Case Report

Karyomegalic tubulointerstitial nephritis with primary focal segmental glomerulosclerosis in a young female: A rare form of steroid-nonresponsive nephrotic syndrome

Rajesh Kumar, Amit Kumar Singh, Gian Prakash, Rajan Duggal[1]

Department of Nephrology and Renal Transplant Medicine, V.M.M.C. and Safdarjung Hospital, New Delhi, [1]NephroCORe Diagnostics, Gurugram, Haryana, India

Abstract Karyomegalic interstitial nephropathy (KIN) is a rare form of chronic tubulointerstitial nephritis initially described as a familial nephropathy in adults. We present a case of KIN with focal segmental glomerulosclerosis in a 15-year-old young female who became late nonresponder and resistant to steroid therapy. To our knowledge, only one case has been reported in literature.

Keywords: Focal segmental glomerulosclerosis, karyomegalic interstitial nephropathy, nephrotic syndrome

Address for correspondence: Dr. Amit Kumar Singh, Department of Nephrology and Renal Transplant Medicine, VMMC and Safdarjung Hospital, New Delhi, India.
E-mail: drtakhele.md@gmail.com
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INTRODUCTION

Karyomegalic interstitial nephropathy (KIN) was first described and named in 1979 by Mihatsch *et al.*[1] The prevalence of the disease is <1%.[2] The disease is characterized by atypical tubular epithelial cells, with large hyperchromatic nuclei having irregular outlines.[3] The disorder has no known treatment. It presents in the 2nd and 3rd decades of life with progressive renal impairment.

CASE REPORT

A 15 -year-old girl presented with a history of generalized body swelling and facial puffiness. There was no history of consanguineous marriage in parents, birth defects, or complicated delivery. She is having two younger siblings without any significant medical history.

Her baseline investigations included hemoglobin of 14.3 g/dl, total leukocyte count of 9.35 × 10^3/μL, platelet count of 246,000 per microlitre, blood urea of 23 mg/dl, and serum creatinine of 0.64 mg/dl; 24-h urinary protein was 5.5 gm; urine showed 4+ protein, normal C3 and C4 levels, and normal thyroid profile but deranged lipid profi le; antinuclear antibody and viral markers were negative; and immunoglobulin (Ig) IgG level was reduced and IgA was normal. On evaluation, she was diagnosed as nephritic syndrome and was started on steroid therapy. The patient achieved partial remission in 8 weeks of full dose of steroid but relapsed on tapering the dose of steroid with heavy proteinuria, hypoalbuminemia, pleural effusion, and diuretic-resistant edema. Even after giving two cycles of steroid, she did not respond, and her renal function started deteriorating.

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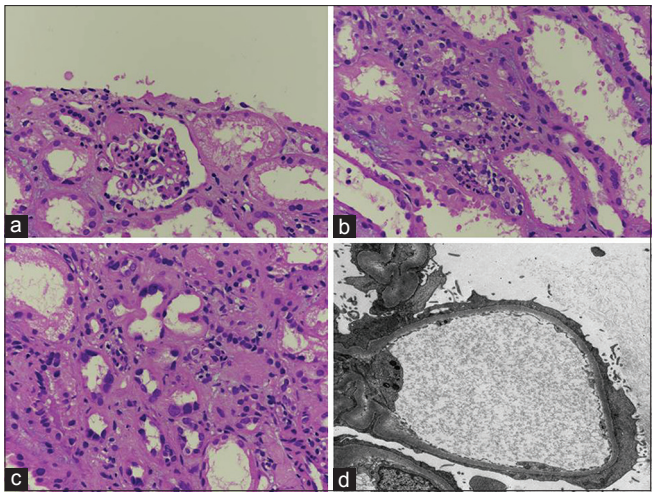

Figure 1: (a) Segmental sclerotic lesion in one glomerulus associated with hyalinosis, diffuse acute tubular necrosis, and interstitial infiltrate (H and E, ×400). (b) The interstitial infiltrate is composed of lymphocytes with few scattered neutrophils and an occasional eosinophil (H and E, ×400). (c) Majority of the tubular nuclei are enlarged, few with conspicuous nucleoli (H and E, ×400). (d) Diffuse podocytic foot process effacement indicating primary podocytopathy (electron microscopy, ×3000)

After taking informed consent, kidney biopsy was performed, and microphotograph panel showed [Figure 1] segmental sclerosis lesion in one glomerulus with associated hyalinosis [Figure 1a; hematoxylin and eosin (H and E) ×400]; diffuse acute tubular injury with associated interstitial infiltrate is seen. The interstitial infiltrate was composed of lymphocytes with few scattered neutrophils and an occasional eosinophil [Figure 1b; H and E ×400]; majority of the tubular nuclei were enlarged, few with conspicuous nucleoli [Figure 1c; H and E ×400]; ultrastructural examination revealed diffuse podocytic foot process effacement indicating primary podocytopathy (electron microscopy, ×3000).

The third trial of steroid therapy was started with 1 mg/kg of body weight, but proteinuria increased from 10 to 17 g/24 h. The patient was then switched to tacrolimus and minimum dose of steroid. She responded to the treatment, and proteinuria after 10 days of starting tacrolimus reached to 7 g/24 h [Table 1]. The patient is stable at present and in close follow-up.

Table 1: Laboratory investigations

Date	Urine protein g/24 h	Blood urea/creatinine
April 9, 2018	5.50	23/0.64
June 13, 2018	2.84	18/0.2
August 16, 2018	6.10	16/0.4
September 6, 2018	2.98	28/0.6
January 7, 2018	10.0	51/1.23
January 24, 2019	17.7	139/1.6
February 11, 2019	7.0	120/1.3

DISCUSSION

Karyomegalic tubulointerstitial nephritis is a rare form of familial chronic tubulointerstitial nephritis. The disease usually presents with normal renal function initially but with proteinuria and may be associated with microhematuria. So far, very few cases have been reported in literature. The classical finding of this disorder is tubulointerstitial nephritis and karyomegaly of tubular epithelium, which is due to increased ploidy of the cells, most likely secondary to cell cycle arrest.[4] The pathogenesis of the disease is not well established. Various toxic substances including medicines, herbs, and viral infections are supposed to be the cause of this disorder. Some cases of KIN are also reported in patients who were treated with ifosfamide.[5,6] The disorder is usually not associated with extrarenal involvement.

An exome sequencing study by Zhou *et al*. identified mutation in FAN1 as a cause of KIN.[7] Genetic defects on MHC locus on chromosome 6 are suspected.[8] Familial clustering is known, and the frequency of HLA A9 and HLA B35 haplotypes suggests the possibility of genetic susceptibility. There is only one case which described the association of KIN and primary focal segmental glomerulosclerosis (FSGS), which was reported by Radha *et al*.[9]

Our patient presented with nephritic syndrome and microscopic hematuria. All predisposing factors linked to the disorder were excluded. There was no history suggestive of renal disease in any family member. There was no history of chronic medication or concurrent infection.

The patient presented with both glomerular and tubulointerstitial involvement, initially with normal renal function but deteriorated later on. She responded to steroid partially, but, later on, became resistant to steroid therapy. She was started on tacrolimus 0.05 mg/kg twice daily. She responded to the treatment, and her proteinuria decreased significantly. Currently, the patient is stable and in regular follow-up.

CONCLUSION

Karyomegalic tubulointerstitial nephritis in association with primary FSGS is a rare entity, not described in literature. There is no clear pathogenesis and treatment available for this disorder. Our patient had a steroid-dependent nephritic syndrome and became nonresponsive later on. She was switched to tacrolimus with a minimum dose of steroid. The patient responded well to tacrolimus and improved clinically. It suggests that calcineurin inhibitor may help in treating such cases.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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