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CLINICAL COURSE OF IDIOPATHIC FSGS

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ABSTRACT Focal segmental glomerulosclerosis (FSGS) is a histopathological diagnosis. FSGS can be idiopathic (primary/unknown cause) or secondary (with underlying cause). The study includes 35 histopathological-proven cases of FSGS. Mean age was 28 years (age range: 18-45 years). There were 20 males and 15 females. About 85.7% patients presented with nephrotic syndrome, 14.2% had sub-nephrotic proteinuria. Patients with nephrotic syndrome were given prednisolone 1 mg/kg/day for 3 months, tapered over next 3 months and response was noted. Complete remission, partial remission and no response was noted in 33%, 25% and 42% patients respectively. Mean follow up of the patients was 30 months. At the end of follow up, 2 of the 14 responders to steroids & 4 of the 10 non-responders to steroids had ESRD (Creatinine Clearance < 15 ml/min). Relapsed and non responders were treated with immunosuppressants. In our study, 24-hour urinary protein bears statistically significant relation (p-value <0.05) with the development of End stage renal disease (ESRD).

KEYWORDS : ESRD, FSGS, Nephrotic syndrome

INTRODUCTION

Focal Segmental Glomerulo Sclerosis (FSGS) is a disease entity defined by histopathological findings. The classical lesion is characterized by the presence of scarring in a portion (segmental) of some (focal), but not all glomeruli.[1,2] The scar comprises increased mesangial matrix, collapsed capillaries, adhesions between tuft & bowman's capsule, hyaline deposits, mesangial hypercellularity and foam cells.[3]

FSGS can be idiopathic (primary or unknown cause) or secondary (with underlying cause). Idiopathic FSGS may be the result of a circulating factor or factors that alter the permeability of glomeruli.[4,5] Evidence supporting this comes from recurrent FSGS after renal transplantation.[6] Serum soluble urokinase receptor (supar) is one such causative factor.[7]

FSGS can occur at any age. Mean age at onset varies between 40-50 years.[8] Primary form often presents with nephrotic syndrome, characterized by proteinuria, edema, hypoalbuminemia, and hypercholesterolemia. Most individuals progress to end-stage renal disease (ESRD) within 5 to20 years.[9] Degree of proteinuria and renal dysfunction, histological findings, and the response to therapy are the factors influencing response to treatment and/or prognosis. Response is reported in terms of degree of reduction in proteinuria.[10] The aim of this study was to describe the clinical course of idiopathic FSGS with particular emphasis on response to steroids & development of ESRD.

MATERIALAND METHODS

The prospective study was undertaken for a period of two and half years from July 2010 to Dec 2012. It includes 35 histopathological-proven cases of FSGS. Cases of secondary FSGS were excluded.

Patient's particulars were recorded in detail on proformas, which includes age, gender, presenting symptoms, and detailed clinical examination and laboratory investigations. The patients were followed for a mean period of 30 months. The confidentiality of the patient's identity was maintained. Data was analyzed using the SPSS (version 20) and presented as frequency and percentage.

RESULTS

A total of 35 patients with biopsy proven FSGS were studied. Mean age of the patients was 28 years with age range of 18-45 years. There were 20 (57.14%) males and 15 (42.85%) females. About 30 (85.71%) patients presented with nephrotic syndrome & 5 (14.28%) had sub-nephrotic proteinuria. Hematuria, hypertension and azotemia were present in 14 (40%), 6 (17.14%) and 6 (17.14%) patients respectively. Mean value of 24-hour urinary protein was 7.82 +/-3.9 gm.

In the present study, 7 patients were lost to follow up. Of the remaining 28 patients, 4 had sub-nephrotic proteinuria & were treated with Angiotensin converting enzyme inhibitors (ACEI) and dietary salt restriction and all had stable serum creatinine level till the end of follow up. The remaining 24 patients who had nephrotic syndrome were given steroids (prednisolone 1 mg/kg/day) for 3 months following which dose was gradually tapered over next 3 months. Out of these, 8 (33%) showed complete remission (CR), 6 (25%) partial remission (PR) & 10 (42%) patients did not respond/ no response (NR). Complete remission was defined by 24-hour urinary protein < 200 mg. Partial remission as >50% reduction in 24-hour urinary protein & no response as <50% reduction in 24-hour urinary protein. About 3 (37.5%) out of 8 showing CR & 2 (33%) out of 6 showing PR had a relapse. Relapsed and non-responders were subsequently treated with other immunosuppressants. The presence of hypertension, hematuria, azotemia at presentation, degree of proteinuria had no statistically significant effect (p-value>0.05) on the response to steroids in the study.

Mean follow up of the patients was 30 months. At the end of follow up, 2 of the 14 responders to steroids & 4 of the 10 non-responders to steroids had ESRD (Creatinine Clearance < 15 ml/min). Age, gender, hypertension and azotemia at presentation, hematuria and response to steroid therapy have statistically insignificant relation (p-value>0.05) with the progression of FSGS to ESRD. In the present study, only degree of proteinuria bears a statistically significant relation (p-value <0.05) with the development of ESRD on univariate analysis (Table 1).

Table 1 shows the relation between 24-hour urinary protein and development of ESRD

Urinary protein (gm/day)	No ESRD	ESRD	Total	p-value
<8	0	19	19	0.000
>8	6	3	9	
Total	6	22	28	

DISCUSSION

Focal segmental glomerulosclerosis (FSGS) is a leading cause of adult nephrotic syndrome. Expert opinion guidelines recommend a trial of oral steroid therapy for at least 6 months, Cyclosporine A (CSA) if steroid-resistant disease is present and, if CSA fails, alternative therapy with other cytotoxics (cyclophosphamide, azathioprine,and chlorambucil).[9]

In our study, we followed up 28 biopsy-proven cases of FSGS for a mean duration of 30 months, and tried to see their clinical course with emphasis on response to steroid therapy & progression to ESRD.

Mean age of presentation as reported in various studies is variable. In the present study, mean age of the patients was 28 years (range = 18-45 years). SK Agarwal et al [11] had mean age of patients with FSGS as 25 years. In the study by Chun MJ et al [13], mean age of adults with FSGS was 23 years. In the present study, 57.14% patients were males and 42.85% were females. Korbet SM et al[12] had 57% male patients. Microscopic hematuria was seen in 14 (40%) patients which is comparable with Aggarwal SK et al (37%).[11]

In the present study, presentation as nephrotic syndrome was seen in 85.7% of our patients. Mean value of 24-hour urinary protein was 7.82 +/- 3.9 gm. These findings were comparable to study by Aggarwal et al. [11] Comparison in response rate to steroids in other studies is shown in Table 2.

Table 2 shows the comparison in response to steroids among different studies.

Authors	Number of cases	CR	PR	NR
Beaufalis et al (1978)[15]	38	6(15.7%)	13(34.2%)	19(50%)
Velosa et al (1983)[16]	38	4(10.5%)	10(20.3%)	24(63.1%)
SK Agarwal et al(1994)[11]	38	12(31%)	10(27%)	16(42%)
Present study (2012)	24	8(33%)	6(25%)	10(42%)

The presence of hypertension, hematuria or azotemia at presentation, degree of proteinuria, had no statistically significant effect on the response to steroids in our study (p-value>0.05) which is comparable with SK Agarwal et al.[11] Also, age, gender, hypertension at presentation, hematuria have statistically insignificant relation with the progression of FSGS to ESRD (p-value > 0.05). This stands in accordance to study by SM Korbet et al.[12]

Earlier studies have proved that factors influencing the development of ESRD in idiopathic FSGS include degree of proteinuria, renal dysfunction & response to therapy.[10] In the present study, only degree of proteinuria bears a statistically significant relation (p-value <0.05) with the development of ESRD on univariate analysis . Serum creatinine at presentation and response to steroid therapy has statistically insignificant relationship (p-value > 0.05) with the development of ESRD. Shorter follow up may be the possible reason behind it. Studies with longer follow up may show significant relation between the two.

CONCLUSIONS

A good number of patients of idiopathic FSGS showed response to steroids. We found stastically significant relation between 24-hour urinary protein and progression of FSGS to ESRD. More studies with longer follow up are advised.

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