

# Association Between Focal Segmental Glomerulosclerosis and Cross-Fused Renal Ectopia: A New Cause of Secondary Focal Segmental Glomerulosclerosis or a Casual Association?

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## Abstract

Cross-fused renal ectopia is a rarely described congenital kidney anomaly. It can occur in association with ureteropelvic obstruction, vesicoureteral reflux, and multicystic dysplasia, which sometimes leads to nephrolithiasis and recurrent urinary infection. However, complications related to glomerulopathies are rare in patients with congenital kidney anomaly. Here, we report a case of cross-fused renal ectopia associated with focal segmental glomerulosclerosis (FSGS). The initial clinical findings suggested the possibility of secondary FSGS; nonetheless immunosuppression was successfully done. The case demonstrates a never-before reported association in an asymptomatic patient.

**Keywords:** Cross-fused renal; FSGS, Glomerulosclerosis; Nephrotic syndrome; Renal ectopia; Secondary FSGS; Kidney anomaly; Renal fusion

## Introduction

Cross renal ectopia is a rare congenital anomaly. It has a reported frequency of 1 case per 700 - 1,000 births, and usually (85-90%) occurs with fusion [1]. Patients with cross renal ectopia may present with ureteropelvic obstruction, vesicoureteral reflux, and multicystic dysplasia, as well as nephrolithiasis and recurrent urinary tract infections [1].

There are only a small number of cases of congenital kidney anomalies in association with glomerulopathies in the literature. Some patients remain asymptomatic until the fourth or fifth decade of life, and 20-30% of cases are only discovered as an accidental finding in routine exams [1, 2]. Here, we report a case of cross-fused ectopic kidneys presenting with focal seg-

mental glomerulosclerosis (FSGS), a combination that has not been described previously in the literature.

## Case Report

A 40-year-old male patient came to the nephrologist for a routine evaluation. He had previously identified cross-fused renal ectopia, but was asymptomatic. Blood tests showed creatinine (SCr) 1.8 mg/dL, blood urea nitrogen (BUN) 66 mg/dL and serum albumin 4.1 mg/dL. Urinalysis revealed proteinuria (++)/4+ and hematuria (10 - 15 red blood cells/field), and 24-h proteinuria was 1.9 g/day. A blood lipid panel demonstrated a high total cholesterol (286 mg/dL) and high triglyceride level (278 mg/dL). The autoimmune workup was negative, serology tests for HIV and hepatitis were non-reactive, and the patient had normal complement levels.

A kidney biopsy was performed after assessment of safety and revealed seven glomeruli, four of which had global sclerosis and two of which had segmental sclerosis, with capillary occlusion and a corresponding increase in the number of mesangial cells with rare podocyte hypertrophy. Tubules with focal points of atrophy and thickening of the basal membrane were observed. There was 70% focal interstitial fibrosis with preserved vessels. Immunofluorescence microscopy demonstrated that the biopsied specimen was positive for C3. Based on these observations, a diagnosis of FSGS with diffuse interstitial fibrosis was made.

An initial treatment of enalapril, spironolactone, and prednisone (1 mg/kg/day) was administered for 16 weeks. The renal function deficit persisted with proteinuria (2.5 g/day). Therefore, we decided to replace the corticosteroid with 2 mg/kg/day of cyclophosphamide. After 2 months, an improvement in renal function and a reduction in proteinuria were documented. A follow-up blood test revealed changes in SCr (1.4 mg/dL) and BUN (100 mg/dL), and a creatinine clearance (CrCl) rate of 42 mL/min. His 24-h proteinuria was brought down to 280 mg. After 1 year, the patient had maintained renal function CrCl rate of 40 mL/min and proteinuria at the level of 220 mg/day.

## Discussion

Congenital renal/ureteral abnormalities, including renal hypo-

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plasia, horseshoe kidney, simple or crossed ectopic kidneys, rotational defects and renal agenesis, occur in 3-4% of newborns [1-3]. Clinical complications of these abnormalities consist of urinary infection, kidney stones, abdominal mass or pain, dysuria, hematuria, and oliguria. There may be anatomical manifestations, such as hydronephrosis in the ureteropelvic junction or vesicoureteral reflux [1, 2].

Although there are numerous descriptions of clinical complications in the literature, there are few reported cases of renal anomalies involving glomerulopathies [4]. A search in the MEDLINE and PubMed databases did not reveal any descriptions of cross-fused renal ectopia with glomerulopathy. We found only four publications describing an association between renal anomalies (horseshoe kidneys in all cases) and glomerulopathies [4-7]. FSGS was the glomerulopathy present in two of these cases, and treatment with immunosuppressant drugs did not improve proteinuria in those two cases, with levels remaining in the range of 1 - 2.5 g [4-7].

In one report, Abson et al described the case of a 52-year-old patient with peripheral edema for 6 months. The patient had proteinuria (7.7 - 14.4 g/day), low serum albumin (2.4 g/dL), high SCr (1.5 mg/dL), and a CrCl of 70 mL/min. Complementary investigation showed horseshoe kidneys with FSGS. After 5 months, the SCr had risen to 1.7 mg/dL and CrCl had fallen to 53 mL/min. The patient was then started on 100 mg cyclosporine. They described resolution of the nephrotic pathology over the first 11 months, after which the patient presented with proteinuria levels of 1 - 2.5 g/day without any relapses [5].

In the second case, Chen and Ko reported the case of 20-year-old man, admitted with repeated instances of swelling of his glans penis. A urinalysis demonstrated proteinuria (300 mg/dL), hematuria (15 - 20 red blood cells/field), and SCr and albumin levels of 0.9 mg/dL and 2.3 mg/dL, respectively. Horseshoe kidneys were observed in a tomography exam, and an open kidney biopsy confirmed membranous glomerulonephritis [6].

In the third case, Fujimoto et al described the case of a 48-year-old woman with proteinuria discovered during a routine annual exam, associated with persistent hypocomplementemia. A urinalysis demonstrated proteinuria (2+/4+) without hematuria, SCr 0.7 mg/dL and proteinuria 600 mg/day. She had normal blood pressure and a CrCl of 82 mL/min, normal C3 (89 mg/dL) and low C4 (10 mg/dL). An abdominal ultrasound and tomography showed horseshoe kidneys, and a percutaneous biopsy revealed global and segmental sclerosis [7].

In the fourth report, Kavukcu et al described the case of an 18-year-old female patient submitted to evaluation of proteinuria and hematuria. She presented with a runny nose, fever, and cough, accompanied by peripheral edema. Urinalysis was 8 - 10 erythrocytes per field, SCr was 0.8 mg/dL, albumin was 2 g/dL and proteinuria was 1,200 mg/day. A renal ultrasound showed evidence of horseshoe kidneys. A kidney biopsy revealed diffuse mesangioproliferative glomerulonephritis. An initial treatment with prednisolone improved the clinical signs and symptoms, although she had two episodes of massive proteinuria during follow-up. The first relapse was treated with prednisolone and the second with a combination of cyclophosphamide and prednisone [4].

It is not possible to correlate the occurrence of kidney anomalies with glomerulopathies; it can occur by chance without a causal relationship as described by Abson et al and Kavukcu et al [4, 5]. However, different from primary FSGS, which is related to minimal changes and profuse proteinuria, secondary FSGS can be associated to pre-existing conditions and occur in various forms. Moreover, these patients are more likely to have mild foot process effacement and to present with subnephrotic-range proteinuria and normal serum albumin [8, 9].

The term FSGS is used to describe a histopathological glomerular sclerosis lesion. It is considered to be secondary when it arises in the presence of a pre-existing pathology, including lymphoproliferative disorder, autoimmune diseases, infection, unilateral renal artery stenosis, increased growth hormone production, dense deposit disease, and lipid deposition. It also includes congenital vesicoureteral reflux and renovascular diseases [10-12].

Secondary FSGS is known to result from hemodynamic adaptations mediated by intrarenal vasodilatation leading to glomerular hypertrophy and hyperfiltration [8-11]. There are no prior descriptions of this occurrence in patients with cross-fused ectopia, although this condition is known to be related to a high variability of vasculature [2, 9] which makes it possible that some degree of hemodynamic adaptation can occur in these cases.

The first line therapy in secondary FSGS is blockade of the renin angiotensin system and dietary sodium restriction. There is no evidence to support administration of glucocorticoid therapy in such cases [8, 9]. Immunosuppressive therapy should be considered if there is progression to full nephrotic syndrome in patients with foot process effacement evidenced by electronic microscopy [9]. Calcineurin inhibitors can be used as an empirical therapy in some genetic forms of the disease [8].

For primary FSGS treatment should start with corticosteroids over a minimum period of 3 months. Immunosuppressant drugs (cyclophosphamide, chlorambucil, or azathioprine) are a second line of treatment for patients that are resistant to corticotherapy, with maximum remission of symptoms occurring within 6 months. Non-specific therapies (ACEIs, angiotensin II receptor blockers, and statins) are often beneficial and should be considered [12].

This present case shows a never-before described association between cross-fused renal ectopia and FSGS. The clinical evolution contributed to our determination of the type of FSGS. Despite an initial failure to respond to steroid treatment, the patient's excellent response to cyclophosphamide characterized by complete remission of proteinuria and maintenance of renal function indicates the possibility of a primary FSGS. Distinguishing between primary and secondary FSGS was somehow difficult in this case because of the initial presentation. Few clinical findings, subnephrotic-range proteinuria, and normal serum albumin associated with kidney anomaly featuring a wide variety of vascularization point to likely secondary FSGS. Although percutaneous kidney biopsy is known to be associated with technical difficulties, it was performed successfully, allowing an accurate diagnosis, adminis-

tration of an appropriate treatment and a stable renal function for at least a year.

### Conflict of Interest

The authors declare that they have no conflict of interest.

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