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RESEARCH ARTICLE

FOCAL SEGMENTAL GLOMERULOSCLEROSIS AND MULTIPLE MYELOMA.

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Abstract

Focal segmental glomerulosclerosis (FSGS) is one of the most important causes of end-stage renal disease in the United States. FSGS is more prevalent in young African American patients. It is commonly associated with various conditions such as genetic abnormalities, metabolic disorders, infections, and drug abuse. FSGS is a rare disease, and its association with hematological disorders is uncommon. In this study, we are documenting a case of the FSGS due to underlying multiple myeloma. The objective of this study is to emphasize the importance of excluding hematologic disorders in the older patients before diagnosing them with idiopathic FSGS. Early diagnosis and treatment of the underlying condition responsible for the FSGS can lead to complete remission of the FSGS, thus preventing complications such as renal failure.

Introduction:-

Focal segmental glomerulosclerosis (FSGS) is one of the most important causes of end-stage renal disease in the United States. FSGS is more prevalent in young African American patients [1]. FSGS is responsible for nephrotic syndrome in 40% of adults [2]. Common etiologies associated with FSGS are genetic abnormalities, metabolic disorders, infections and drug abuse [3]. However, FSGS has rarely been reported in association with hematologic malignancies such as lymphoproliferative, myeloproliferative and plasma cell disorders. In this study, we are documenting a case of FSGS in association with multiple myeloma in a 55-year-old male Asian patient.

Case Presentation:-

A 55-year-old male Asian patient was referred to the nephrology department by his primary care physician for the evaluation of incidental proteinuria. The patient experienced no associated symptoms such as fever, weight/appetite changes, cough, or any antecedent infection. His past medical, surgical and family history was unremarkable, and he had no modifiable or non-modifiable risk factors. He never smoked cigarettes or used any illicit drugs. The physical examination revealed a blood pressure of 170/100 mm Hg and +2 bilateral pitting edema in his lower limbs. The rest of the systemic examination was unremarkable.

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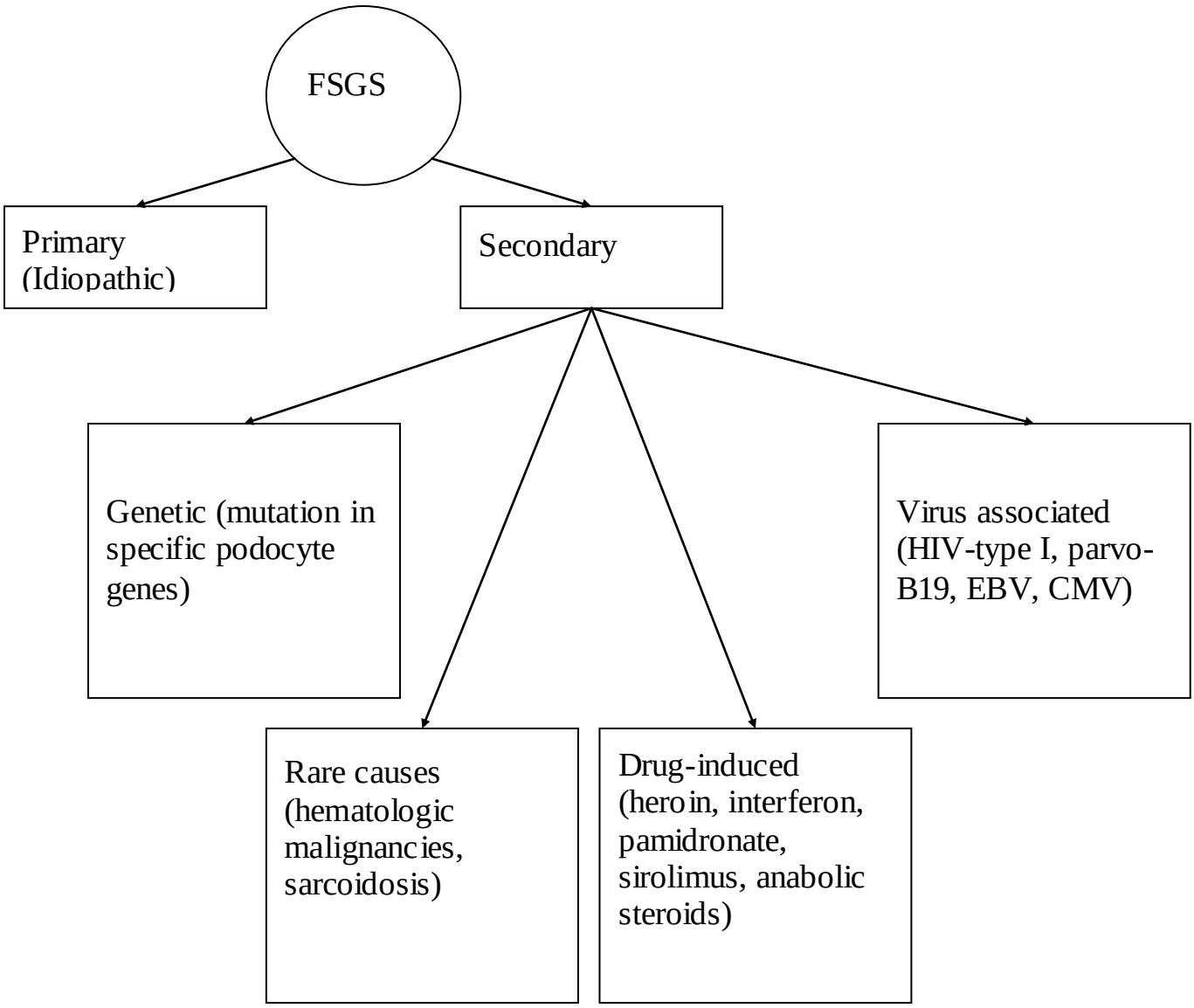
The patient was asked to follow-up with his urine and blood tests. Laboratory investigations revealed creatinine 1.3 mg/dl, blood urea nitrogen (BUN) 20 mg/dl and proteinuria 2400 mg/24 hours. The patient was admitted to the hospital for additional investigations. The patient was administered angiotensin-converting enzyme inhibitor (ACEI) to control his high blood pressure. Additionally, he was scheduled for a renal biopsy. The patient was diagnosed with FSGS based on his histopathological findings. At his follow-up visit one month later, the patient's high blood pressure was controlled. However, proteinuria and serum creatinine were slightly increased.

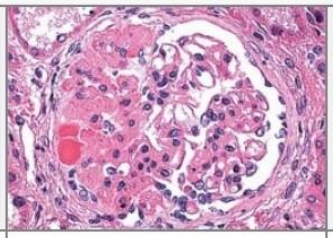
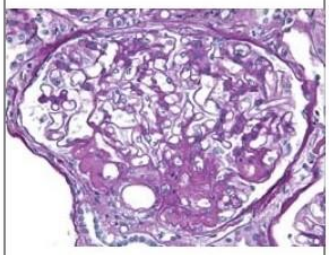
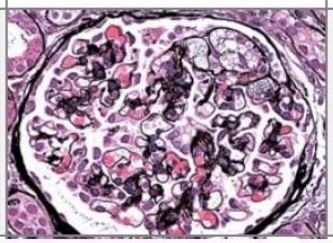
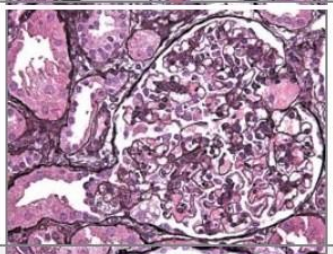
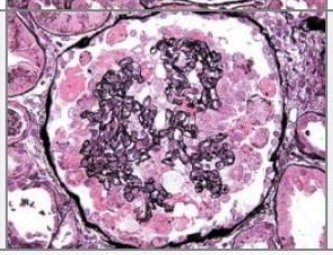
Seven months after his last visit, the patient visited the hospital again for a complaint of back pain for the last one month. The pain was constant, dull, 6/10 in intensity, aggravated by movement and occurs at night. An X-ray of the spine revealed lytic lesions on the lumbar spine. Laboratory investigations revealed serum calcium levels of 14.5 mg/dl (calcium normal levels 8.5-12.2 mg/dl). Considering the probability of multiple myeloma, a urine protein electrophoresis was ordered and the patient was scheduled for a bone marrow aspiration and biopsy. The electrophoresis revealed light chains in immunofixation of urine. Bone marrow aspiration and biopsy revealed more than 35% kappa positive plasma cells. Based on the clinical features, pathological findings, and investigations, the patient was diagnosed with multiple myeloma. The patient was started on thalidomide, dexamethasone, and pamidronate. After two weeks of his treatment, the calcium level came down to normal and the patient felt a considerable improvement in his back pain as well. In the following visit, his proteinuria had also decreased and repeated biopsy of the kidney showed resolution of the FSGS.

Discussion:-

FSGS is a type of glomerular disease and is characterized by sclerosis in small sections of each glomerulus. It is one of the most important causes of end-stage renal disease. FSGS is associated with various etiologies, which are summarized below in figure *1*.



Histologically, FSGS is defined as the segmental obliteration of glomerular capillaries by the extracellular matrix [4-5]. The histologic variants of the FSGS are described in figure *2*[6].

Histologic Subtype	Glomerular Lesion	Defining Features	Associations	Clinical Features
NOS		The usual generic form of FSGS. FSGS(NOS) does not meet defining criteria for any other variant. Foot-process effacement is variable.	Primary or secondary (including genetic forms and other diverse secondary causes). Cross-sectional studies suggest this is the most common subtype. Other variants can evolve into FSGS (NOS) over time.	May present with the nephrotic syndrome or subnephrotic proteinuria.
Perihilar		Perihilar hyalinosis and sclerosis involving the majority of glomeruli with segmental lesions. Perihilar lesions are located at the glomerular vascular pole. In adaptive FSGS, there is usually glomerular hypertrophy (glomerulomegaly). Foot-process effacement is relatively mild and focal, which probably reflects the heterogeneous adaptive responses of glomeruli.	Common in adaptive FSGS associated with obesity, elevated lean body mass, reflux nephropathy, hypertensive nephrosclerosis, sickle cell anemia, and renal agenesis. Predisposition for vascular pole is probably due to normally increased filtration pressures at the proximal afferent end of glomerular capillary bed, which are heightened under conditions of compensatory demand and vasodilatation of the afferent arteriole.	In adaptive FSGS, patients are more likely to present with subnephrotic proteinuria and normal serum albumin levels.
Cellular		Expansile segmental lesion with endocapillary hypercellularity, often including foam cells and infiltrating leukocytes, with variable glomerular epithelial-cell hyperplasia. There is usually severe foot-process effacement.	Usually primary, but also seen in a variety of secondary forms. This is the least common variant. It is thought to represent an early stage in the evolution of sclerotic lesions.	Usually presents with the nephrotic syndrome.
Tip		Segmental lesion involving the tubular pole, with either adhesion to tubular outlet or confluence of podocytes and tubular epithelial cells. Compared with other variants, it has the least tubular atrophy and interstitial fibrosis. There is usually severe foot-process effacement.	Usually primary. Probably mediated by physical stresses on the paratubular segment owing to the convergence of protein-rich filtrate on the tubular pole, causing shear stress and possible prolapse.	Usually presents with abrupt onset of the nephrotic syndrome. More common in white race. Best prognosis, with highest rate of responsivity to glucocorticoids and lowest risk of progression.
Collapse		Implosive glomerular-tuft collapse with hypertrophy and hyperplasia of the overlying visceral epithelial cells. Hyperplastic glomerular epithelial cells may fill the urinary space, resembling crescents. Severe tubular injury and tubular microcysts are common. There is usually severe foot-process effacement.	Primary or secondary to Viruses: HIV-1, parvovirus B19, SV40, EBV, CMV, hemophagocytic syndrome Drugs: pamidronate and interferon Vaso-occlusive disease: atheroemboli, calcineurin inhibitor nephrotoxicity, and chronic allograft nephropathy	Most aggressive variant of primary FSGS with black racial predominance and severe nephrotic syndrome. Worst prognosis, with poor responsivity to glucocorticoids and rapid course to renal failure.

In our case report, the patient was diagnosed with the FSGS based on his clinical and histopathological findings. The patient was diagnosed with tip variant FSGS, which has a good prognosis and higher remission rates compared with other variants [7]. FSGS is commonly seen in young African Americans with conditions like genetic abnormalities, metabolic disorders, infections, or drug abuse. However, the association of the FSGS with hematologic malignancies is rarely seen especially in the older Asian population [2]. Few studies have documented that the FSGS and hematologic malignancies are epidemiological and temporally linked.

Shah S et al. in his study reported a case of collapsing FSGS in association with multiple myeloma that underwent partial remission following the treatment for the underlying disease [8]. Similarly, in another retrospective study by Dingli D et al. identified 13 patients with the FSGS and a monoclonal plasma cell disorder. Out of 13 patients, four patients had multiple myeloma and nine patients had monoclonal gammopathy of undetermined significance.

Patients treated for multiple myeloma experienced improvement in their renal lesion, and the latter relapsed when the multiple myeloma relapsed [3]. In another study by Calvo JV et al. they discovered an association between FSGS and non-Hodgkin's lymphoma [9].Similarly, one study published by Ashrafi F et al. reported a case report of FSGS who developed the manifestation of amyloidosis in his course of disease. Following urine protein electrophoresis and bone marrow study confirmed the diagnosis of multiple myeloma [10].

The authors of the above-mentioned studies concluded that before diagnosing patients with Idiopathic FSGS, especially adults and the elderly, hematologic disorders (especially plasma cell disorders) must be excluded. The occurrence of these two conditions may not be as a result of chance [3]. In our patient, after initiation of treatment for multiple myeloma, his proteinuria decreased and FSGS resolved afterward. Thus, early diagnosis and treatment of the underlying disease responsible for the FSGS can reduce the chances of the renal complications due to FSGS.

Conclusion:-

FSGS is a rare disease, and its association with hematological disorders is rarer. In this study, we want to highlight that in older patients, hematologic disorders must be ruled out before diagnosing them with idiopathic FSGS. This is because early diagnosis and treatment of the underlying condition responsible for FSGS can completely resolve FSGS and prevent its complications.

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