

A RARE CASE REPORT OF KARYOMEGALIC INTERSTITIAL NEPHRITIS WITH FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS

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Implication for health policy/practice/research/medical education:

The case (40 years, female) of karyomegalic interstitial nephritis (KIN) with focal and segmental glomerulosclerosis (FSGS) is rare. It was reported, which was second case in Indian subcontinent after doing series of tests with examination.

Article Info

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Abstract

Karyomegalic interstitial nephritis (KIN) is a rare form of progressive chronic interstitial nephritis. We present a case of KIN in an adult, who also have nephrotic syndrome. Only one case has been reported of KIN associated with FSGS in the literature. Our case also exhibited similar condition with focal and segmental glomerulosclerosis with KIN, which was second association reported from India.

Key words: Rare association, Karyomegalic interstitial nephritis (KIN), Focal and segmental glomerulosclerosis (FSGS).

Introduction:

Karyomegalic interstitial nephritis (KIN) is uncommon cause of chronic interstitial nephritis. It was first described in 1974 [1]. The term of "KIN" was introduced by Mihatsch *et al* [2] in 1979 who described three cases of systemic karyomegaly associated with chronic interstitial nephritis. The prevalence of this disease is less than 1% [3]. The pathogenesis of KIN is unclear. The disease has no known treatment. More recently, the disease has been linked to mutations in the FAN1 (FANCD2/FANCI-Associated Nuclease 1) gene, a gene involved in the DNA damage response pathway, particularly in the kidney, shedding new lights on the potential link between defective DNA repair and chronic kidney disease progression. Extrarenal features are absent or mild, consisting of recurrent upper respiratory tract infections and abnormal liver function tests. The case under discussion has associated glomerulopathy causing nephrotic syndrome and altered renal function, which is showing gradual deterioration. Normal renal function at the time of diagnosis is known and in one large series published by Bhandari *et al*. [4] one out of the six cases presented with microhematuria and normal renal function.

Case Report:

A 40 year-old woman presented with generalized edema. On evaluation she was found to have nephrotic proteinuria and impaired renal function. She had no familial history of nephropathy, no exposure to nephrotoxic medications, heavy metals, environmental or agricultural toxins, and no consumption of Chinese herbal medicine. Physical examination was unremarkable. Serum creatinine was at 1.6 mg/dl. Serum electrolytes, calcium levels were normal. Hemoglobin level was 12 g/dl (normal range 12-15 g/dl). The platelet and leukocyte counts were normal. Liver functions revealed hypoalbuminemia of 2.6 g/dl. Her liver enzymes were within normal limits. Urinalysis showed proteinuria (+++). No glucosuria was detected. Immunological tests were negative. Tests for human immunodeficiency and hepatitis B and C viruses were negative. Ultrasound revealed mild bulky kidneys with normal echo texture.

First Renal biopsy was done outside, and was reported as focal and segmental glomerulosclerosis with moderate acute tubular necrosis. So she was on steroid for 1 year and Mofetil since 6 months. However, there was no response even after 6 months. Hence a repeat (Second) Renal biopsy was done. Biopsy showed 12 glomeruli, 02 of whom showed segmental sclerosis (Figures 1 and 2). Basement membrane and cellularity were normal in the uninvolved glomeruli. Tubular epithelial cells revealed changes diffusely. The lining cells in many, revealed enlarged nuclei with lobulated appearance. These cells are larger than the normal tubular epithelial cells (Figures 3). There was chromatin clumping giving a hyperchromatic appearance. Mitoses are sparse. There is interstitial edema and distalization of proximal tubules with acute tubular necrosis (ATN). (Figure 4). Serum viral load was negative. Immunofluorescence did not reveal any significant immune deposits (Cohort-1).

Discussion:

KIN is a rare disorder characterized by enlarged tubular epithelial cell nuclei and chronic interstitial nephritis. These patients present with renal impairment and rarely with extra renal manifestations. Histologically, presence of interstitial nephritis along with karyomegaly in the tubular epithelial cells is characteristic of this disorder. Karyomegalic cells have been identified in various other tissues like astrocytes, Schwann cells, intestinal smooth muscle and bile duct epithelium, but no clinical significance has been identified with these changes. Sclare [5] described pneumopathy, characterized by pulmonary karyomegalic cells at autopsy. Transient elevation of liver enzymes is described [6]. Pathogenesis of this disease is unclear and controversial. Toxins or viral infections are suggested as cause of this disorder [2]. Exposure to herbs, ochratoxins is also implicated.

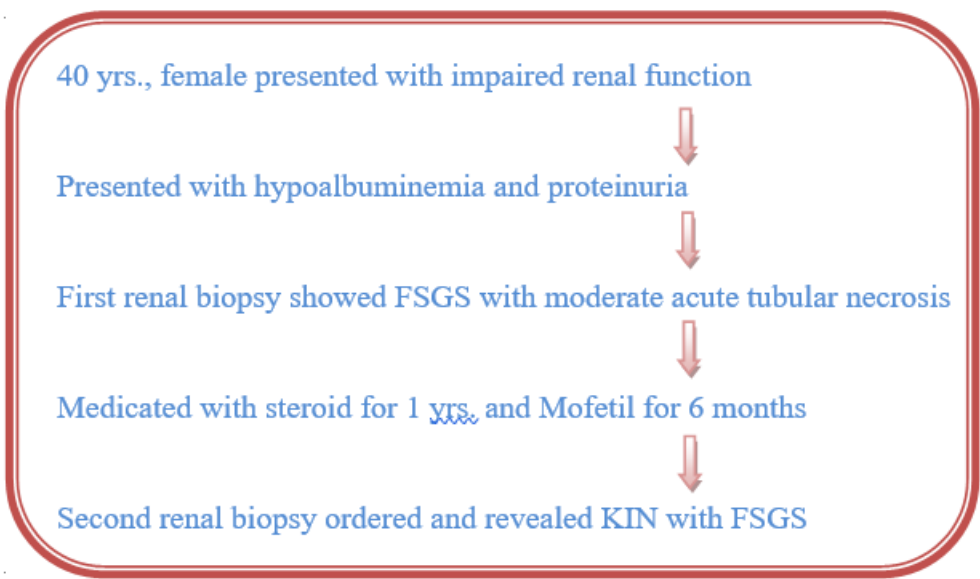
McCulloch *et al.*, reported KIN in three adolescent patients treated with ifosfamide for Ewing's sarcoma [7]. All patients progressed to renal failure. A familial clustering is known and frequency of human leukocyte antigen (HLA)-A9 and HLA-B35 haplotypes suggest the possibility of genetic susceptibility [4]. Another genetic defect on chromosome 6, linked to major histocompatibility complex locus is also suspected [8]. Abnormal deoxyribonucleic acid ploidy and distribution with high ploidy values is described. Exome sequencing study by Zhou *et al.*, identified mutations in FAN1 as cause of KIN [9]. Moreover, the disease has been linked to mutation in this FAN1 (FANCD2/FANCI-Associated Nuclease 1) gene in the progression of this disease involving defective DNA repair [10]. The morphological alterations in renal epithelial cells are thought to be the initial damage caused by either chemicals or viral agents, which in susceptible individuals lead to disruption of cells. Advanced glomerulopathy as initial change is unlikely. Immunofluorescence and histological findings support focal and segmental glomerulosclerosis (FSGS). No positive family history or drug history and exposure to toxins are implicated and this case probably represents a sporadic occurrence. KIN is an increasingly recognized entity although is under diagnosed. It is important to diagnose this entity as it is a progressive disorder leading to irreversible renal damage. First such case was reported in 8 year old male child [11].

The case under discussion has both glomerular and tubulo-interstitial pathology. Common etiological factors for both these lesions are toxins and drugs, patient on repeated questioning denied any history of drug or herbal medicine intake. Heredo-familial occurrence is described both in FSGS and KIN. There is no history of renal disease in the Spoendlin *et al.*, [8] reported four patients who were asymptomatic initially, but later experienced progressive renal failure.

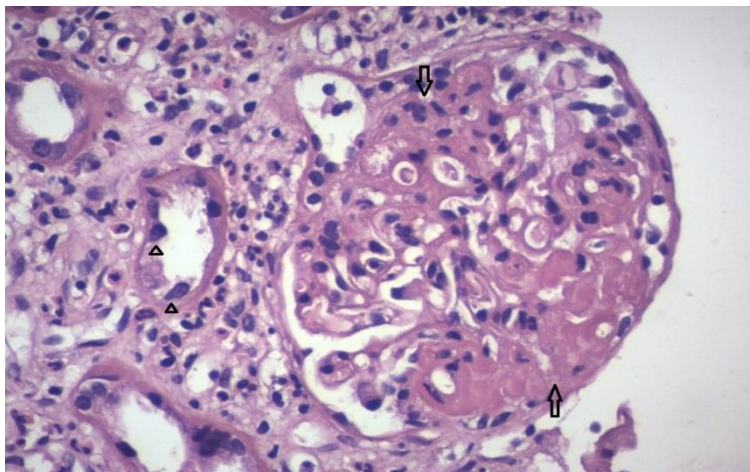
Conclusion:

We present a rare case of KIN who initially presented with normal renal parameters; interestingly, this patient's clinical presentation was of nephrotic syndrome whose biopsy also revealed FSGS. Only one

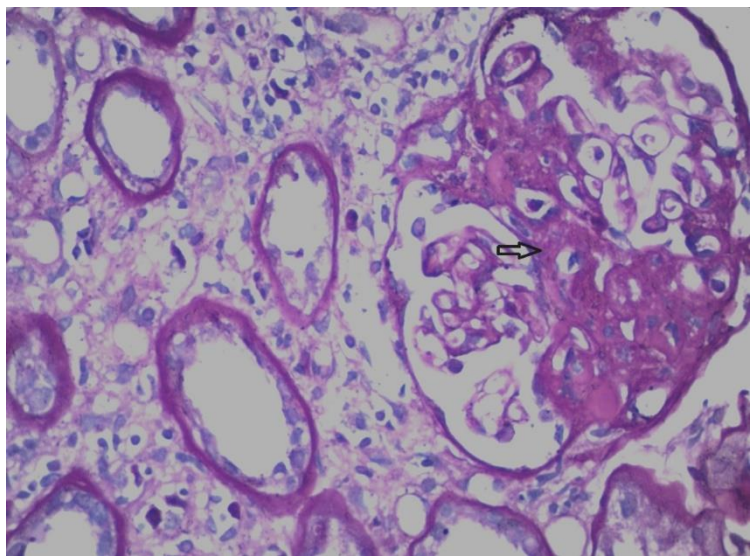
case of KIN and FSGS is described in the literature earlier [10] and this is a second report from Indian subcontinent.



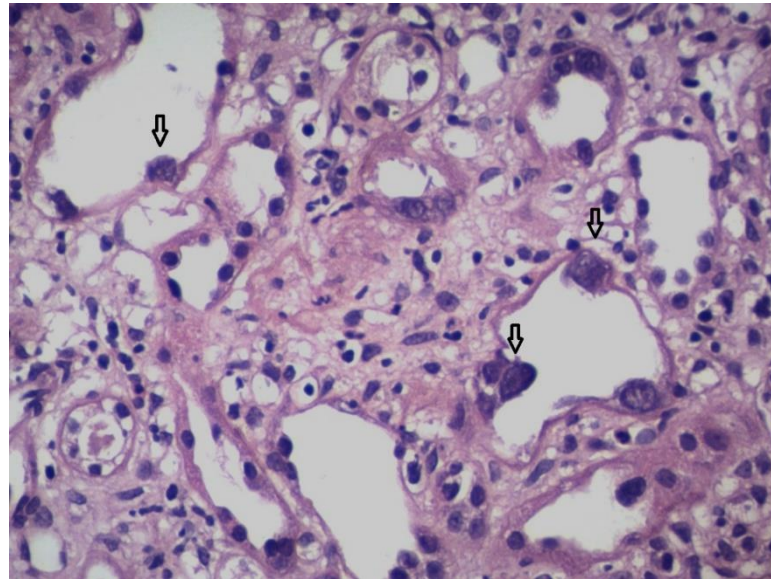
Cohort -1: Depicting progressed renal anomaly



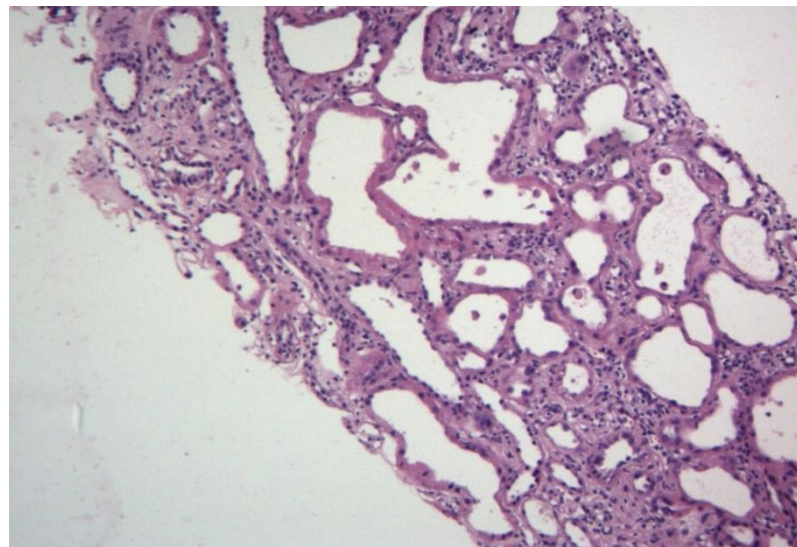
1.FSGS (arrow) and Karyomegalic cells (arrowhead), H&E stain x400.



2.FSGS (arrow) PAS stain x400.



3. Karyomegalic cells (arrow), H&E stain x400.



4. Tubules with changes of ATN, x100 H&E stain

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author. The patient gave the consent to publish as a case report.

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