].

Other conditions described with nodular glomerulopathy (monoclonal immunoglobulin deposition disease, membranoproliferative glomerulonephritis, amyloidosis, cigarette smoking, obesity, severe hypertension) were excluded in the patient, on clinical history and kidney biopsy findings (light microscopy, immunofluorescence, and electron microscopy) [11].

In conclusion, CF LTx recipients may develop renal disorders specifically linked to CF, such as nodular glomerulopathy. Given the high risk of rapid decline of kidney function in CF LTx recipients [4,12], early and in-depth evaluation of any kidney abnormality (not only increased serum creatinine) and regular follow-up could allow prompt implementation of renoprotective strategies and help minimize chronic kidney disease development and progression. Finally better understanding of the mechanisms underlying nodular nephropathy in CF patients without overt diabetes, could lead to improved outcomes.

References

1. Ojo AO, Held PJ, Port FK, Wolfe RA, Leichtman AB, et al. (2003) Chronic renal failure after transplantation of a nonrenal organ. *N Eng J Med* 349: 931.
2. Yusen RD, Christie JD, Edwards LB, Kucheryaavaya AY, Benden C, et al. (2013) The registry of the International Society for Heart and Lung Transplantation. Thirtieth lung and heart-lung transplant report- 2013; focus theme: age. *J Heart and Lung Transplant* 32: 965-978.
3. Yusen RD, Edwards RB, Dipchant AI, Goldfarb S, Kucheryaavaya AY, et al. (2016) The registry of the International Society for Heart and Lung Transplantation: thirty-third adult lung and heart-lung transplant report- 2016; focus theme: primary diagnostic indication for transplant. *J Heart and Lung Transplant* 35: 1158-1169.
4. Lefaucheur C, Nochy D, Amrein C, Chevalier P, Guillemain R, et al. (2008) Renal histopathological lesions after lung transplantation in patients with cystic fibrosis. *Am J Transplant* 8: 1901-1910.
5. Yahiaoui Y, Jablonski M, Hubert D, Mosnier-Pudar H, Noël LH, et al. (2009) Renal involvement in cystic fibrosis: disease spectrum and clinical relevance. *Clin J Am Soc Nephrol*. 4: 921-928.

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6. Westall GP, Binder J, Kotsimbos T, Topliss D, Thomson N, et al. (2004) Nodular glomerulosclerosis in cystic fibrosis mimics diabetic nephropathy. *Nephron Clin Pract.* 96: c70-75.
7. O'Connell O, Magee CN, Fitzgerald B, Burke L, Plant WD, et al. (2010) A CF patient with progressive proteinuric disease: a CF specific nodular glomerulosclerosis? *NDT Plus* 3: 354-356.
8. Lalayiannis AD, Thompson C, Malcomson R, Milford DV. (2016) Nodular glomerulosclerosis in a patient with cystic fibrosis but not diabetes mellitus: a paediatric case. *Respir Med Case Report* 19: 58-60.
9. Granados A, Chan CL, Ode KL, Moheet A, Moran A, et al. (2019) Cystic fibrosis related diabetes: pathophysiology, screening and diagnosis. *J Cystic Fibros* 18: S3-S9.
10. Sidhaye A, Goldsweig B, Kaminski B, Blackman SM, Kelly A. (2019) Endocrine complications after solid-organ transplant in cystic fibrosis. *J Cyst Fibros.* 18: S111-S119
11. Alsaad KO, Herzenberg AM. (2007) Distinguishing diabetic nephropathy from other causes of glomerulosclerosis: an update. *J Clin Pathol* 60: 18-26.
12. Soulsby N, Greville H, Coulthart K, Doecke C. (2009) Renal dysfunction in cystic fibrosis. *Pediatr Pulmonol* 44: 947-953.