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Clinical characteristics and outcome of chronic lymphocytic leukemia patients with renal involvement in the era of target drugs

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OBJECTIVES

- To understand the clinical features, pathological types and prognosis of renal involvement in CLL patients treated with new drugs, and to provide the basis for timely diagnosis and individualized treatment of renal involvement in CLL.

CONCLUSIONS

- Majority of CLL patients with renal involvement were with IGHV mutated status and often with favorable prognosis according to CLL-IPI low risk The most renal pathological type was primarily interstitial infiltration nephritis and membranoproliferative glomerulonephritis. The outcome of CLL and improvement of renal abnormalities were satisfied under treatment of new drugs.

INTRODUCTION

- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma(SLL) is a clonal proliferative tumor of mature B lymphocytes, which can involve the kidney in some patients. This study reported the clinical characteristics, pathological types, treatment and prognosis of CLL patients with renal dysfunction and pathological diagnosis of renal disease in China.

METHODS

- From January 2017 to October 2024, 13 patients with CLL/SLL who underwent renal biopsy in four centers in China and were pathologically confirmed as having renal lesions were included. The indications for renal biopsy included hematuria, proteinuria, renal insufficiency, or nephrotic syndrome, and all other secondary causes leading to chronic kidney disease were excluded. Clinical data such as complete blood count, biochemical profile, urinalysis, 24-hour urine protein, peripheral blood flow cytometry, IGHV mutation, chromosomal analysis, and genetic mutations were collected. Pathological markers of the kidneys, including CD20, CD3, CD5, CD10, CD23, LEF-1, and CyclinD1, were also analyzed. The clinical characteristics, pathological features of the kidneys, and treatment outcomes of these patients were evaluated.

RESULTS

- Thirteen CLL/SLL patients with renal involvement were included in the study, nine were CLL and four were SLL, with a median age of 58 years (range 40-72 years). Proteinuria, hematuria, renal dysfunction and nephrotic syndrome were found in 92.3%, 38.5% ,50% and 7.7% respectively. The median time from diagnosis to renal biopsy was 40.7 months (range 0.2-159 months). Interstitial infiltration by tumor cell, membranoproliferative glomerulonephritis and membranous nephropathy were identified in 38.5% (5/13) ,23.1% (3/13) and 15.4% (2/13) of patients respectively. Ninety-nine percent (10/11) of patients were IGHV mutated and 62.5% (5/8) was low risk stratified by CLL-IPI. Meanwhile, 23.1% (3/13) were with monoclonal immunoglobulin and 15.4% (2/13) had cryoglobulinemia.All but one patient received a targeted agent-based regimen, including six patients with BTK inhibitors (BTKi) plus CD20 monoclonal antibody, two patients with BTKi monotherapy, one with CD20 monotherapy antibody, one with BTKi plus Fludarabine, cyclophosphamide, obinutuzumab, another with BTKi plus Bendamustine, obinutuzumab, and the other with venetoclax plus obinutuzumab. As of May 15, 2025, with a median follow-up of 18.5 months (range, 8-31 months), 11 patients were available for efficacy evaluation.According to iwCLL criteria for CLL and Lugano criteria for SLL, best overall response rate was 100% and complete remission was 67%;As for the improvement for renal according to KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases, best overall response rate was 100% and complete remission was 33.3%. Four patients achieved CR in both CLL and kidney efficacy assessments. The median time to PR in the renal efficacy assessment was 6.03 months(range3.1-13.3months); The median time to achieve PR and CR in the efficacy evaluation of CLL/SLL was 3.47 months(range2.52-6.07months),and 6.27months(4.03-14.9) months,respectively.The median PFS was not reached.

Table1. Baseline characteristics of CLL/SLL

	N=13
Demographic characteristics	
Median age ,years(range)	58[47-72]
femal,%	6/13(46.15%)
male,%	7/13(53.85%)
Comorbidity	
diabetes	4/13(30.8%)
hypertension	5/13(38.5%)
obesity	4/13(30.8%)
the second tumor	1/12(8.3%)
Laboratory data	
white blood cell count,*10^9/L	31[3.4-291.99]
Lymphocyte count, *10^9/L	23[0.7-283.2]
Hemoglobin, g/L	171[78-138]
blood platelet, *10^9/L	115[78-279]
Serum albumin, g/L	38[23.4-47.8]
Serum globulin, g/L	21.4[17.7-50.5]
Serum creatinine, umol/l	99.7[51.5-516.3]
Serum urea, mmol/l	7.39[3.8-16.15]
eGFR, mL/min/1.73 m2	60.46[7.19-108.27]
Proteinuria, g/24h	1.6[0.16-4.27]
Hematuria	5/13(38.5%)
Proteinuria	12/13(92.3%)
Nephrotic syndrome	1/13(7.7%)
β2-MG>3.5mg/L	5/12(41.7%)
LDH>265U/L	0/13
SIFE	
IgG-k	3/13(23.1%)
Cryoglobulinemia	2/13(15.4%)
Large mass lesion>5cm	0/13(0)
Splenomegaly	5 /13(38.5%)

eGFR, estimated glomerular filtration rate;SIFE, serum immunofixation electrophoresis.Unless otherwise indicated, values for categorical variables are given as number or number/number analyzed (percentage); values for continuous variables, as median [range].

Table2. Baseline and demographic characteristics at the time of kidney biopsy

	n/N(%)
Diagnose	
CLL	9/13(69.2%)
SLL	4/13(30.8%)
Binet stage	
A	2/9(22.2%)
B	2/9(22.2%)
C	5/9(55.6%)
Rai stage	
0-II	2/9(22.2%)
III-IV	7/9(77.8%)
Lugano	
0-II	0/4(0)
III-IV	4/4(100%)
CD38 postive	2/12(16.7%)
CD49d postive	4/13(30.8%)
CD200 postive	10/11(90.9%)
CLL-IPI	
low(0-1)	4/7(62.5%)
intermediate(2-3)	1/7(12.5%)
high (4-6)	1/7(12.5%)
very high(7-10)	1/7(12.5%)
Complex karyotypes	4/13(30.8%)
IGHV mutated	10/11(90.9%)
IGHV 4-34	4/10(40%)
TP53 mutated	0/12 (0)
FISH	
del 13q14	5/10(50%)
+12	1/10(10%)
del 11q	0/10(0)
del 17p	1/10(10%)
all negative	4/10(40%)

Table3. The kidney biopsy pathology and molecular biological characteristics

Case	Age/Sex	eGFR (mL/min/1.73 m²)	UTP (g/24 h)	SIFE	Cryo(mg/L)	C3(g/L)	C4(g/L)	Time (months)	Diagnosis by renalbiopsy
1	53/M	41.98	2.02	N		0.95	0.12	159.0	IgA nephropathy
2	59/F	77.15	1.92	IgG-K		1.05	0.196	1.8	Lymphoma infiltration
3	42/M	108.27	1.695	N		1.480	0.339	48.4	MN
4	40/M	60.46	1.09	N		0.371	0.0557	10.3	Lymphoma infiltration
5	55/M	100.04	0.58	IgG-K		0.427	0.0341	58.0	C3 glomerulonephritis
6	58/F	53.97	3.07	N		0.453	0.147	49.7	Lymphoma infiltration, MPGN
7	59/M	7.19	1.60	N	482.07	0.606	0.123	40.7	Cryoglobulinemic,MPGN
8	67/F	89.64	4.27	N		0.728	0.154	49.8	MN
9	45/F	101.39	1.78	N	536.82	0.454	0.172	43.6	Cryoglobulinemic,MPGN
10	61/M	11.30	0.41	N		1.040	0.328	26.0	AIN
11	45/F	37.55	1.36	N		0.760	0.182	0.2	Lymphoma infiltration
12	59/F	46.23	0.16	IgG-K		0.85	0.05	2.2	Lymphoma infiltration
13	72/M	93.74	0.47	N		1.370	0.44	2.2	IN

Notes: Time: time from diagnosis of CLL/SLL to renal biopsy;Treatment：treatment Before Renal biopsy：N:negative;NA: not available

Abbreviations:eGFR, estimated glomerular filtration rate;UTP;urine total protein, SIFE, serum immunofixation electrophoresis; Cryo;cryoglobulinemia；MN, membranous nephropathy;MPGN：membrano proliferative glomerulonephritis;AIN, acute interstitial nephritis;IN:interstitial nephritis.

Table4. Treatment and follow-up after renal biopsy

Case	Haematological diagnosis	Diagnosis by renal biopsy	Treatmet Regimens	Follow up (months)	Best response in CLL	Renal response	Patient outcome
1	CLL	IgA nephropathy	ZR	17.6	CR	PR	Alive
2	SLL	Lymphoma infiltration	COP→IR	99	CR	PR	Alive
3	CLL	MN	OFCG	33.9	CR	CR	Alive
4	CLL	Lymphoma infiltration	R+Ibrutinib	72.8	CR	CR	Alive
5	CLL	C3 glomerulonephritis	GV	6.5	CR	CR	Alive
6	SLL	Lymphoma infiltration, MPGN	zebrutinib	20.1	PR	PR	Alive
7	SLL	Cryoglobulinemic,MPGN	ZR	20.3	PR	PR	Alive
8	CLL	MN	rituximab	10.2	CR	CR	Alive
9	CLL	Cryoglobulinemic,MPGN	ZR	7.3	PR	PR	Alive
11	CLL	Lymphoma infiltration	OBG	41.6	CR	PR	Alive
12	CLL	Lymphoma infiltration	ZG	13.4	CR	PR	Alive
13	SLL	IN	zebrutinib	5.5	PR	PR	Alive

MN, membranous nephropathy,MPGN:membrano proliferative glomerulonephritis;IN:interstitial nephritis;
ZR:zebrutinib+rituximab;COP: cyclophosphamide+vincristine+ prednisone;
OFCG:Obrutinib+fludarabine+cyclophosphamide+obinutuzumab;
GV:Obinutuzumab+venetoclax;
OBG:Obrutinib+ bendamustine+obinutuzumab;ZG:zebrutinib+obinutuzumab;
CR: complete remission; PR: partial remission.

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