

INTRODUCTION:

- Monoclonal immunoglobulin deposition disease (MIDD) in kidney is characterised by the deposition of monoclonal immunoglobulins on glomerular basement membrane and tubular basement membrane
- Monoclonal immunoglobulins are secreted as a result of clonal proliferation of abnormal plasma cell or B cell lineage
- MIDD comprises 3 subtypes
- Light chain deposition disease (LCDD) with deposits of either kappa or lambda
- Heavy chain deposition disease (HCDD) with deposits of single heavy chain
- Light and heavy chain deposition disease (LHCDD) with deposits of monoclonal light chain and heavy chain
- LCDD could reportedly have concomitant light chain cast nephropathy (LCCN) in the biopsy

METHODS:

- We conducted observational study of all the native kidney biopsies reported as monoclonal immunoglobulin deposition disease from 2018 to 2024
- The panel for immunofluorescence study included IgG, IgA, IgM, C3, C1q, kappa and lambda light chains
- All the pathology slides were reviewed
- The clinicopathologic parameters were analysed based on the glomerular morphologies as well as between MIDD and MIDD+LCCN groups
- The statistical analysis was performed using SPSS software version 21. p value of <0.05 is statistically significant

RESULTS:

- 23,182 biopsies were reviewed. 60 cases of MIDD and 73 cases of MIDD+LCCN were identified, the biopsy incidence being 0.25% and 0.31% respectively.
- Of the total 133 cases, 94 were males
- 65.4% presented with acute kidney injury and 53.3% required haemodialysis
- All the cases had proteinuria while 45.1% were in nephrotic range
- The mean serum creatinine at presentation was 5.2 ± 3.5 mg/dl
- 35.3% were known cases of multiple myeloma and one patient had Hodgkin lymphoma at the time of biopsy

Pathologic spectrum of MIDD group and MIDD+LCCN group

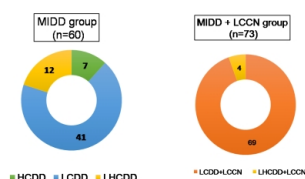


Table 1 Analysis of clinicopathologic features in study cohort vs glomerular morphologic patterns

CLINICOPATHOLOGIC FEATURES		GLOMERULAR MORPHOLOGY			p VALUE
		NORMOCELLULAR	NODULAR	MILD INCREASE MESANGIUM	
		n (%)	n (%)	n (%)	
Age (years)		56.6 (±11.9)	52.4 (±13)	60.1 (±10.1)	0.052
Gender	Males	51 (70.8%)	36 (81.8%)	7 (41.2%)	0.041
	Females	21 (29.2%)	8 (18.2%)	10 (58.8%)	
Acute kidney injury	Yes	50 (69.4%)	24 (54.5%)	13 (76.5%)	0.155
	No	22 (30.6%)	20 (45.5%)	4 (23.5%)	
Hypertension	Present	27 (37.5%)	37 (84.1%)	6 (35.3%)	0.001
Diabetes	Present	15 (20.8%)	6 (13.6%)	6 (35.3%)	0.095
Proteinuria	Nephrotic	24 (33.3%)	30 (68.2%)	6 (35.3%)	0.001
	Sub nephrotic	48 (66.7%)	14 (31.8%)	11 (64.7%)	
Serum Creatinine (mg/dl)		5.5 (±3.5)	4.9 (±3.5)	4.7 (±3.6)	0.588
Immuno-fluorescence	Kappa	32 (44.4%)	22 (50%)	7 (41.2%)	0.774
	Lambda	33 (45.8%)	9 (20.5%)	7 (41.2%)	0.032
	Gamma, lambda	4 (5.6%)	3 (6.8%)	2 (11.8%)	0.323
	Gamma kappa	2 (2.8%)	1 (2.3%)	1 (5.9%)	0.749
	Gamma	0 (0%)	7 (15.9%)	0 (0%)	0.001
	Alpha, lambda	0 (0%)	2 (4.5%)	0 (0%)	0.128
	Alpha, kappa	1 (1.4%)	0 (0%)	0 (0%)	0.652
Interstitial fibrosis	> 25%	8 (11.1%)	8 (18.2%)	6 (35.3%)	0.01
tubular atrophy IF/TA	≤ 25%	64 (88.9%)	36 (81.8%)	11 (64.7%)	
Dialysis at Presentation	Yes	40 (55.6%)	23 (52.3%)	8 (47.1%)	0.806
	No	32 (44.4%)	21 (47.7%)	9 (52.9%)	

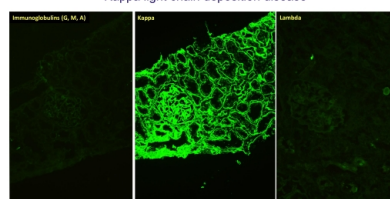
REFERENCES:

- Nasr SH, Valeri AM, Sethi S, et al. Clinicopathologic correlations in multiple myeloma: a case series of 190 patients with kidney biopsies. Am J Kidney Dis. 2012;59(6):786-794
- Zand L, Nasr SH, Gertz MA, et al. Clinical and prognostic differences among patients with light chain deposition disease, myeloma cast nephropathy and both. Leukemia & Lymphoma. 2015;56(12):3357-3364

Table 2 Analysis of clinicopathologic features in MIDD vs MIDD+LCCN

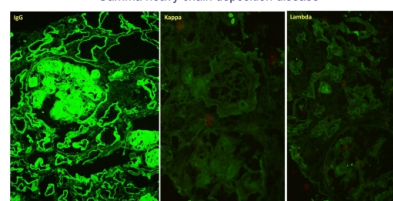
CLINICOPATHOLOGIC FEATURES		CLASSIFICATION		p VALUE	
		MIDD n (%)	MIDD+LCCN n (%)		
Age (years)		54.93 (± 13.31)	56.27 (± 11.35)	0.53	
Gender	Males	50 (83.3%)	44 (60.3%)	0.004	
	Females	10 (16.7%)	29 (39.7%)		
Acute kidney injury	Present	30 (50%)	57 (78.1%)	0.001	
Hypertension	Present	42 (70%)	28 (38.4%)	0.001	
Diabetes	Present	14 (23.3%)	13 (17.8%)	0.431	
Proteinuria	Nephrotic	37 (61.7%)	23 (31.5%)	0.001	
	Sub nephrotic	23 (38.3%)	50 (68.5%)		
Morphology	Normocellular	20 (33.3%)	52 (71.2%)	0.001	
	Nodular	32 (53.3%)	12 (16.4%)	0.001	
	Mild mesangial matrix increase	8 (13.3%)	9 (12.3%)	0.862	
Serum Creatinine (mg/dl) mean		3.61 (± 2.77)	6.52 (± 3.53)	0.001	
Immuno-fluorescence	Kappa	31 (51.7%)	30 (41.1%)	0.223	
	Lambda	10 (16.7%)	39 (53.4%)	0.001	
	Gamma, lambda	7 (11.7%)	2 (2.7%)	0.010	
	Gamma kappa	3 (5%)	1 (1.4%)	0.201	
	Gamma	7 (11.7%)	0 (0%)	0.003	
	Alpha, lambda	1 (1.7%)	1 (1.4%)	0.498	
	Alpha, kappa	1 (1.7%)	0 (0%)	0.451	
Interstitial fibrosis	> 25%	12 (20%)	10 (13.7%)	0.33	
	tubular atrophy IF/TA	<= 25%	48 (80%)		63 (86.3%)
Dialysis at Presentation		Yes	19 (31.7%)	52 (71.2%)	0.001

Kappa light chain deposition disease



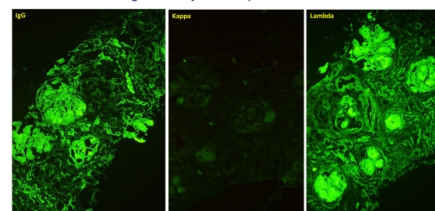
Immunoglobulins are negative (left), Kappa shows linear positivity on the glomerular basement membrane and tubular basement membrane (centre), lambda is negative (right)

Gamma heavy chain deposition disease



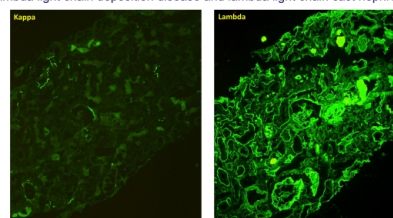
IgG shows linear positivity on the glomerular basement membrane and tubular basement membrane (left), kappa and lambda light chains are negative (centre, right)

Light & heavy chain deposition disease



IgG and lambda show linear positivity on the glomerular basement membrane and tubular basement membrane (left, right), kappa is negative (centre)

Lambda light chain deposition disease and lambda light chain cast nephropathy



Kappa is negative (left), lambda shows linear positivity on the glomerular basement membrane, tubular basement membrane and tubular luminal casts

CONCLUSIONS:

- Renal biopsy with a systematic analysis of the immunofluorescence findings is essential for the diagnosis of MIDD
- Only 35% of patients with MIDD had clinical or laboratory features of multiple myeloma
- There is a wide spectrum of renal histopathological lesions in MIDD
- MIDD with concomitant light chain cast nephropathy is associated with normal glomeruli in the biopsy and presents with acute kidney injury, higher serum creatinine and increased dialysis requirement than isolated MIDD