CLINICAL COURSE AND RESPONSE TO TREATMENT OF FAMILIAL FORM OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS CAUSED BY MUTATION IN THE INF2 GENE – A CASE REPORT

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Introduction

Focal segmental glomerulosclerosis has become one of the most common causes of steroid-resistant nephrotic syndrome in children and adults frequently progressing to end stage renal disease (ESRD). The etiology of FSGS is not completely understood. However, recent advances in molecular genetics show that defects in the podocyte play a major role in its pathogenesis. In the recent years, many inheritable forms of FSGS caused by mutations in proteins important for podocyte function have been reported.

Objective: we are presenting two cases (mother and son) with familial form of FSGS caused by INF2 mutation, their clinical course and effect of different treatment regimens.

Clinical course

A 19-year–old patient was admitted to our Department for evaluation of 24h-proteinuria 2.2 g/dU and slightly decreased eGFR (75 ml/min). At admission he had normal serum creatinine (sCr) (108 μmol/l), urine sediment was unremarkable and blood pressure was normal. A renal biopsy revealed FSGS (figure 1 and 2). He was treated with ACE inhibitor. After one year of follow-up sCr increased to 144 μmol/l and 24h-proteinuria to 3.9 g/dU. Moreover, he had remarkable family history. At age of 20 yrs. patient s mother was also diagnosed with FSGS and had similar clinical course - from non-nephrotic to nephrotic proteinuria, gradually progressing over 10 years to ESRD. She was transplanted and until now no relapse in transplanted kidney was observed. Interestingly, she was also resistant to immunosuppressive treatment (steroids, cyclosporine).Clinical course and positive family history were indicative for inherited FSGS (particularly the INF2 gene mutation). Analysis of the INF2 gene was performed in the Molecular Biology Laboratoryof Fundacio Puigvert in Barcelona, Spain. Genetic analysis revealed that the consultant carries the sequence variant c.658G >A>C (p.E220K) in heterozygosity in exon 4 of the INF2 gene. Observed mutation was found in affected mother but not in his father who had normal renal function without proteinuria. Two years after kidney biopsy progression of kidney disease was observed (sCr 166 μmol/l, eGFR 61 ml/min, 24-h proteinuria 4.93 g/dU). Although data from the literature are scarce and sometimes contradictory we introduced a trial of cyclosporine 5 mg/kg and after 6 months observed moderate decline in proteinuria to 3.0 g/dU however accompanied with further deterioration of kidney function (SC 181 μmol/l ,eGFR 54.9 ml/min). .

Figure 1. Kidney biopsy findings. The micrograph shows a glomerulus with two segmental lesions of sclerosis with accompanying deposition of hyaline (arrow). (Periodic acid Schiff staining, magnification 63x)

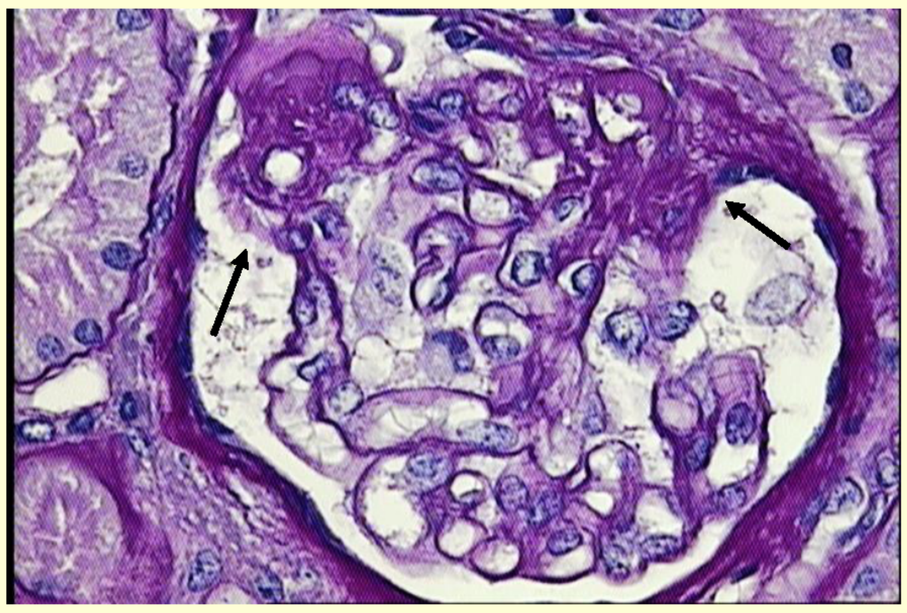


Figure 2. Kidney biopsy findings. The electron micrograph shows focal moderate effacement of irregularly shaped podocyte foot processes (arrow). Glomerular basement membranes were normal, as well as mesangium. (magnification 3500x)

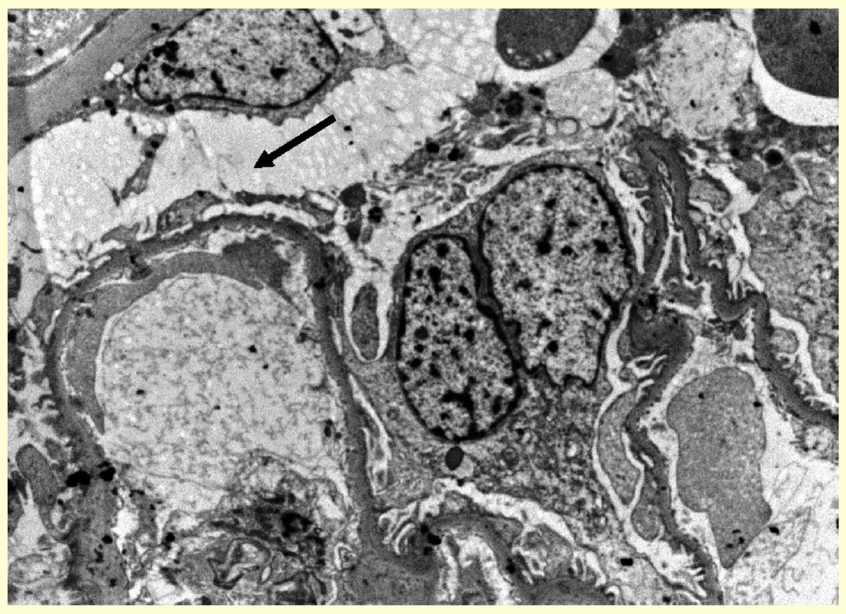
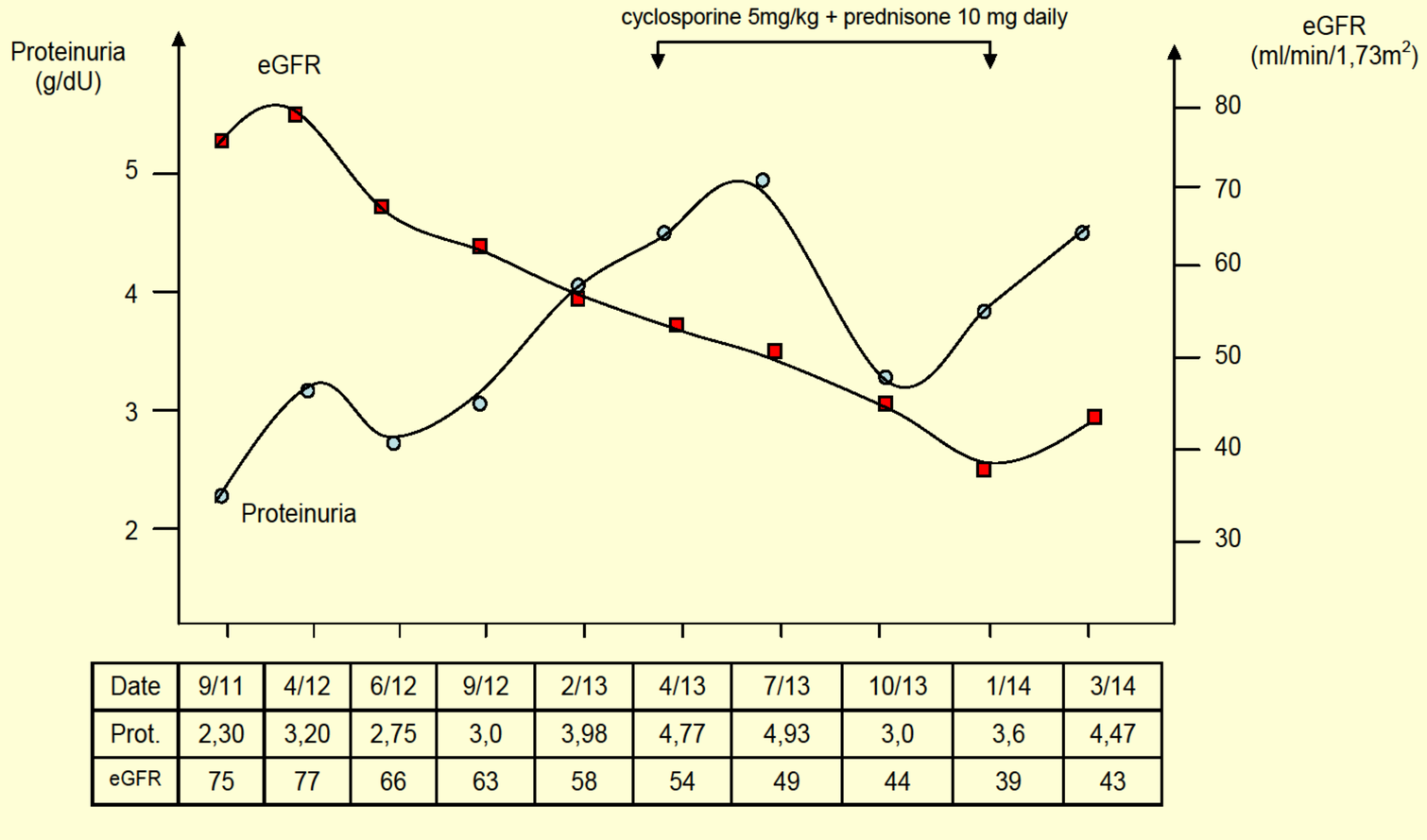


Figure 3. Clinical course and response to treatment



Date	9/11	4/12	6/12	9/12	2/13	4/13	7/13	10/13	1/14	3/14
Prot.	2,30	3,20	2,75	3,0	3,98	4,77	4,93	3,0	3,6	4,47
eGFR	75	77	66	63	58	54	49	44	39	43

Conclusion

This case report emphasized the importance of family history in renal disorders especially in young patients. Genetic screening is justified in particular group of patients where it might have crucial role in making treatment decision and avoiding of prolonged unhelpful exposure to corticosteroids or cyclophosphamide.

Finally, this case report adds evidence for potential antiproteinuric effect of cyclosporine treatment.

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