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Graft loss from a living donor due to flash recurrence of focal segmental glomerular sclerosis — case report

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ABSTRACT

Focal segmental glomerular sclerosis is a pattern of histological damage of the kidney. The most common clinical manifestation is proteinuria, however, it can frequently progress to full nephrotic syndrome. Glucocorticosteroids are the first line of treatment and, in case of resistance, calcineurin inhibitors are used. In some patients, despite treatment, focal segmental glomerular sclerosis leads to end-stage renal disease, in which organ transplantation is the only therapeutic option. In several cases, relapse occurs in the transplanted organ. The following paper presents a case report of a patient treated for focal segmental glomerular sclerosis since the age of 21, who developed end-stage renal failure after seven years of disease despite immunosuppressive treatment. Although there was a significant risk of recurrence, it was decided to transplant a kidney from a family donor — the patient's mother. From about one week after transplantation, progressive deterioration of graft function was observed.

Keywords: focal segmental glomerular sclerosis, graft loss, kidney transplantation

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Introduction

Focal segmental glomerulosclerosis (FSGS) is not a distinct disease entity, rather it is a pattern of histological damage in the kidney [1]. It is defined as the sclerosis of the glomerular vascular bundle with the formation of an adhesion with Bowman's capsule, accompanied at a later stage by an increase in the extracellular matrix, as well as the deposition of vitreous deposits. Sclerosis primarily affects the area of the corticomedullary border [2]. Focal segmental glomerulosclerosis lesions have shown an increasing incidence over the past few decades and are considered the most common glomerular cause leading to end-stage renal failure [3]. Depending on the aetiology, a classification is made into primary-idiopathic FSGS, genetic FSGS—usually caused by mutation of podocyte and slit membrane structural proteins—and secondary FSGS, caused by factors that damage the glomerulus, i.e. post-infectious, drug-induced damage (e.g., pamidronate, lithium, interferon alfa, tacrolimus, sirolimus,

cyclosporin A), renal mass reduction and hyperfiltration (dysplasia, agenesis, progressive renal damage with reduction of active nephrons, chronic dysfunction of the transplanted kidney), as well as hypertension, obesity, renal artery stenosis, certain haematopoietic diseases [4]. The most common clinical manifestation of FSGS is proteinuria. Patients with primary FSGS often present with full nephrotic syndrome, accompanied by hypertension and microscopic haematuria [5]. In patients with nephrotic syndrome, due to the high loss of albumin in the urine, there may be a reduction in vascular oncotic pressure, leading to a decrease in circulating blood volume. This decrease is detected by the renal juxtaglomerular apparatus, which stimulates the renin-angiotensin-aldosterone system, leading to fluid retention which can result in the development of peripheral oedema and hypertension. Additionally, patients develop hypercoagulability associated with urinary loss of protein S and antithrombin. Nephrotic syndrome additionally leads to increased production of cholesterol and low-density lipoproteins resulting in the

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Table 1. Results of selected laboratory tests after transplantation

Day after transplant	Serum creatinine concentration [mg/dL]	Serum urea concentration [mg/dL]	Haemoglobin concentration in venous blood [g/dL]
0	7.4	50.3	11.8
1	6.6	58.6	11.9
6	2.6	71.5	9.8
8	2.2	93.1	8.9
13	4.8	145.5	7.5

development of hyperlipidaemia [6]. During diagnosis, the clinical picture and laboratory findings, such as urine and blood albumin levels, urinalysis and blood lipids, can guide the diagnosis, but a renal biopsy is required to differentiate FSGS from other glomerulopathies. The first-line treatment of FSGS is high-dose glucocorticosteroids, or calcineurin inhibitors (in case of glucocorticosteroid resistance or intolerance) [7].

Case report

Patient treated for chronic glomerulonephritis since the age of 21 years, FSGS biopsy without immune deposits. In addition, had a history of hypertension, inflammation of the duodenal mucosa and nicotine use. In family history, his father was also diagnosed with the disease, although the course of the disease was lighter (haemodialyzed, currently after a deceased donor kidney transplant, with normal graft condition). Immunosuppressive treatment included a number of drugs: steroids, temporary azathioprine and chlorambucil, and mycophenolate mofetil (MMF). In addition to treatment, frequent relapses of severe nephrotic syndrome requiring hospitalisation were reported. After 7 years of disease progression, a patient with end-stage renal failure on a haemodialysis programme was approached for renal transplantation. Qualified for organ transplantation from the patient's living mother donor. The patient received induction treatment with rabbit anti-human T-lymphocyte immunoglobulin, the perioperative course was uncomplicated, the patient did not require haemodialysis after the procedure, a diuresis of approximately 2,500 mL and a gradual decrease in serum creatinine levels were observed (lowest level of 2.2 mg/dL on the eighth day after transplantation) (Tab. 1). This was followed by a reduction in diuresis to around 500 mL/day and a gradual increase in creatininaemia, as well as the appearance of lower extremity oedema. On postoperative day 13, an angio-CT scan was performed — stenosis of the renal artery of the transplanted kidney was excluded. A biopsy of the transplanted kidney was performed, an infusion of 500 mg of methylprednisolone was given,

and the MMF dose was planned to be increased to 2×1 g/day, but the dose was reduced to 2×500 mg due to the observed leukopenia. Methylprednisolone infusions were continued for a further two days; despite treatment, the patient was reported to have an increase in serum creatinine to 5.8 mg/dL, increasing peripheral oedema and body weight, and elevated blood pressure values. Two haemodialysis procedures with ultrafiltration were performed on days 15 and 16 post-transplant, and a gradual increase in diuresis was observed. Due to the non-diagnostic result of the biopsy with high immunization of the patient, it was decided to perform another biopsy on day 22 after transplantation — in the biopsy taken, only 1 glomerulus was described — damage to the tubular epithelium as in severe ischaemia. Ultrasound-doppler was performed — renal vascular flow was preserved. After the treatment, serum creatinine dropped to 2.6 mg/dL. Approximately 3 months after transplantation, another graft biopsy: image consistent with chronic glomerulopathy, type of damage: focal segmental glomerular sclerosis. No glomerular deposits were found. In addition, acute damage to the tubular epithelium. Given the above, 5 plasmapheresis procedures were performed with the exchange of 1.5 plasma volumes for 5% albumin and 500 mg of rituximab was administered. Due to the depletion of the CD19 lineage of B lymphocytes, rituximab therapy was cancelled. Immunosuppressive treatment was changed from tacrolimus to a cyclosporine preparation. In the further course of the disease, serum creatinine increased to 7.4 mg/dL. Due to moderate anaemia, the patient qualified for stimulant treatment after ruling out iron deficiency. In addition, there was a need to modify hypertension treatment due to unsatisfactory control. The patient was qualified for haemodialysis.

Discussion

Focal segmental glomerulosclerosis in the transplanted kidney may occur as a recurrence of the disease, or secondary to the organ-damaging processes accompanying transplantation. It is diagnosed based on histopathological examination and analysis of risk

factors [4]. The recurrence rate of FSGS in allografts is 20–40%, and graft failure occurs in 40–50% of these cases. In cases of graft failure due to relapse, the risk of recurrence in a second transplantation approaches 80% [8]. In patients who lost their previous transplant for reasons other than recurrent FSGS, the incidence of FSGS recurrence in the new allograft was significantly lower — 14% [9]. The familial donor should also be considered as a factor increasing the risk of recurrence, as normal renal function and absence of proteinuria at the time of assessment do not exclude a genetic predisposition to FSGS [10]. Other unfavourable prognostic criteria are a young age of onset of the described glomerulopathy, rapid progression to end-stage renal failure, resistance to treatment, and a living organ donor [11]. However, the risk of relapse will not contraindicate transplantation [12]. In the face of a rapidly deteriorating organ and poor response to treatment, transplantation from a family donor should be considered after a careful analysis of the benefits and potential risks. In individual cases, after obtaining conscious consent from the donor and recipient, it may be advisable to further diagnose the condition of the donor organ by genetic testing and biopsy [11]. Given the inevitable exposure of the donor to surgical complications, pain, the need for hospitalisation and even the risk of death (90-day mortality estimated at approximately 3.1 per 10,000) associated with transplantation and the small but significant risk of end-stage renal failure [13], in the face of the likelihood of relapse in the transplanted kidney, the ethical concerns associated with transplantation should also be considered. After transplantation, the recipient's condition should be closely monitored, as recurrence can occur in the first hours after transplantation [12]. At present, no official guidelines have been created for the treatment of FSGS recurrent after transplantation. Most centres use plasmapheresis treatment with or without rituximab. The intensity and duration of treatment vary considerably between centres. The percentage of complete or partial remission with the above treatment is estimated at 57% [9]. The described patient had most of the risk factors listed above. In the absence of therapeutic options and having a potential family donor, the decision was made to organ transplantation. After the operation, the condition of the graft was monitored, and when a significant deterioration in organ function was observed, treatment and diagnosis for recurrent glomerulopathy was initiated. Despite plasmapheresis and rituximab, the renal status deteriorated and the patient required haemodialysis.

Conclusions

Focal segmental glomerulosclerosis is not a contraindication to kidney transplantation, however, the

significant risk of recurrence of this glomerulopathy in the transplanted organ, especially from a family, living donor should lead clinicians to very careful consideration and discussion of the potential benefits and risks of the procedure. Other factors that increase the risk of recurrence are the young age of onset of FSGS, resistance to treatment, rapid progression to end-stage renal failure and subsequent transplantation due to recurrence in the transplanted kidney. After surgery, the recipient requires close monitoring, as the risk of relapse in the transplanted organ exists from the first hours after surgery. Currently, no clear recommendations established by specialists are available for the treatment of FSGS in the transplanted kidney.

Article information

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