Spectrum Of Renal Disease In Visceral Leishmaniasis

J Prakash, S Sundar, B Kar, N Sharma, R Raja, Usha

Citation

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Abstract

Background: Renal involvement in Visceral Leishmaniasis has been reported in the form of proteinuria, microscopic haematuria, acute renal failure and histologic abnormalities in kidney biopsy. However, renal disease in Visceral Leishmaniasis is not widely documented from India, despite kala-azar being endemic in this country.

Material methods: We have studied incidence and spectrum of clinical renal disease in patients with Visceral Leishmaniasis (VL). This study included 240 (Male: 154 and Female: 86) patients with parasitological confirmed diagnosis of VL over a period of two years (April 2002 – April 2004). The presence of oliguria, edema, proteinuria, elevated serum creatinine and haematuria either alone or in combination were taken as evidence of clinical renal disease. Renal tissue under light microscope was studied in six cases.
Observation: The renal involvement was documented in 37/240 (15%) patients. The age (Male:32; Female:05) of the patient ranged between 15-36 years. The spectrum of renal diseases included; proteinuria in the range of 1-2 gm/day (15%), abnormal urinary sediment (4%), edema (9%) and acute renal failure (15%) of cases. Dialytic support was not needed. All patients received Amphotericin B (1.0 mg per kg body wt.) as anti-leishmanial treatment for 15 infusions. Renal histology in six patients revealed; ATN (4), AIN (01) and thrombotic microangiopathy in (01) patients. Glomerular lesions were not observed in our study. There was no mortality.
Conclusion: Renal disease can occur during the course of Visceral Leishmaniasis. They were of mild nature and reversible with treatment of Kala-azar without specific treatment. Acute renal failure is mostly related to prerenal factors and overall renal disease carry good prognosis in patient with Visceral Leishmaniasis.

INTRODUCTION

Visceral leishmaniasis (VL) is a disseminated protozoal infection of reticuloendothelial system caused by Leishmania donovani and characterized by fever, hepatosplenomegaly, anaemia, leucopenia, thrombocytopenia and hyperglobulinemia ([1]). Renal involvement in the form of proteinuria (usually < 1gm/24hrs) and acute renal dysfunction have been reported in Indian patients with Kala-azar ([2]). Different patterns of renal histological lesions had been described in experimental animals ([3], [4]). Acute interstitial nephritis related to visceral leishmaniasis was described in autopsy study of 21 patients from Sao Paulo general hospital ([5]). Immune complex mediated glomerulonephritis was reported in patients with VL by other workers as well ([6], [7]). Visceral leishmaniasis causing graft dysfunction is reported in renal transplant recipient ([8], [9]). However, renal disease is not well documented from India, despite VL being endemic disease in eastern part of the country. We have studied incidence and spectrum of clinical renal disease in patients with VL at Kala-azar unit of our hospital.

MATERIAL METHODS

This study was carried in the Department of Nephrology and Kala-azar unit of Institute of Medical Sciences, Banaras Hindu University, Varanasi, India between April 2002 to May 2004. Two hundred and forty (male: 154; female: 86) patients with parasitologically confirmed diagnosis of VL were included in the study. Diagnosis of Kala-azar was proved by demonstration of Leishmania Donovani (LD) bodies in bone marrow/spleenic aspirate. All patients were screened for the presence of clinical renal disease during the course of hospital stay. The presence of hematuria, proteinuria, edema, elevated serum creatinine and abnormal urine sediments were taken as evidence of clinical renal disease. The patients with VL and clinical renal disease were subjected to detailed physical examination and following laboratory tests were carried in all such cases; urinalysis for cells, casts and crystals, 24 hours urinary excretion of protein, serum creatinine, blood urea, serum protein and

albumin, serum electrolyte, serum calcium, phosphorous, alkaline phosphatase, total and differential leucocyte and platelet count, serum bilirubin, SGOT, SGPT and serum lactate dehydrogenase (LDH).

TREATMENT

All patients were treated with amphoterecin-B 1.0mg/kg body weight for a total of 15 infusions. During treatment regular monitoring of vital signs, spleen size, urinalysis, serum creatinine estimation and adverse reaction to drug were recorded. Urinalysis, hematological profile, renal and liver function were repeated at end of therapy.

RENAL BIOPSY

Patients with proteinuria of >2 gm/24 hrs, impaired renal function (S.Creatinine > 3 mg/dl), and delayed recovery of renal function were subjected to kidney biopsy. Renal biopsy was carried in six patients and tissue was studied under light microscope using H&E, PAS and massion trichome stains.

RESULTS

The study cohort included 240 (male: 154, female: 86) patients with proven diagnosis of Visceral Leishmaniasis of all age group and both genders. The age ranged from 2 to 60 years. Finally 37 patients of VL with clinical renal diseases were subjected to detailed analysis.

CLINICAL PRESENTATION OF KALA-AZAR

The clinical feature of Visceral leishmaniasis was fever of 3-6 months of duration in all the cases (100%), of which 148 (61.6%) presented with chills and vomiting. Hepatosplenomegaly and anemia were seen in all the patients. Dehydration, icterus and lymphadenopathy were seen in 44 (18%), 13 (5.46%) and 56 (23%) cases respectively. The bleeding manifestation and hypotension occurred in 3 (1.25%) cases only. Anemia, thrombocytopenia and leucopenia were seen in all cases (100%). Hypoalbuminemia was seen in 30 (12.5%) cases, serum bilirubin and elevated SGOT/SGPT were recorded in 12 (5%) and 3 (1.25%) cases respectively. High serum LDH was seen in 3 (1.25%) cases.

CLINICAL RENAL DISEASE IN VISCERAL LEISHMANIASIS

The evidence of clinical renal disease was noted in 37 (15%) cases. Oliguria/oligoanuria and elevated serum creatinine were observed in all 37 (15%) patients. However, oedema and haematuria was observed in 23 (9%) and 3 (1.25%) cases respectively. Proteinuria of varying grade was noted in all (100%) cases. On radiological study the kidneys were echogenic and enlarged in 25 (10.4%), and corticomedullary differentiation was maintained. However, one case was noted to have small and contracted kidneys with loss of corticomedullary differentiation, which was unrelated to the disease (Table 1).

Figure 1

Table 1: Clinical renal Disease in Visceral leishmaniasis (n=37/240)

CLINCAL MANIFESTATION	No.	PERCENTAGE
Oliguria/Oligoanuria	37	15.41
Edema	23	9.58
Proteinuria	37	15.41
Hematuria	03	1.25
Elevated creatinine	37	15.41
Enlarged kidney with increased echogenecity	25	10.41
Small and contracted kidney	01	0.41

URINARY ABNORMALITIES IN PATIENTS WITH VISCERAL LEISHMANIASIS

Urinary abnormalities were observed in all 37 cases with clinical renal disease. Proteinuria in the range of 1.2±0.69 gm was observed in all cases. Pyuria was noted in 6 (2.5%) patients of which 3 (1.25%) cases were positive for E. coli (1%). However, haematuria was observed in 3 (1.25%) cases (Table 2).

Figure 2

Table 2: Urinary Abnormality in Patients with Visceral Leishmaniasis (n=37/240)

ABNORMALITY	No.	PERCENTAGE
Microscopic hematuria (RBC/hpf)	03	1.25
Pyuria (WBC/hpf)	06	2.2
24 hr urinary protein (1 to 2 gm/24 hrs)	37	15
Urine culture (growth of E.coli)	03	01

RENAL SYNDROME IN VISCERAL LEISHMANIASIS

The renal involvement was documented in 37 (15%) cases. The spectrum of renal disease included; proteinuria in the range of 1-2gm/day (15%), abnormal urinary sediment (4%), and acute renal failure (15%) of cases. Dialytic support was not needed (Table 3).

Figure 3

Table 3: Renal Syndromes in Patients with Visceral Leishmaniasis (n=37/240)

SYNDROME	No.	PERCENTAGE
Proteinuria (1-2gm/day)	37	15
Abnormal Urinary Sediments	10	4
Acute Renal Failure	36	15
Acute on Chronic Renal Failure	01	0.42

RENAL HISTOLOGY IN PATIENTS WITH VISCERAL LEISHMANIASIS TREATMENT (N=6/37)

Six (16%) patients were subjected to kidney biopsy. The renal tissue was studied under light microscopy, which revealed acute tubular necrosis ([4]) and acute interstitial nephritis in one patient. Glomerular lesion was not seen in our study. Evidence of thrombotic microangiopathy was seen in one patient. This case had proteinuria, haematuria and urinary abnormalities returned to normal with cure of leishmaniasis.

LABORATORY PARAMETERS OF PATIENTS BEFORE AND AFTER TREATMENT

The laboratory parameters before and after the antileishmaniasis treatment were evaluated in all patients. Hemoglobin concentration was increased after the treatment from 6.4 ± 1.6 gm/dl to 10.1±1.82 gm/dl. Total leukocyte count was noted to increase from 3.52±0.62 x 10^3 /cm of blood to 7.04 ± 0.69 x 10^3 . Platelet count was observed to increase to 3.41 ± 0.42 (10^9 /L) from 1.21 ± 0.066 (10^9 /L)

Twenty-four hour urinary protein came to normal values 0.08 ± 0.02 gm/24 hour from 1.2 ± 0.69 gm/24 hour after antileishmanial therapy. Serum creatinine reduced to 0.82 ± 0.39 mg/dl from 2.8 ± 0.8 mg/dl, after antileishmanial therapy in patients with acute renal failure due to visceral leishmaniasis. Serum LDH came down to 67.30 IU/l from 740 ± 175 IU/l after treatment of leishmaniasis. Serum albumin was noted to increase after therapy from 3.16 gm/l to 3.51gm/l. Serum concentration of SGOT and SGPT were reduced from 185 ± 60 IU/L and 176 ± 34 IU/L to 37 ± 11 IU/L and 45 ± 07 IU/L respectively. It was also observed that the concentration of Serum bilirubin reduced to 0.73 ± 0.21 mg/dl from 21 ± 0.58 mg/dl. Serum Alkaline phosphatase which was elevated (357 ± 23 IU/lt) prior to therapy, reduced to 126 ± 16 IU/lt after treatment (Table 4).

Figure 4

Table 4: Lab parameters before and after anti-leishmaniasis treatment

PARAMETRES	BEFORE TREATMENT	AFTER TREATMENT
Hb (gm/dl)	6.4±1.67	10.1±1.82
WBC count (x 10^3 per cu mm of blood)	3.52±00.62	7.04±0.69
Platelet count (10^9 / l)	1.21±0.0.66	3.41±0.82
24 hrs urinary protein (gm)	1.2±0.69	0.08±0.02
LDH (IU/l)	740±175	67±30
S.Creatinine (mg/dl)	2.8±0.8	0.82±0.39
S.Albumin (gm/l)	3±1.6	3.5±1
S.Bilirubin (mg / dl)	2.1±0.58	0.73±0.21
SGOT (IU/l)	185±60	37±11
SGPT (IU/L)	176±34	45±04
S. Alkaline phosphatase (IU/l)	357±23	126±16

All thirty seven patients with clinical renal disease improved with anti-kala azar treatment. There was no mortality. None of the patients of visceral leishmaniasis with acute renal failure required dialytic support. Thus, this study emphasized that, renal disease in visceral leishmaniasis do not adversely affect the prognosis of Kala-azar.

DISCUSSION

Leishmaniasis is group of disease caused by intracellular obligate protozoa of genus leishmania and disease occurs in three distinct clinical forms viz., visceral, cutaneous and mucocutaneous leishmaniasis. Cutaneous leishmaniasis is most common worldwide but in India visceral form, commonly known as Kala-azar is most prevalent. Visceral leishmaniasis is intracellular protozoal infection which is fatal without treatment. We have studied renal involvement in patients with Kala-azar in the present study.

Renal involvement in visceral leishmaniasis has been reported in the form of urinary abnormalities, acute renal failure and histological abnormalities in kidney biopsy ([2], [5], [7], [10]). ARF has been noted in 24% of cases and dehydration and volume loss was responsible for tubular lesion in majority of cases ([2]). We observed clinical renal disease in 37/240 (15%) cases of visceral leishmaniasis. The reported incidence of renal disease in VL varied from 40 to 60% ([2], [10], [11]). The spectrum of renal disease in our patients included, acute renal failure (15%), abnormal urinary sediments (9%), proteinuria < 2gm/24 hrs (15%) and oedema in (9%) of cases. Acute renal failure occurred in 15% of cases of VL in

present study. The reported incidence of acute renal failure in visceral leishmaniasis varied from 4.2 to 16.3% ([2], [11]). This variable incidence of ARF, in patients with visceral leishmaniasis may be related to criteria defining acute renal failure, severity of acute renal failure and etiological factors causing ARF. Dutra et al reported elevated blood urea above 60mg/dl in 42/100 (4.2%) cases and 12 patients had decreased glomerular filtration rate as well ([11]). These changes were reversible with cure of Kala-azar ([2]). There are reports of 18 cases of visceral leishmanisis and graft dysfunction in organ transplant recipient ([12]). Acute graft dysfunction has been described due to visceral leishmaniasis in renal allograft recipient from our country ([8], [9], [13]). Visceral leishmaniasis should be considered in the differential diagnosis of febrile transplant recipient with pancytopenia and allograft dysfunction ([9]). Acute renal failure related to sodium antimony gluconate therapy has been reported in patients with Kala-azar ([10]). The acute renal failure in our patients mostly related to prerenal factors like, fluid loss from vomiting, dehydration, and poor fluid balance. We have used fat emulsified Amphotericin B to treat visceral leishmaniasis in our patients and noted serum creatinine returned to normal with cure of Kala-azar using Amphotericin B. This shows ARF is not related to nephrotoxicity of Amphotericin B in the present study. The renal function was reversible with treatment of visceral leishmaniasis in our study, similar to other observations. ([2], [10]).

Abnormal urinary sediments (microscopic hematuria and proteinuria) was observed by several investigators in visceral leishmaniasis ([2],[5],[7]). There are reports of Acute GN, Acute TIN and nephritic syndrome in visceral leishmaniasis ([14]). Microscopic haematuria and pyuria were observed in 1.6% and 2.2% of cases respectively. Acute nephritic presentation was reported in visceral leishmaniasis ([7],[14]). We have not observed acute nephritic syndrome in our study. Proteinuria ranged between 1.2-1.8gm/24 hrs was observed in 15% of cases in present study. The finding of urinary protein excretion of less than 2 gm/24hrs in our study was similar to other workers ([2], [7], [11], [14]). The nephritic syndrome is not reported in visceral leishmaniasis similar to our observation ([6]).

Renal biopsy in patients with visceral leishmaniasis revealed membranous, hyaline, fibrilar, mesangial thickening and normal glomerular basement membrane. Renal histology in 7 patients of visceral leishmaniasis revealed glomerular lesions consisting of mesangial proliferation ([3]), focal proliferative GN ([2]) and minimal change lesion in two cases ([6]). They also reported interstitial nephritis in all 7 patients along with glomerular lesions. Deposition of IgG, IgM, C_3 was documented in kidney tissue along with electron dense deposit in basement membrane mainly in the proximity of mesangium([6],[7],[15]). Autopsy study of 21 patient of visceral leishmaniasis showed diffuse interstitial infiltrate without any significant glomerular lesion ([5]). Six patient in our study were subjected to kidney biopsy because of delayed recovery of renal function. The histology reveals ATN ([4]) cases, AIN ([1]), TMA ([1]) case. Renal biopsy demonstrated interstitial nephritis without glomerular involvement in a patient with visceral leishmaniasis and acute renal failure ([16]). The interstitial nephritis was reported by various workers in patients with visceral leishmaniasis, a finding similar to our observation ([5],[16]). We have not observed glomerular lesions in our study.

CONCLUSION

In summary, renal disease can occur during the course of visceral leishmaniasis. They were of mild nature and reversible with treatment of Kala-azar without specific treatment. Acute renal failure is mostly related to prerenal factors and overall renal disease carry good prognosis in patients with VL and do not adversily affect the course of disease. However, further extensive study is required to address the nature of the glomerular and tubular lesions observed in patients with visceral leishmaniasis.

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CORRESPONDENCE TO

Dr. Jai Prakash MD, DM, FISN Professor and Head Department of Nephrology Institute of Medical Sciences Banaras Hindu University Varanasi-221005 (INDIA) Tel no.:91-542-2575508 Fax no: 91-542-2367568 e-mail: jaiprakashbhu@hotmail.com

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Author Information

Jai Prakash, MD, DM
Professor, Department Of Nephrology, Institute of Medical Sciences, Banaras Hindu University

Shyam Sundar, M.D.
Professor, Department Of General Medicine, Institute of Medical Sciences, Banaras Hindu University

B. Kar, M.D.
Senior resident, Department Of Nephrology, Institute of Medical Sciences, Banaras Hindu University

Naveen Sharma, MBBS
Junior Resident, Department Of General Medicine, Institute of Medical Sciences, Banaras Hindu University

R. Raja, MBBS
Junior Resident, Department Of Nephrology, Institute of Medical Sciences, Banaras Hindu University

Usha, MD
Professor, Department Of Pathology, Institute of Medical Sciences, Banaras Hindu University