Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

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To cite this article: Pallav Gupta, D. S. Rana, A. K. Bhalla, Ashwini Gupta, Manish Malik, Anurag Gupta & Vinant Bhargava (2014) Renal failure due to granulomatous interstitial nephritis in native and allograft renal biopsies: experience from a tertiary care hospital, Renal Failure, 36:9, 1468-1470, DOI: 10.3109/0886022X.2014.950975

To link to this article: https://doi.org/10.3109/0886022X.2014.950975

Published online: 26 Aug 2014.

RENAL FAILURE

http://informahealthcare.com/rnf
ISSN: 0886-022X (print), 1525-6049 (electronic)

Ren Fail, 2014; 36(9): 1468–1470
 DOI: 10.3109/0886022X.2014.950975

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BRIEF REPORT

Renal failure due to granulomatous interstitial nephritis in native and allograft renal biopsies: experience from a tertiary care hospital

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Abstract

Granulomatous interstitial nephritis is a rare cause of renal failure in both native and allograft renal biopsies. Drugs and sarcoidosis are the commonest causes of granulomatous interstitial nephritis as reported in Western countries. Unlike the west, tuberculosis is the commonest cause of granulomatous interstitial nephritis in Indian subcontinent. The etiological factors, clinical course, glomerular and tubulointerstitial changes associated with granulomatous interstitial nephritis have been analyzed in the present study along with the outcome in patients with granulomatous interstitial nephritis.

Keywords

Allograft, granulomatous, interstitial, native, nephritis, tuberculosis

History

Received 5 May 2014
Revised 23 July 2014
Accepted 30 July 2014
Published online 21 August 2014

Introduction

Granulomatous interstitial nephritis is a rare cause of renal failure. It is an uncommon histological diagnosis and is seen in <1% of both native and allograft renal biopsies.[1–3] Common etiologies associated with this condition include drugs, infections, immunologic disorders, foreign body reaction and idiopathic. Of these drugs are most common cause accounting for about 38% cases.[1] Limited studies are published in literature on this subject including both native and allograft renal biopsies.[4–8]

Materials and methods

Records of all the patients who underwent renal biopsy between (January 2009 and December 2013) were reviewed. Sixteen patients with a biopsy-proven diagnosis of granulomatous interstitial nephritis (14 native biopsies and 2 allograft renal biopsies) were included in the study. Clinical and biochemical records were reviewed and histopathology slides were re-examined. Histopathology slides were evaluated for presence of epithelioid cell granuloma, giant cells, necrosis, glomerular pathology (including crescents), eosinophil, and Schumann and asteroid bodies. Extent of tubular atrophy and interstitial fibrosis was also assessed in all these cases and was graded as mild (up to 25%), moderate (26–50%) and severe (>50%). Zeihl–Neelsen stain for acid fast bacilli was performed in all the cases.

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Results

A total of 1484 renal biopsies were performed between January 2009 and December 2013 including both native and allograft renal biopsies. Granulomatous interstitial nephritis was diagnosed in 16 cases (14 in native biopsies, two in allograft renal biopsies) accounting for 1.08% of total renal biopsies. There were 10 males and 6 females. Mean age of the patients was 34 ± 3.97 years with age range from 12 to 68 years. Majority of the patients presented with advanced renal failure with mean serum creatinine of 6.25 ± 3.53 mg/dL at presentation. Twenty-four hours urine protein ranged from 0.327 g to 3.5 g. Nine of the sixteen cases (9/16) were confirmed to have tuberculosis (Table 1). Of the remaining seven patients, two had granulomatous interstitial nephritis associated with pauci-immune crescentic glomerulonephritis. There were two cases of drug-induced granulomatous interstitial nephritis. Both patients had history of non-steroidal anti-inflammatory drug (NSAID) intake. *Klebsiella pneumonia*-associated urinary tract infection was seen in one patient. Remaining two patients had idiopathic granulomatous tubulointerstitial nephritis. Serum calcium levels were performed in 10 patients (all within normal range) and angiotensin-converting enzyme (ACE) levels were done in four patients (normal in all four cases). Patient data are summarized in Table 1. Two of the cases (2/16) of granulomatous interstitial nephritis were seen in renal allograft biopsies. One of these patients had evidence of miliary tuberculosis (confirmed by computed tomography (CT) thorax and positive QuantiFERON-TB gold test). The other patient had evidence of urinary tract infection secondary to *K. pneumoniae* (confirmed by urine culture).

Table 1. Demographic, clinical and pathological details of patients with granulomatous interstitial nephritis.

Age	Sex	S.Creatinine mg/dL	Diagnosis/confirmatory test	Interstitial fibrosis/tubular atrophy	Treatment	Follow-up	Outcome creatinine mg/dL
32	f	3.89	Tuberculosis/AFB positive mediastinal lymph node	Mild	Anti-tubercular	9 months	2.5
57	m	6.70	Drug	Mild	Steroids	5 months	2.3
30[a]	m	2.49	Klebsiella/urine Culture+	Mild	Antibiotics	7 months	1.4
35[a]	M	1.90	Tuberculosis/QuantiFERON-TB Gold+	Moderate	Anti-tubercular	8 months	Transplant
22	m	15.2	Tuberculosis/QuantiFERON-TB Gold+	Mild	Anti-tubercular	–	No follow-up
37	M	11.2	Tuberculosis/QuantiFERON-TB Gold+	Moderate	Anti-tubercular	18 months	Dialysis dependent
12	F	7.30	Tuberculosis/QuantiFERON-TB Gold+	Mild	Anti-tubercular	18 months	1.3
21	F	7.60	Tuberculosis/QuantiFERON-TB Gold++	Moderate	Anti-tubercular	14 months	Dialysis dependent
34	F	4.20	Tuberculosis/QuantiFERON-TB Gold+	Mild	Anti-tubercular	30 months	2.6
27	f	5.45	Tuberculosis/QuantiFERON-TB Gold+	Mild	Anti-tubercular	28 months	2.7
45	M	4.10	Drug	Mild	Steroids	12 months	1.4
20	m	5.40	Idiopathic	Mild	Steroids	9 months	1.3
29	m	4.80	Idiopathic	Mild	Steroids	11 months	1.4
39	f	9.70	Tuberculosis/QuantiFERON-TB gold+	Mild	Anti-tubercular	–	No follow-up
35	m	7.70	Pauci-immune GN	Mild	Steroids, cyclophosphamide	–	No follow-up
68	m	2.40	Pauci-immune GN	Mild	Steroids, cyclophosphamide	–	No follow-up

Notes: S.creatinine, serum creatinine; Pauci-immune GN, pauci-immune glomerulonephritis.
[a]Renal allograft recipients.

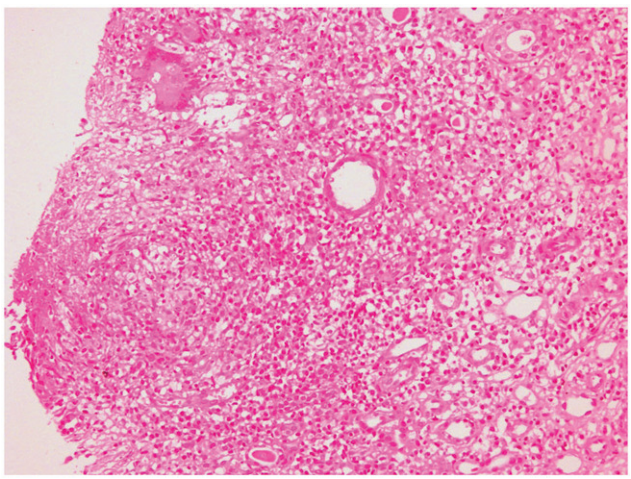

Figure 1. Renal biopsy showing interstitial epithelioid cell granuloma, Langhan's giant cell and focal necrosis along with atrophic tubules (Hematoxylin and eosin, ×200).

Histopathology

All the 16 cases showed presence of epithelioid cell granulomas (Figure 1). Necrosis was associated with granuloma in seven cases. Langhan's giant cells were seen in nine cases (all nine cases with tubercular etiology), foreign body type of giant cells in two cases and giant cells were absent in five cases. Zeihl–Neelsen stain for acid fast bacilli was negative in all the cases. Acute tubular necrosis like change was seen in nine patients. Two cases had pauci-immune crescentic glomerulonephritis [cytoplasmic anti-neutrophil cytoplasmic antibody (c-ANCA) + in one case, perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA)+] in one case. One of the patients with tuberculous granulomatous interstitial nephritis had focal segmental glomerulosclerosis with 24-h urine protein of 3.5 g. There were no significant glomerular changes in remaining cases.

All but three cases showed mild tubular atrophy and interstitial fibrosis. Only three cases had moderate tubular atrophy and interstitial fibrosis (two native and one allograft biopsy).

Treatment

All eight patients diagnosed with tubercular granulomatous interstitial nephritis on native renal biopsies received standard anti-tubercular treatment with isoniazid, rifampicin, pyrazinamide and ethambutol. Renal transplant patient with tubercular granulomatous interstitial nephritis received ofloxacin instead of rifampicin as a part of anti-tubercular treatment. Patients with drug-induced granulomatous interstitial nephritis and idiopathic granulomatous tubulointerstitial nephritis were treated with steroids. Patients having pauci-immune crescentic glomerulonephritis with granulomatous tubulointerstitial nephritis received steroids along with cyclophosphamide. Patient with Klebsiella associated urinary tract infection received antibiotics. Twelve of the 16 patients also received one or more sessions of hemodialysis initially (12/16).

Follow-up

Of the 16 patients, follow-up was available in 12 patients. The follow-up duration ranged from 5 months to 30 months. Two of these 12 patients progressed to end stage-renal disease and were dialysis dependent at last follow-up (14 months and 18 months after being diagnosed as tubercular granulomatous interstitial nephritis). One of the renal transplant patients with tubercular granulomatous interstitial nephritis became dialysis dependent and underwent second renal transplant 8 months following diagnosis of granulomatous interstitial nephritis. The follow-up creatinine of the remaining nine patients ranged from 1.3 to 2.7 mg/dL, mean 1.87 ± 0.62 mg/dL.

Discussion

Drugs, infection and sarcoidosis have been identified as the common causes of granulomatous interstitial nephritis in Western literature. NSAID is commonly associated with

drug-induced granulomatous interstitial nephritis. Drugs like allopurinol used in treatment of gout have been shown to cause granulomatous interstitial nephritis.[9] In Indian subcontinent, tuberculosis has been reported as the commonest cause of granulomatous interstitial nephritis in native renal biopsies.[10] Our study is in agreement with the prior study from India. Majority of the patients in our series presented with advanced renal failure with minimal proteinuria as described in the study by Joss et al.[11] Chapagain et al.[12] have described 25 cases of tuberculous tubulointerstitial nephritis of which 17 patients had biopsy proven granulomatous interstitial nephritis. Majority of the patients in this series were of Indian origin. Nine of these patients required renal replacement therapy at presentation and four patients required renal replacement therapy subsequently. Five of these patients had to undergo renal transplantation at follow-up. Even though large number of patients in our study required dialysis initially as a result of advanced renal failure only two patients were dialysis dependent at 14 and 18 months of follow-up, respectively, and one underwent renal transplantation. Glomerular changes were studied in all the patients with granulomatous interstitial nephritis. Two patients had pauci-immune crescentic glomerulonephritis. One of the patients with tubercular granulomatous interstitial nephritis had an associated focal segmental glomerulosclerosis with a 24-h proteinuria of 3.5 g. Patients were also assessed for the severity of tubulointerstitial fibrosis. In present study, we found that majority of patients had mild interstitial fibrosis and tubular atrophy (13/16) at the time of biopsy. Only three patients had moderate tubular atrophy and interstitial fibrosis and they became dialysis-dependent at follow-up. One of these underwent renal transplantation at follow-up. This observation emphasizes that the extent of tubular atrophy and interstitial fibrosis at the time of biopsy influences outcome in patients with granulomatous interstitial nephritis. Even though majority of patients presented with advanced renal failure, only those with more severe interstitial fibrosis and tubular atrophy progressed to end-stage renal disease.

To conclude, present study highlights that tuberculosis is the most common cause of granulomatous interstitial nephritis in India. It also discusses the spectrum of glomerular and tubulointerstitial changes that can be seen in patients with granulomatous interstitial nephritis and its effect on clinical outcome.

Declaration of interest

Authors have no conflict of interest.

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