MONOCLONAL GAMMOPATHY OF RENAL SIGNIFICANCE

Depositi non organizzati

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Andrea Airoldi
SCDU Nefrologia e Trapianto – Novara
Dir Prof. V. Cantaluppi

MONOCLONAL GAMMOPATHY OF RENAL SIGNIFICANCE

Definizione

Monoclonal gammopathy of renal significance: when MGUS is no longer undetermined or insignificant

Nelson Leung,[1,2] Frank Bridoux,[3] Colin A. Hutchison,[4] Samih H. Nasr,[5] Paul Cockwell,[4] Jean-Paul Fermand,[6] Angela Dispenzieri,[2] Kevin W. Song,[7] and Robert A. Kyle,[2] on behalf of the International Kidney and Monoclonal Gammopathy Research Group

Blood 2012

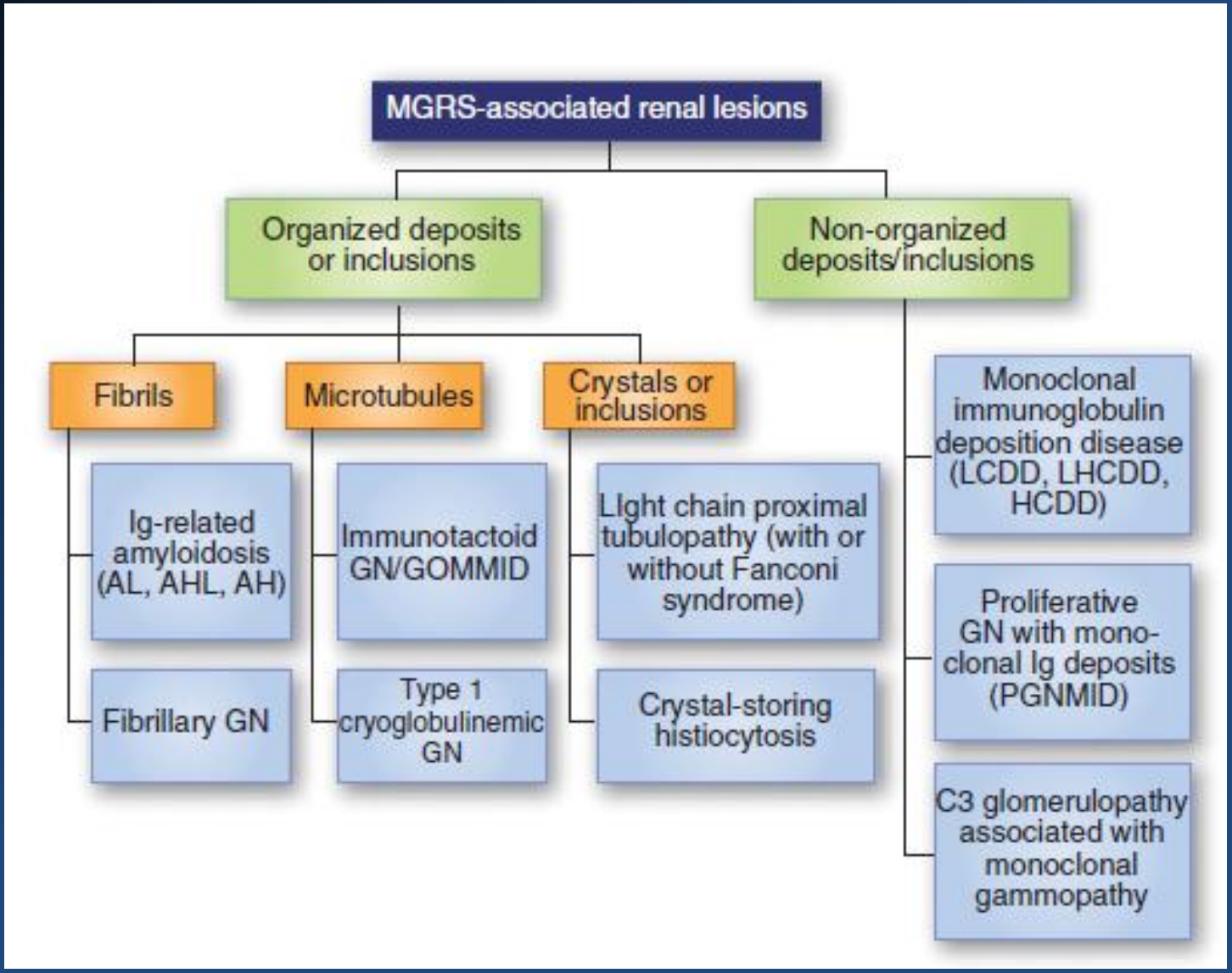
MGUS should not be used to describe hematologic disorders that result in kidney disease. It is because of this necessity that we propose the term "monoclonal gammopathy of renal significance" (MGRS) to discriminate the pathologic nature of these diseases from the truly benign MGUS.

Monoclonal gammopathy of renal significance (MGRS) is defined by the causal relationship between a small B-cell clone and renal disease, usually through deposition of the secreted monoclonal immunoglobulin (MIg) or a fragment thereof.

Cast nephropathy, which almost always complicates high tumor mass myeloma, should not be included in MGRS

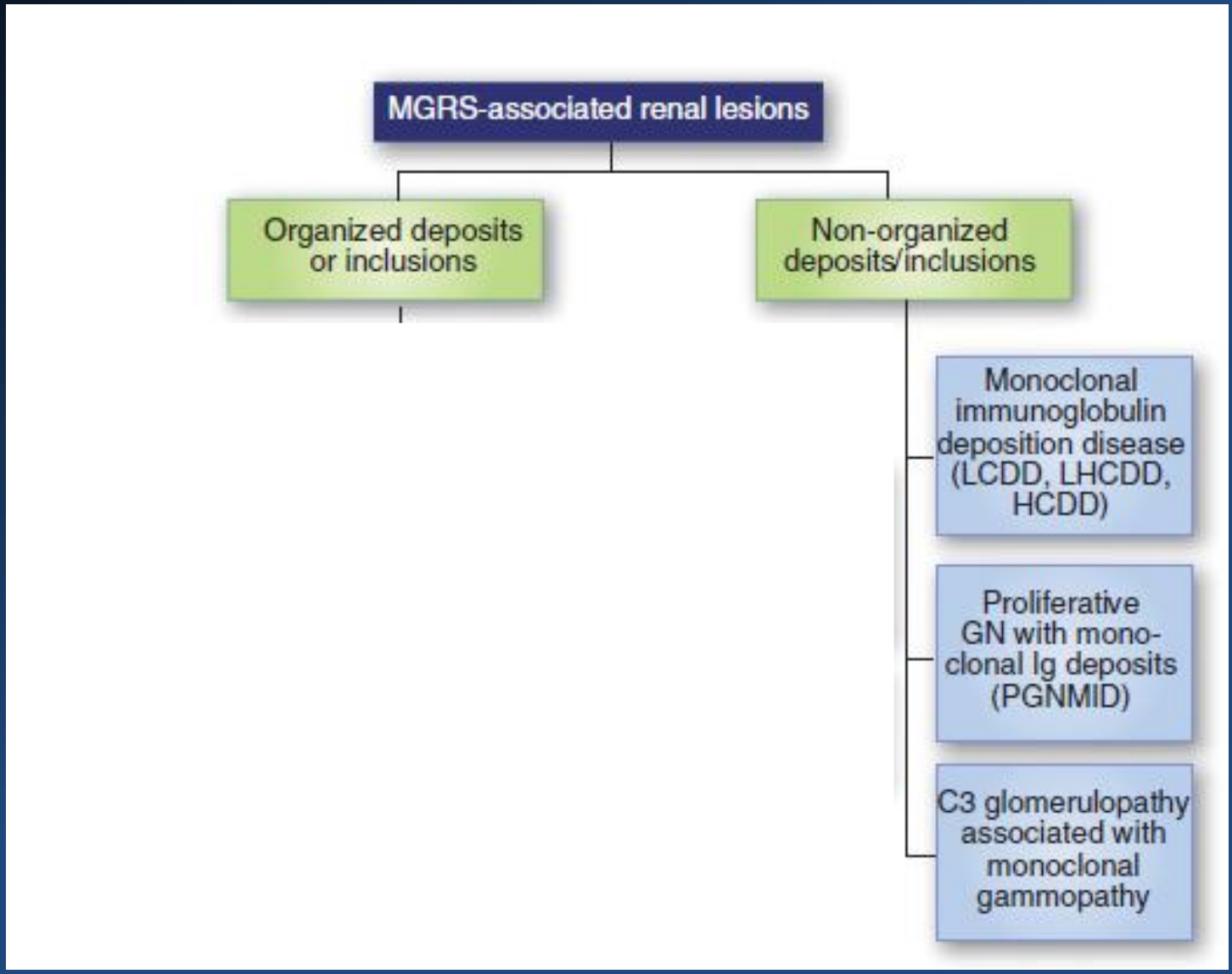
Diagnosis of monoclonal gammopathy of renal significance

Kidney Int 2015

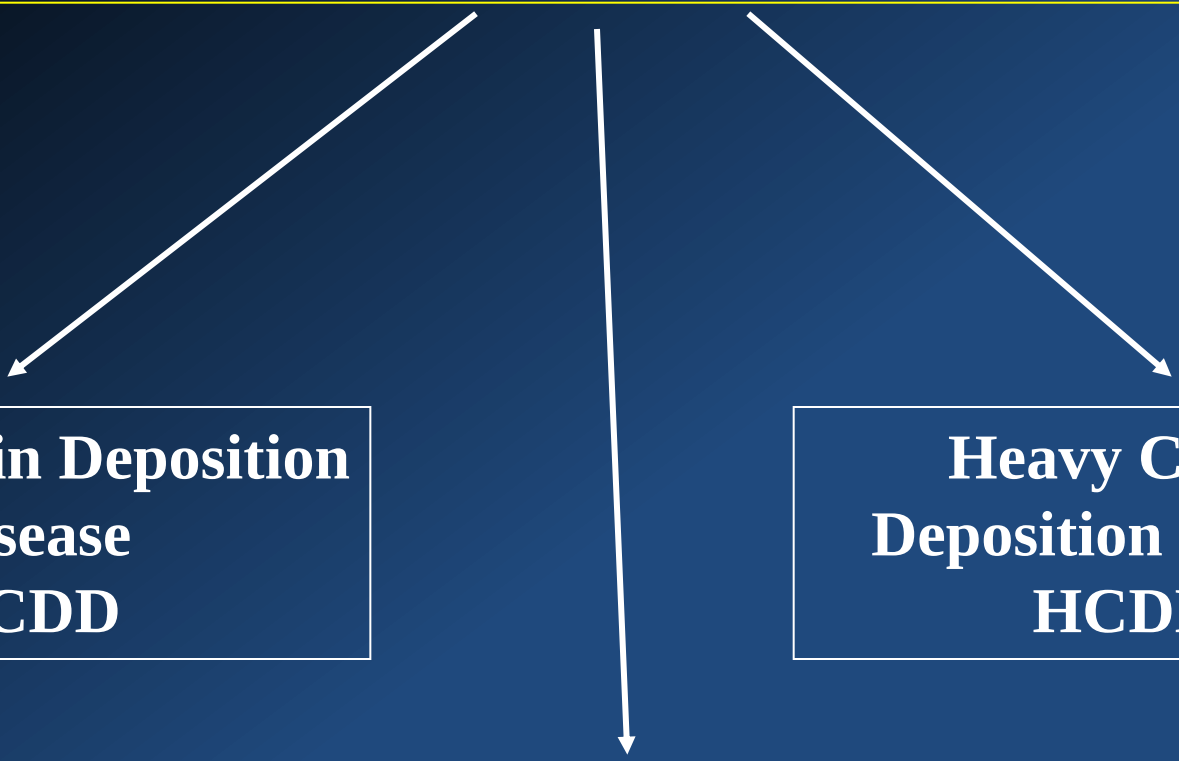


Diagnosis of monoclonal gammopathy of renal significance

Kidney Int 2015



Monoclonal Ig deposition disease (MIDD)



Light Chain Deposition Disease
LCDD

Heavy Chain Deposition Disease
HCDD

Light and Heavy Chain Deposition Disease
LHCDD

DEFINIZIONE

Deposito granulare di

- **catene leggere monoclonali non amiloidotiche (Rosso Congo neg),**
- **catene pesanti monoclonali o**
- **entrambe**

in diversi organi oltre al rene che è sempre coinvolto.

EPIDEMIOLOGIA

5% in riscontri autoptici di pz con Mieloma Multiplo

*Arch Pathol Lab Med **114**: 986– 987,1990*

0,47 -0,7% delle casistiche bioptiche

J Am Soc Nephrol 12: 1482–1492, 2001
Clin J Am Soc Nephrol 7: 231–239, 2012.

LCDD > HCDD ≥ LHCDD

Età media: 56-57.4 anni (22-83 aa)
M > F

J Am Soc Nephrol 12: 1482–1492, 2001
Clin J Am Soc Nephrol 7: 231–239, 2012.

CARATTERISTICHE CLINICHE

- **Insufficienza renale**
- **Proteinuria**
- **Sindrome nefrosica**
- **Microematuria**
- **Ipertensione arteriosa**

Renal Monoclonal Immunoglobulin Deposition Disease: A Report of 64 Patients from a Single Institution

Clin J Am Soc Nephrol 7: 231–239, 2012.

Table 2. Demographics and clinical renal characteristics

Characteristic	LCDD	HCDD	LHCDD	All MIDD Patients	*P* Value
Number of patients	51	7	6	64	
Hypertension	41 (80)	7 (100)	5 (83)	53 (83)	0.60
Mean SCr in mg/dl (range)	3.8 (0.9–9.9)	5.6 (2.5–15)	3.1 (1.4–5.9)	3.9 (0.9–15)	0.23
Renal insufficiency (SCr >1.2 mg/dl)	47/49 (96)	7/7 (100)	6/6 (100)	60/62 (97)	1.00
Dialysis at biopsy	8 (16)	2 (29)	0 (0)	10 (16)	0.47
Mean 24-h urine protein (g)	3	11.5	4.8	4.1	0.004[a]
Nephrotic-range proteinuria	17/47 (36)	6/6 (100)	2/6 (33)	23/59 (39)	0.009[b]
Mean serum albumin (g/dl)	3.6	2.8	3	3.5	0.18
Edema	24/47 (51)	7 (100)	5 (83)	36/60 (60)	0.01[c]
Full nephrotic syndrome	8/48 (17)	4/6 (67)	2 (33)	14/60 (23)	0.02[d]
Microscopic hematuria	29/49 (59)	5 (71)	4/5 (80)	38/61 (62)	0.70
Leukocyturia	11/48 (23)	1 (14)	2/5 (40)	14/60 (23)	0.72

Table 4. Treatment and outcomes

Characteristic	LCDD	HCDD	LHCDD	All MIDD Patients	*P* Value
Number of patients	45	7	4	56	
Mean/median duration of follow-up, mo (range)	35/26 (2–140)	20/12 (5–53)	53/58 (1–97)	34/25 (1–140)	0.65
Treatment, *n* (%)					0.55
none	6 (13)	2 (29)	0 (0)	8 (14)	
chemotherapy without SCT	25 (56)	4 (57)	3 (75)	32 (57)	
SCT	14 (31)	1 (14)	1 (25)	16 (29)	
Renal outcome, *n* (%)					0.98
stable/improved	26 (58)	4 (57)	2 (50)	32 (57)	
worsening renal function[a]	2 (4)	0 (0)	0 (0)	2 (4)	
progression to ESRD	17 (38)	3 (43)	2 (50)	22 (39)	
mean time to ESRD (mo)	6	12	6	7	
Patient deaths, *n* (%)	15/48 (31)	1/7 (14)	3/5 (60)	19/60 (32)	0.27
Mean time to death (mo)	20	12	7	18	
Renal survival, mo (mean ± SEM)	67.7±8.7	26.4±7.7	36.0±24.9	64.0±8.1	0.79
Patient survival, mo (mean ± SEM)	91.1±10.7	42.8±10.7	42.0±20.0	90.4±9.6	0.42

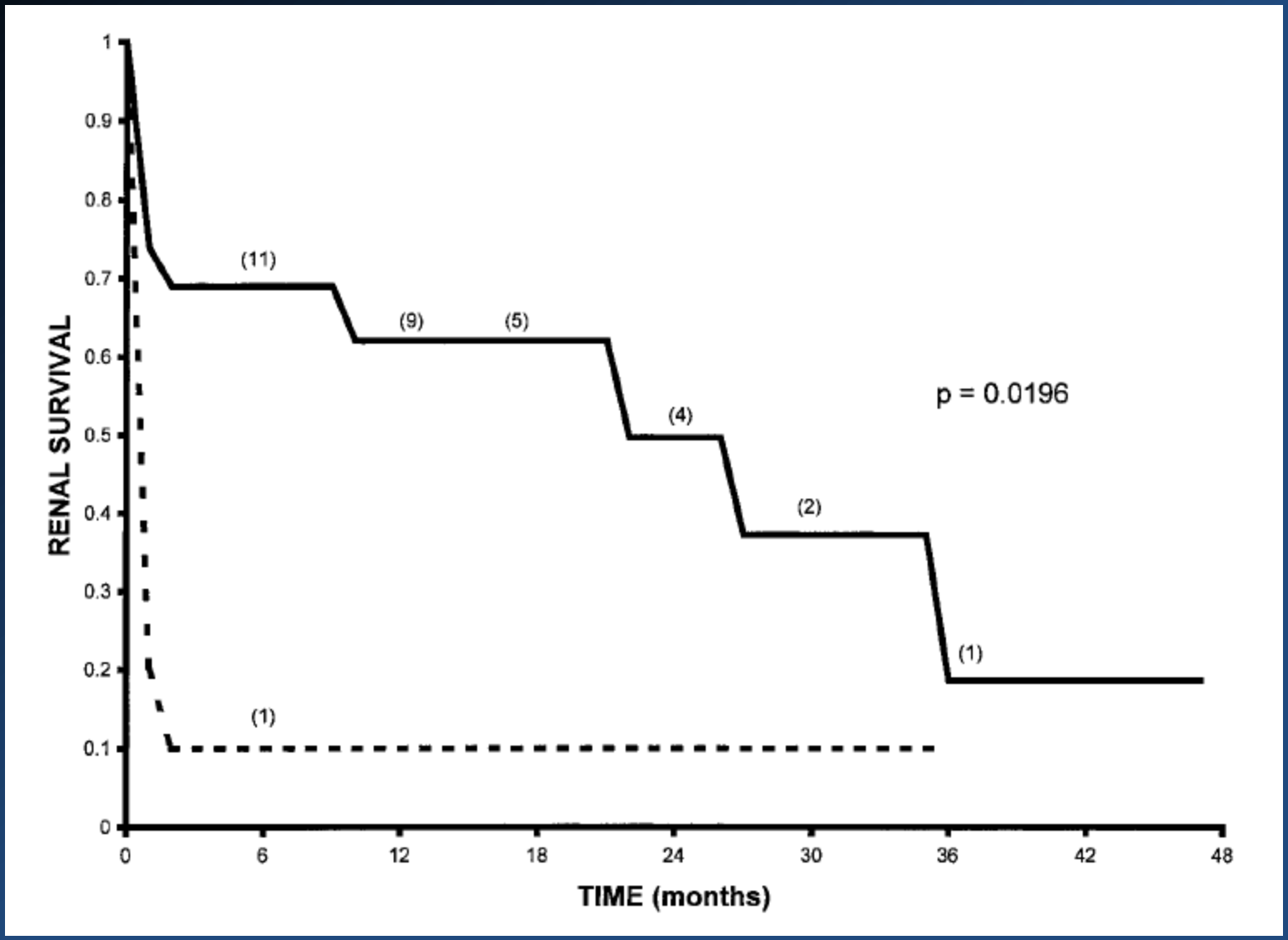
LCDD, light chain deposition disease; HCDD, heavy chain deposition disease; LHCDD, light and heavy chain deposition disease; MIDD, monoclonal immunoglobulin deposition disease; SCT, stem cell transplant.

[a]Defined as >50% increase in final serum creatinine from creatinine at kidney biopsy.

Renal Monoclonal Immunoglobulin Deposition Disease: The Disease Spectrum

J Am Soc Nephrol 12: 1482–1492, 2001

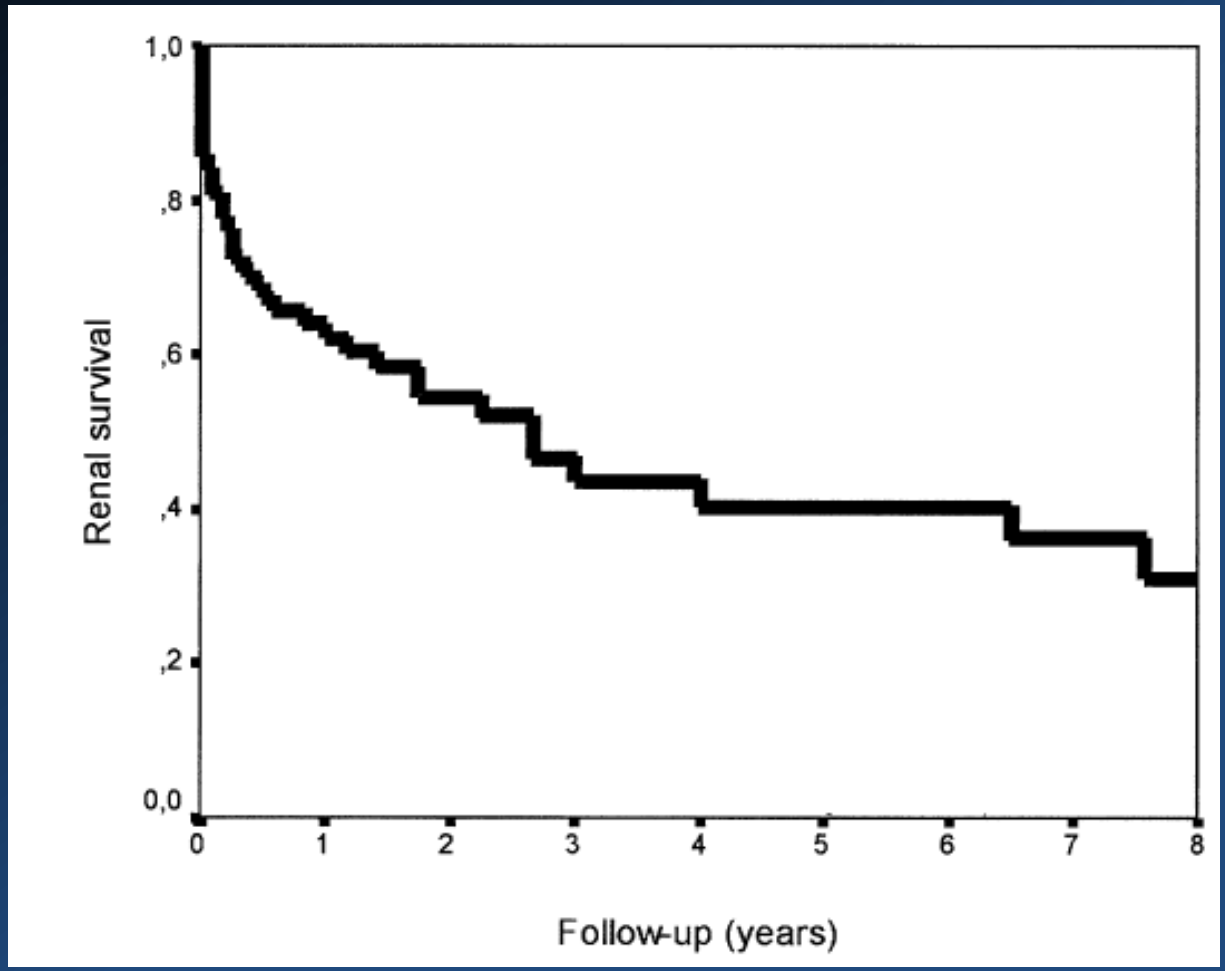
Characteristic	LCDD (n = 12)	LHCDD (n = 5)	HCDD (n = 6)	Pure MIDD (n = 23)	LCDD & MCN (n = 11)	P Value
Gender (M/F)	7/5	2/3	3/3	12/11	5/6	NS
Age (yr)	56.6 ± 2.87	63.8 ± 5.88	53.8 ± 2.63	57.4 ± 2.12	67.1 ± 3.92	0.066[b]
Hypertension	10 (83%)	2 (40%)	6 (100%)	18 (78%)	7 (64%)	0.03[c]
Creatinine (mg/dl)	4.0 ± 0.9	5.3 ± 2.0	4.8 ± 1.5	4.5 ± 0.7	7.8 ± 1.2	0.01[b]
Renal insufficiency (sCr ≥1.2 mg/dl)	11 (92%)	5 (100%)	6 (100%)	22 (96%)	11 (100%)	NS
Proteinuria (g/24 h)	4.2 ± 0.8	2.9 ± 1.0	5.3 ± 2.2	4.2 ± 0.7	2.2 ± 0.7	0.01[b]
Nephrotic proteinuria (≥3 g/24 h)	6 (50%)	1 (20%)	4 (67%)	11 (48%)	2 (18%)	NS
Albumin (g/dl)	3.6 ± 0.2	2.8 ± 0.2	2.9 ± 0.3	3.2 ± 0.2	3.6 ± 0.2	NS
Cholesterol (mg/dl)	275.4 ± 17.2	215 ± 12.1	212.5 ± 26.7	246.3 ± 14.0	218 ± 23.1	0.05[d]
Edema	5 (42%)	5 (100%)	5 (83%)	15 (65%)	2 (18%)	0.01[b]
Nephrotic syndrome	2 (17%)	1 (20%)	3 (50%)	6 (26%)	0 (0%)	NS
Microhematuria (>5 RBC/hpf)	5 (42%)	3 (60%)	4 (67%)	12 (52%)	4 (36%)	NS
Hypocomplementemia	0 (0%)	1 (20%)	3 (50%)	4 (17%)	0 (0%)	NS
Acute renal failure	4 (33%)	1 (20%)	2 (33%)	7 (30%)	9 (82%)	0.02[b]
Dialysis at time of biopsy	2 (16%)	2 (40%)	2 (33%)	6 (26%)	7 (64%)	0.053[b]


RENAL SURVIVAL
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
(11)
(9)
(5)
(4)
(2)
(1)
(1)
p = 0.0196
0
6
12
18
24
30
36
42
48
TIME (months)

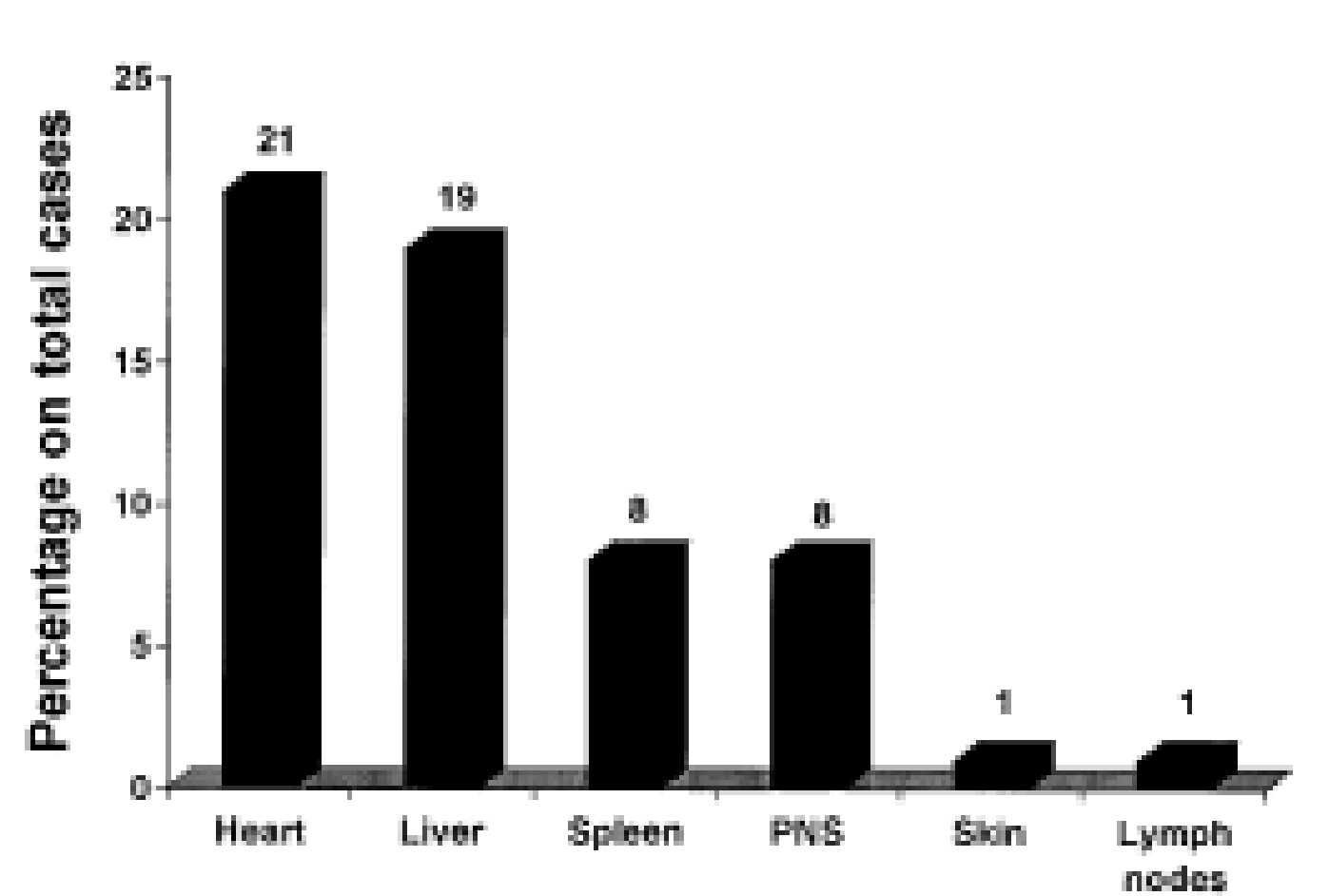
Light Chain Deposition Disease With Renal Involvement: Clinical Characteristics and Prognostic Factors

AJKD, Vol 42, No 6, 2003: pp 1154-1163

Variable	
No. of patients	63
Age (y)	58 ± 14.2
Sex (M/F %)	63.5/36.5
Renal function (%)	
Acute/rapidly progressive renal insufficiency	52
Chronic renal insufficiency	44
Normal	4
Serum creatinine (mg/dL)	3.8 (25^{th}, 75^{th} percentiles: 2.3, 7)
Proteinuria (%)	
>3.5 g/d	40
1-3.5 g/d	44
<1 g/d	16
Proteinuria (g/d)	2.7 (25^{th}, 75^{th} percentiles: 1.5, 5.2)


1,0
,8
,6
,4
,2
0,0
Renal survival
0
1
2
3
4
5
6
7
8
Follow-up (years)

DEPOSITI EXTRARENALI - LCDD



AJKD, Vol 42, No 6, 2003: pp 1154-1163

DEPOSITI EXTRARENALI - HCDD

- **Cuore**
  Scand J Rheumatol 1998

- **Tessuto sinoviale**
  Scand J Rheumatol 1998
  Curr Opin 2000

- **Cute**
  NDT 1998
  Hum Pathol 1988

- **Muscolo striato**
  NDT 1998

CARATTERISTICHE EMATOLOGICHE

Characteristic	LCDD	HCDD	LHCDD	All MIDD Patients
Number of patients	51	7	6	64
Clinical evidence of dysproteinemia	49 (96)	7 (100)	6 (100)	62 (97)
positive SPEP/SIFE	35 (69)	6 (86)	6 (100)	47 (73)
positive UPEP/UIFE	40 (78)	5/6 (83)	6 (100)	51/63 (81)
abnormal FLC ratio (<0.26 or >1.65)	43/43 (100)	4/4 (100)	4/4 (100)	51/51 (100)
markedly abnormal FLC ratio (<0.125 or >8)	34/43 (79)	3/4 (75)	3/4 (75)	40/51 (78)
multiple myeloma (≥10% plasma cells on bone marrow biopsy)	33 (65)	2 (29)	3 (50)	38 (59)
lytic lesions on skeletal survey	12 (24)	0 (0)	1 (17)	13 (20)
hypercalcemia at renal biopsy	4/45 (9)	0/5 (0)	0 (0)	4/56 (7)
mean hemoglobin at renal biopsy (g/dl)	10.2	10.5	10.2	10.2
Light chain type, κ/λ	40/9 (82/18)	5/2 (71/29)	5/1 (83/13)	50/12 (81/19)

Clin J Am Soc Nephrol 7: 231–239, 2012.

Findings and Outcomes	LCDD (n = 12)	LHCDD (n = 5)	HCDD (n = 6)	Pure MIDD (n = 23)	LCDD & MCN (n = 11)
Clinical diagnosis[a]					
multiple myeloma	7 (58%)	1 (20%)	1 (17%)	9 (39%)	10 (91%)
MGUS[b]	2 (17%)	3 (60%)	4 (66%)	9 (39%)	0 (0%)
isolated HCDD	0 (0%)	0 (0%)	1 (17%)	1 (4%)	0 (0%)
insufficient data	3 (25%)	1 (20%)	0 (0%)	4 (17%)	1 (9%)

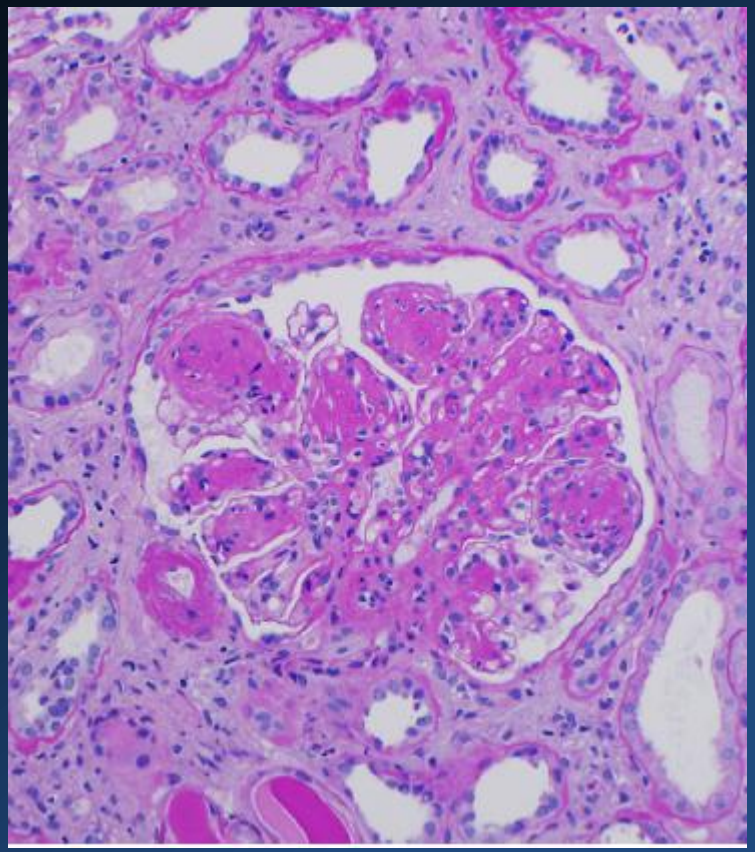
J Am Soc Nephrol 12: 1482–1492, 2001

Variable	
No. of patients	63
Age (y)	58 ± 14.2
Sex (M/F %)	63.5/36.5
Type of LC (κ/λ %)	68/32
Underlying disease (%)	
Idiopathic LCDD	32
MM	65
Lymphoproliferative disorders	3

AJKD, Vol 42, No 6, 2003: pp 1154-1163

ANATOMIA PATOLOGICA

- Glomerulosclerosi nodulare
- Aumento di cellularità mesangiale
- Ispessimento di MB tubulare
- Atrofia tubulare / fibrosi interstiziale
- IF: depositi lineari lungo GBM e TBM di LC/HC
- ME: depositi elettrondensi granulari in GBM e TBM



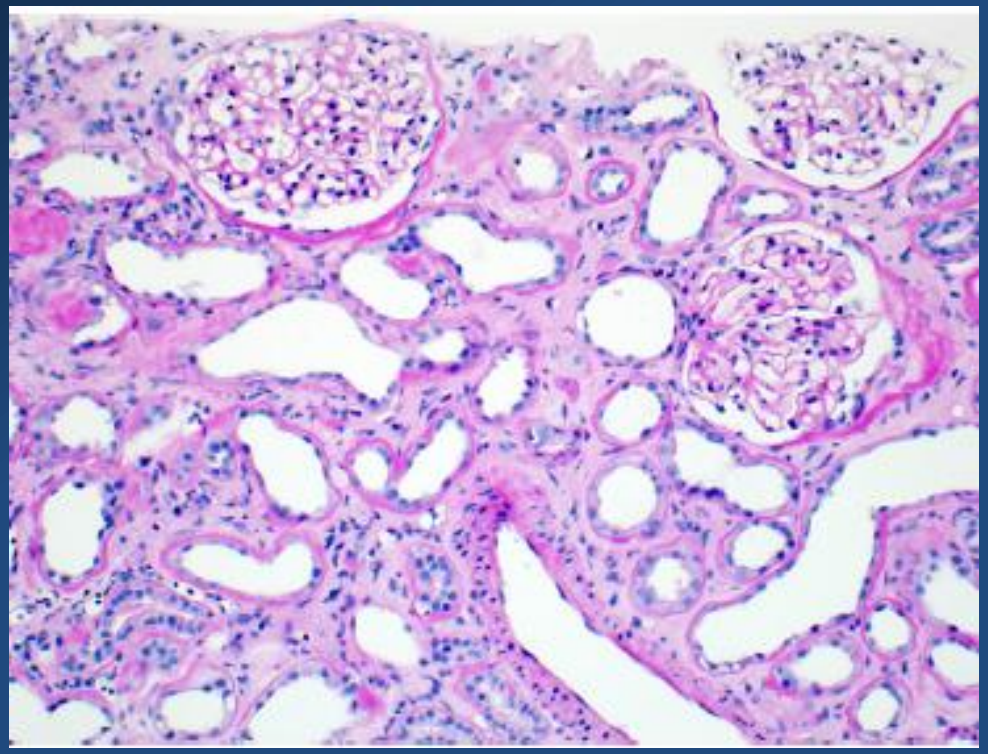
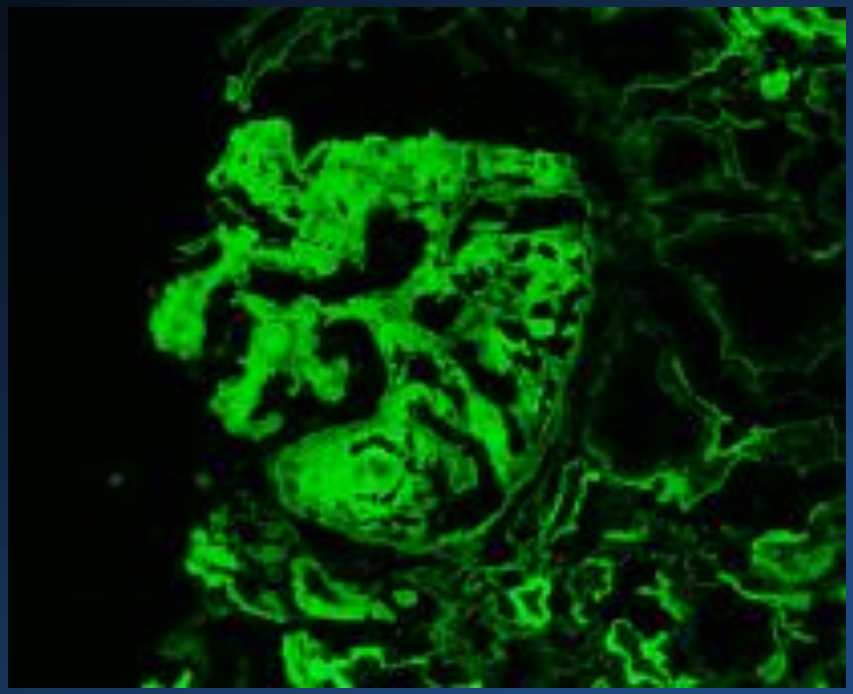
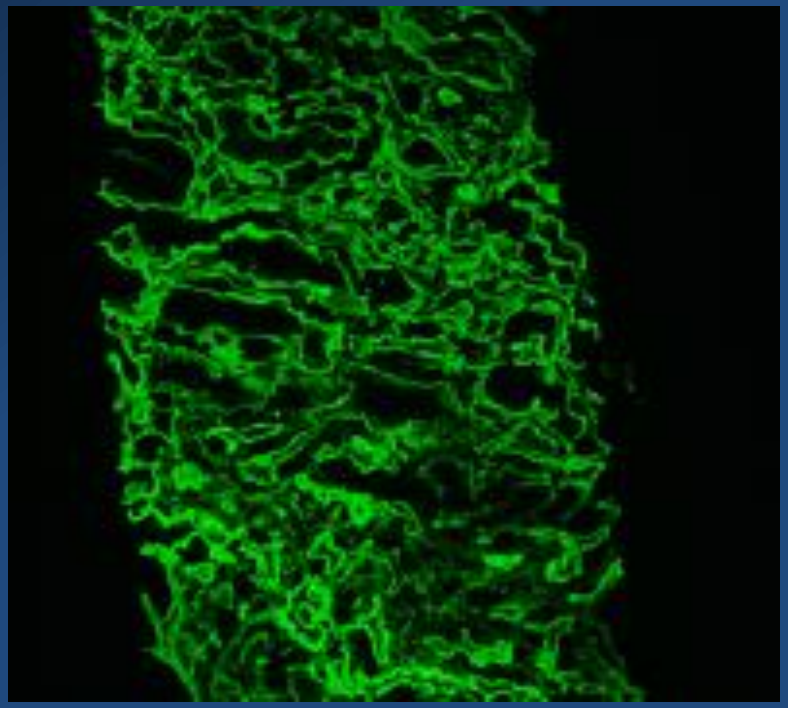


Table 1. Pathologic findings

Characteristic	LCDD	HCDD	LHCDD	All MIDD Patients
Number of patients	51	7	6	64
Mean number of glomeruli	18 (2–150)	15 (9–25)	12 (3–25)	17 (2–150)
Mean % of globally sclerotic glomeruli	24 (0–95)	15 (0–50)	21 (0–63)	23 (0–95)
Nodular mesangial sclerosis	30 (59)	6 (86)	3 (50)	39 (61)
interstitial fibrosis				
none	1 (2)	0 (0)	1 (17)	2 (3)
mild	15 (29)	3 (43)	3 (50)	21 (33)
moderate	16 (31)	4 (57)	0 (0)	20 (31)
marked	19 (37)	0 (0)	2 (33)	21 (33)
Degree of arteriosclerosis				
none	7 (14)	0 (0)	2 (33)	9 (14)
mild	19 (37)	6 (86)	3 (50)	28 (44)
moderate	23 (45)	0 (0)	1 (17)	24 (38)
marked	2 (4)	1 (14)	0 (0)	3 (5)
Monoclonal protein components detected by immunofluorescence	43 κ (84);8 λ (16)	6 γ (86); 1 α (14)	4 γ and κ (67); 1 α and κ (17); 1 α and λ (17)	43 κ (67); 8 λ (13); 6 γ (9); 4 γ and κ (6); 1 α (2); 1 α and κ (2); 1 α and λ (2)
Mesangial deposits on electron microscopy	31/48 (65)	7 (100)	6 (100)	44/61 (72)
GBM deposits on electron microscopy	46/48 (96)	6 (86)	6 (100)	58/61 (95)
TBM deposits on electron microscopy	46/46 (100)	7 (100)	5/5 (100)	58/58 (100)

Nasr et al - cJASN 2012



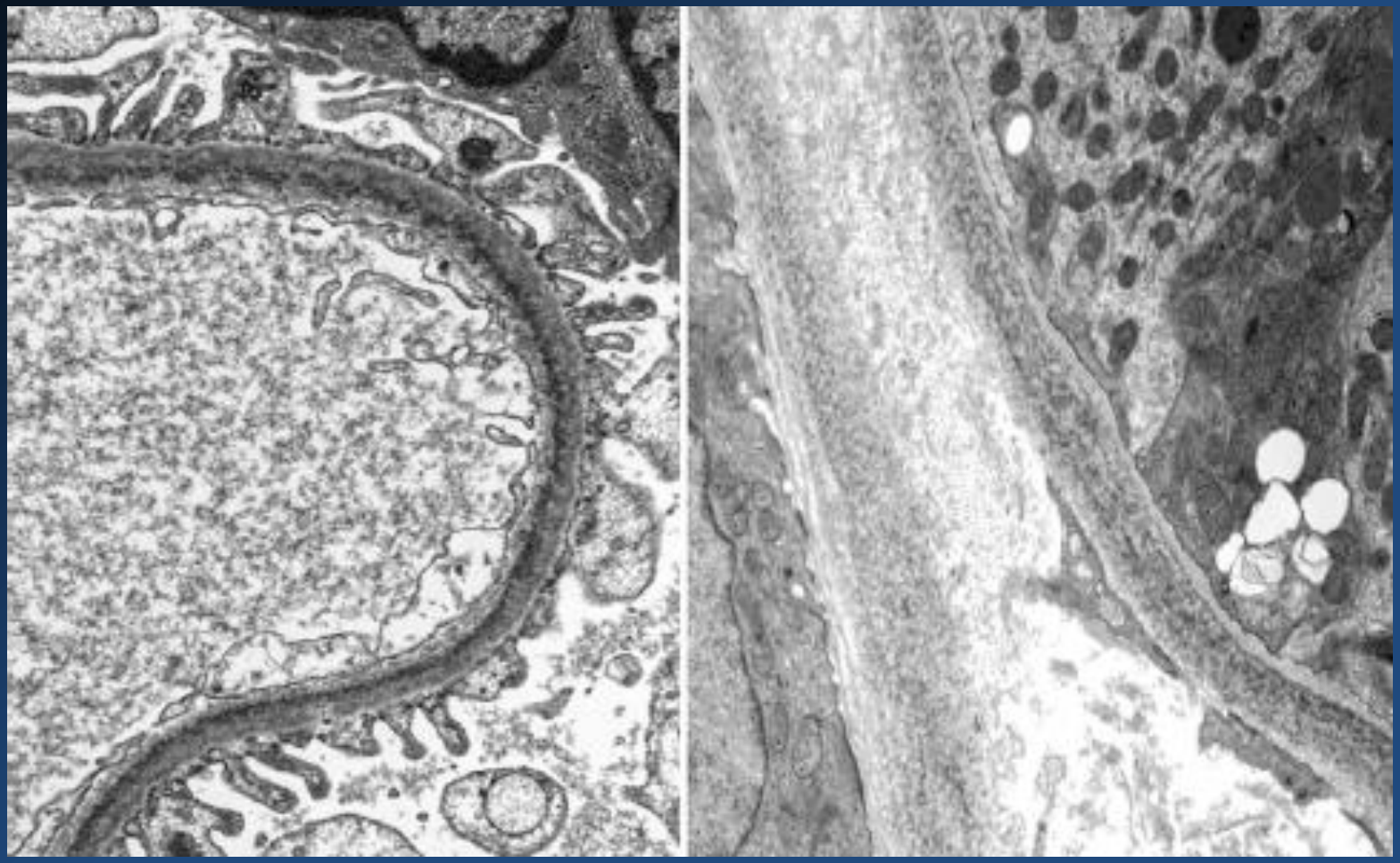


Depositi lineari diffusi di catena monoclonale lungo MB glomerulari e tubulari

Table 1. Pathologic findings

Characteristic	LCDD	HCDD	LHCDD	All MIDD Patients
Number of patients	51	7	6	64
Mean number of glomeruli	18 (2–150)	15 (9–25)	12 (3–25)	17 (2–150)
Mean % of globally sclerotic glomeruli	24 (0–95)	15 (0–50)	21 (0–63)	23 (0–95)
Nodular mesangial sclerosis	30 (59)	6 (86)	3 (50)	39 (61)
Degree of tubular atrophy and interstitial fibrosis				
none	1 (2)	0 (0)	1 (17)	2 (3)
mild	15 (29)	3 (43)	3 (50)	21 (33)
moderate	16 (31)	4 (57)	0 (0)	20 (31)
marked	19 (37)	0 (0)	2 (33)	21 (33)
Degree of arteriosclerosis				
none	7 (14)	0 (0)	2 (33)	9 (14)
mild	19 (37)	6 (86)	3 (50)	28 (44)
moderate	23 (45)	0 (0)	1 (17)	24 (38)
Monoclonal protein components detected by immunofluorescence	43 κ (84);8 λ (16)	6 γ (86); 1 α (14)	4 γ and κ (67); 1 α and κ (17); 1 α and λ (17)	43 κ (67); 8 λ (13); 6 γ (9); 4 γ and κ (6); 1 α (2); 1 α and κ (2); 1 α and λ (2)
microscopy				
GBM deposits on electron microscopy	46/48 (96)	6 (86)	6 (100)	58/61 (95)
TBM deposits on electron microscopy	46/46 (100)	7 (100)	5/5 (100)	58/58 (100)

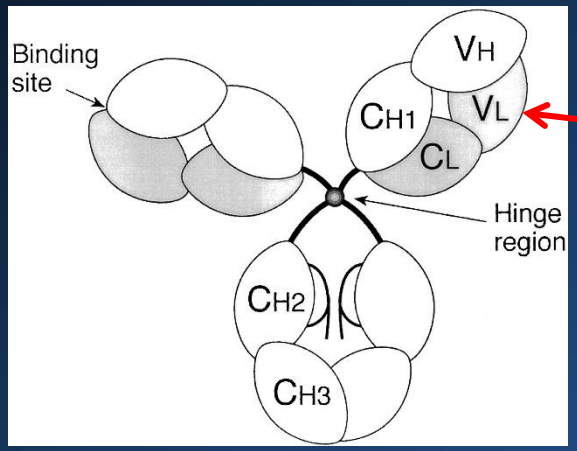
Nasr et al - cJASN 2012



PATOGENESI

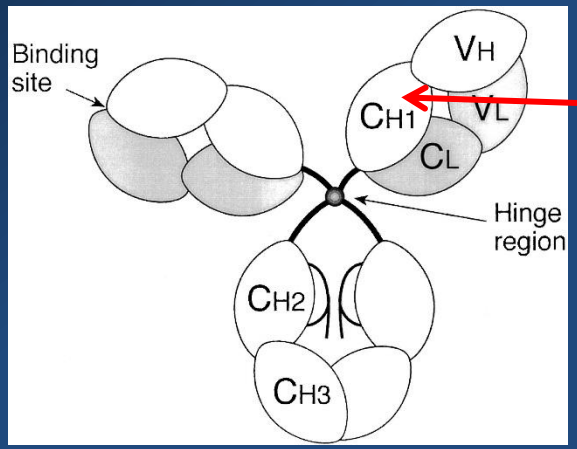
↑ di matrice extracellulare a livello mesangiale e interstiziale indotto da deposito di catena leggera/pesante monoclonale

LCDD



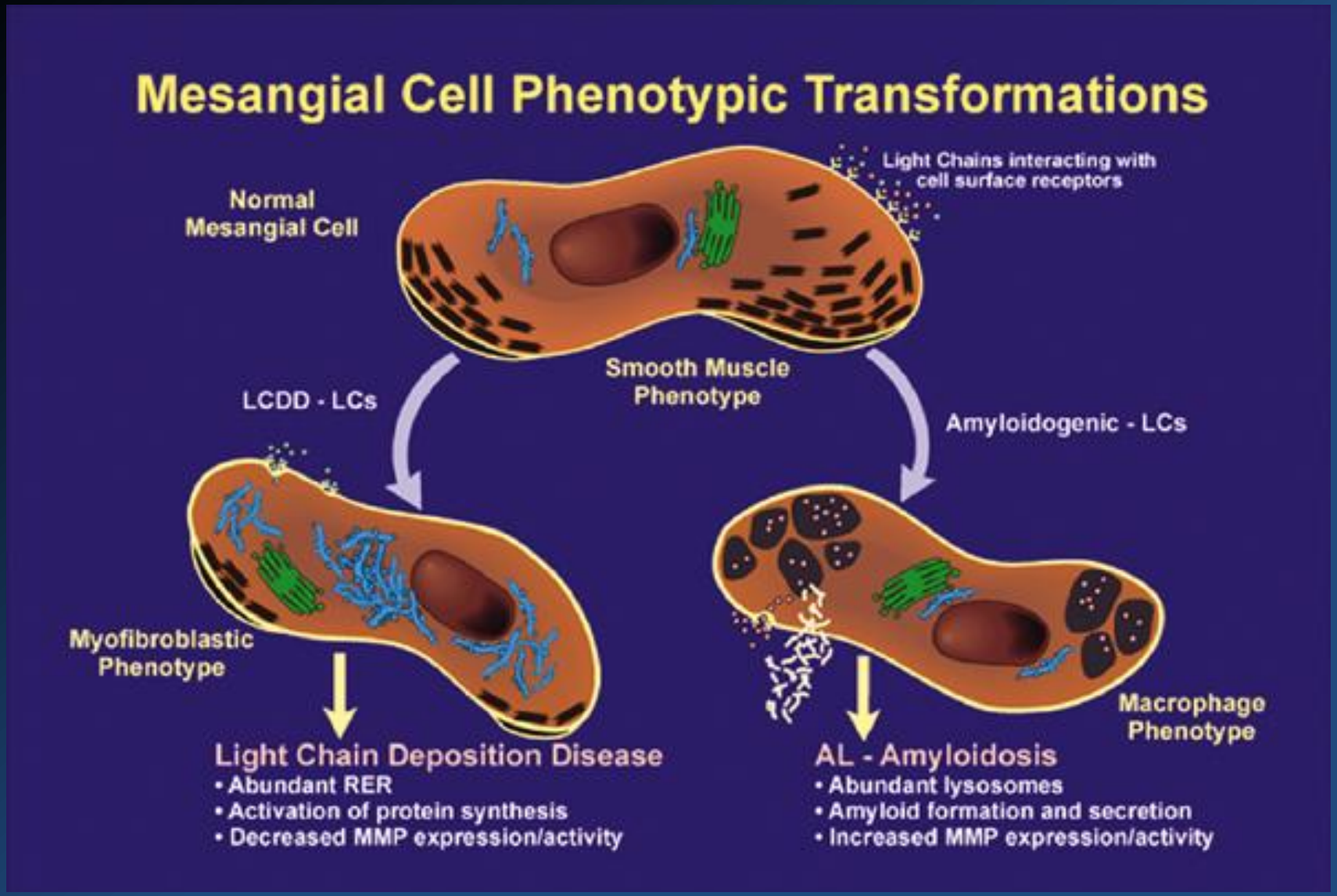
Alterata glicosilazione di regione variabile di LC

HCDD



Delezione a livello di regione costante 1 di HC

Ronco P. JASN 2001
Ronco P cJASN 2006



Keeling J. Lab Invest 2004

PROGNOSI

Table 5. Outcome and prognostic indicators in MIDD in this study and in previous reports

	Pozzi *et al.* (7)[a]	Lin *et al.* (1)	This Study
Study period	1972–2002	1982–2002	1992–2011
Number of patients	63	23	64
MIDD subtype (*n*)	62 LCDD, 1 LHCDD	12 LCDD, 6 HCDD, 5 LHCDD	51 LCDD, 7 HCDD, 6 LHCDD
Duration of follow-up (mo)	Median 28	Mean 22	Mean 34 (median 25)
Patients who reached ESRD on follow-up (%)	57	48	39
Patients who died on follow-up (%)	59	43	32
Predictors of renal survival on multivariate analysis	Lower initial serum creatinine Younger age	Lower initial serum creatinine	Lower initial serum creatinine
Predictors of patient survival on multivariate analysis	Younger age Absence of MM Absence of extrarenal involvement	Lower initial serum creatinine	Absence of lytic bone lesions

MM concomitante **65%** **39%** **59%**

Nasr et al - cJASN 2012

GLOMERULONEFRITE PROLIFERATIVA CON DEPOSITI DI IgG MONOCLONALI

Proliferative Glomerulonephritis with Monoclonal IgG Deposits

Samih H. Nasr,* Anjali Satoskar,† Glen S. Markowitz,* Anthony M. Valeri,‡
Gerald B. Appel,‡ Michael B. Stokes,* Tibor Nadasdy,† and Vivette D. D'Agati*

JASN 20: 2055–2064, 2009

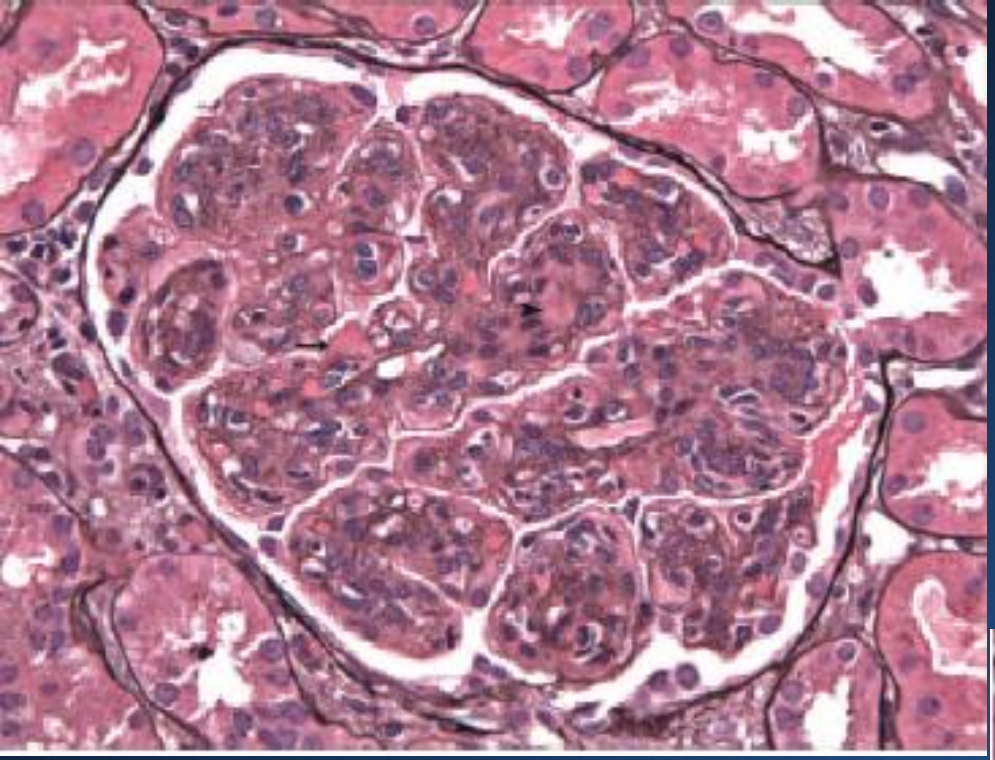
37 pazienti valutati retrospettivamente

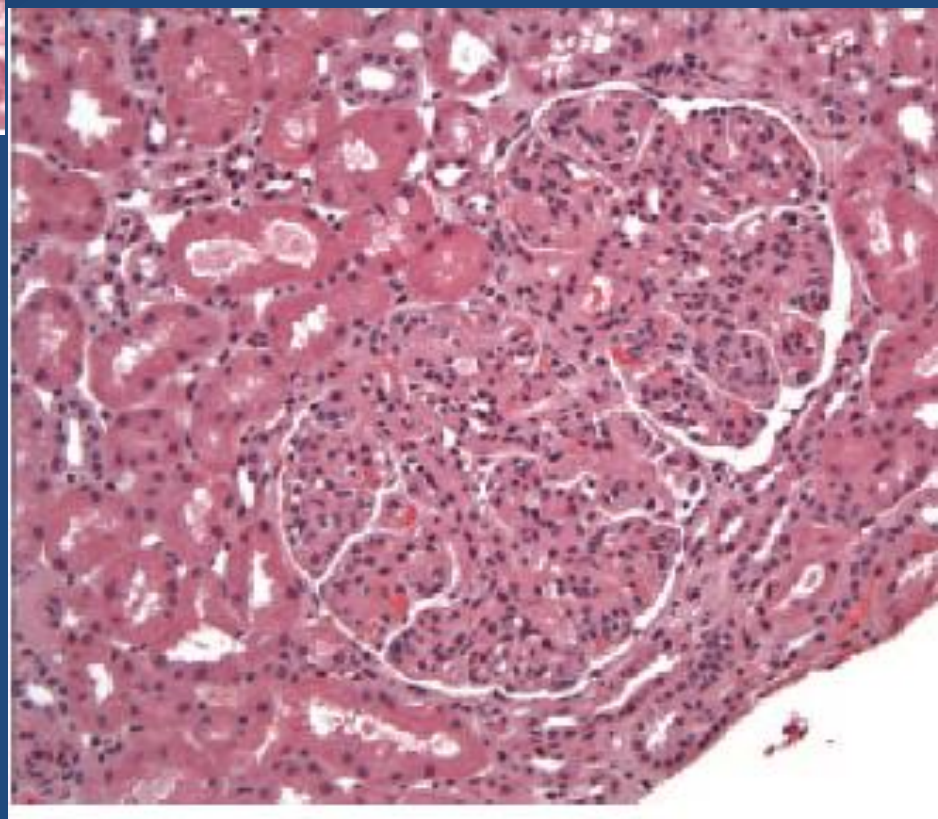
Table 2. Clinical characteristics at presentation

Characteristic	Value
Peripheral edema (*n* [%])	23 (62.2)
24-h urine protein (g/d; mean [range])	5.70 (0.36 to 17.00)
Proteinuria <1 g/24 h (*n* [%])	1/35 (2.9)
Proteinuria 1–3g/24 h (*n* [%])	10/35 (28.6)
Proteinuria >3g/24 h (*n* [%])	24/35 (68.6)
Full nephrotic syndrome (*n* [%])	17/35 (48.6)
Serum albumin (g/dl; mean [range])	3.1 (1.1 to 4.9)
Hematuria (*n* [%])	27/35 (77.1)
Serum creatinine at biopsy (mg/dl; mean [range])	2.77 (0.70 to 17.00)
Renal insufficiency at presentation (*n* [%])	25 (67.6)
Evidence of dysproteinemia (*n* [%])[a]	11/37 (29.7)
Serum paraprotein only	4
Serum and urine paraprotein	7
Multiple myeloma	1
AL-amyloid	1
Low C3 (*n* [%])	3 (8.1)
Low C4 (*n* [%])	3 (8.1)
Low C3 and C4 (*n* [%])	4 (10.8)
Positive serum cryoglobulin (*n* [%])[b]	0 (0.0)
Positive hepatitis C antibody (*n* [%])	1/30 (3.3)
Positive rheumatoid factor (*n* [%])	1/18 (5.5)

Table 3. Light microscopic findings[a]

Pathologic Findings	Value
No. of glomeruli (mean)	17.7
% of globally sclerotic glomeruli (mean)	17.5
Predominant histologic pattern	
membranoproliferative GN[b]	21 (56.8)
endocapillary proliferative GN[b]	13 (35.1)
mesangial proliferative GN	1 (2.7)
membranous GN	2 (5.4)
Crescents[c]	12 (32.4)
focal	10
diffuse	2
Interstitial inflammation: None/focal/diffuse[d]	4/28/5 (10.8/75.7/13.5)
Tubular atrophy and interstitial fibrosis: None/mild/moderate/severe[e]	2/25/6/4 (5.4/67.6/16.2/10.8)
Arteriosclerosis and arteriolar hyalinosis: None/mild/moderate/severe	9/16/11/1 (24.3/43.2/29.7/2.7)
Concurrent vascular amyloid	1 (3)

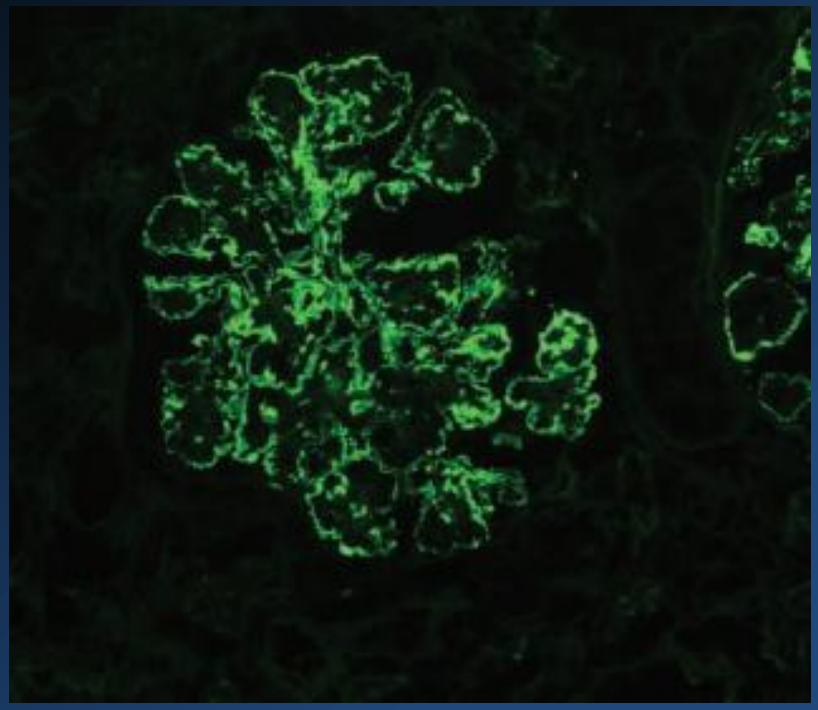


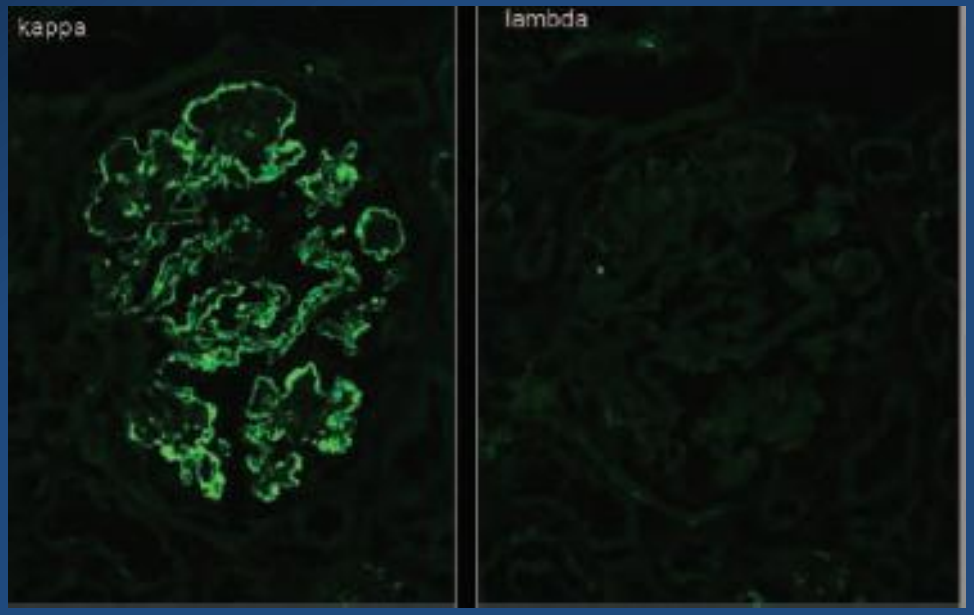


Immunofluorescenza

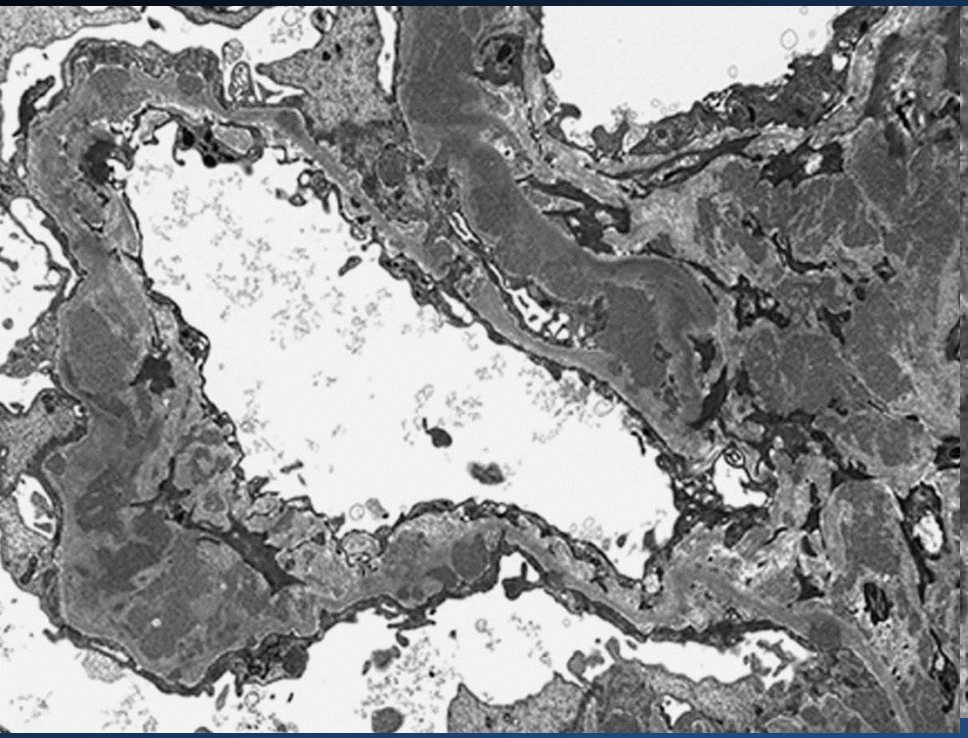
Depositi granulari /semilineari
a livello di capillari glomerlari e mesangiale
di IgG con restrizione clonale κ >λ e C3

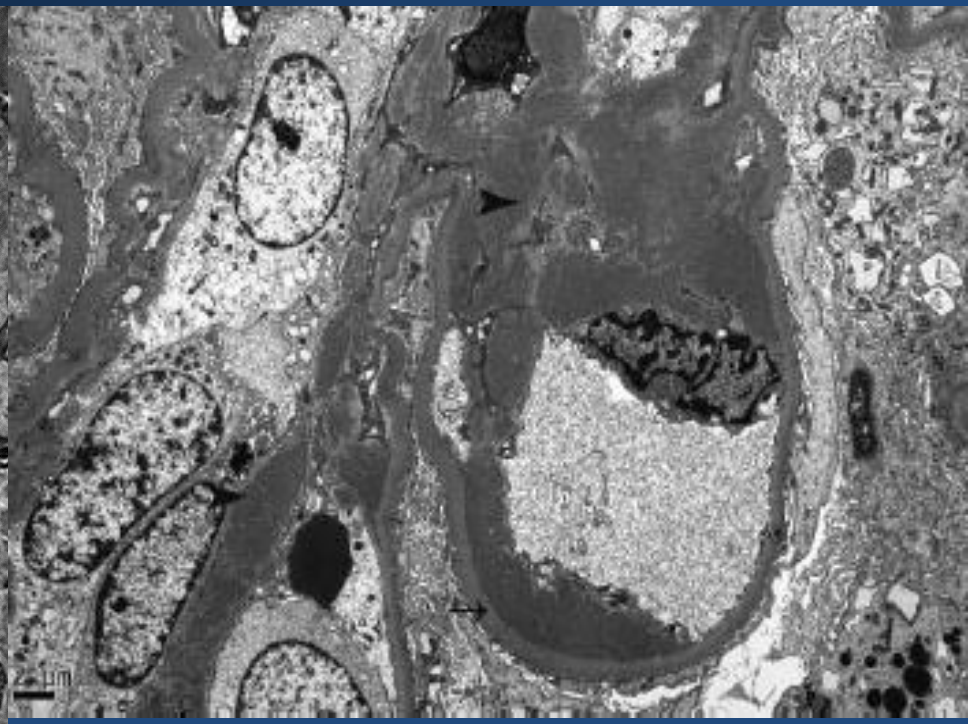
Parameter	No. of Patients	% of Patients
IgG[a]	37	100
IgG1 κ	7/32	21.9
IgG1 λ	2/32	6.3
IgG2 λ	2/32	6.3
IgG3 κ	17/32	53.1
IgG3 λ	4/32	12.5
C3	36	97.3
C1q	23/36	63.9




kappa
lambda

Microscopia elettronica





Depositi elettrondensi mesangiali, subepiteliali e intramembranosi con reduplicazione di GBM

Terapia e prognosi

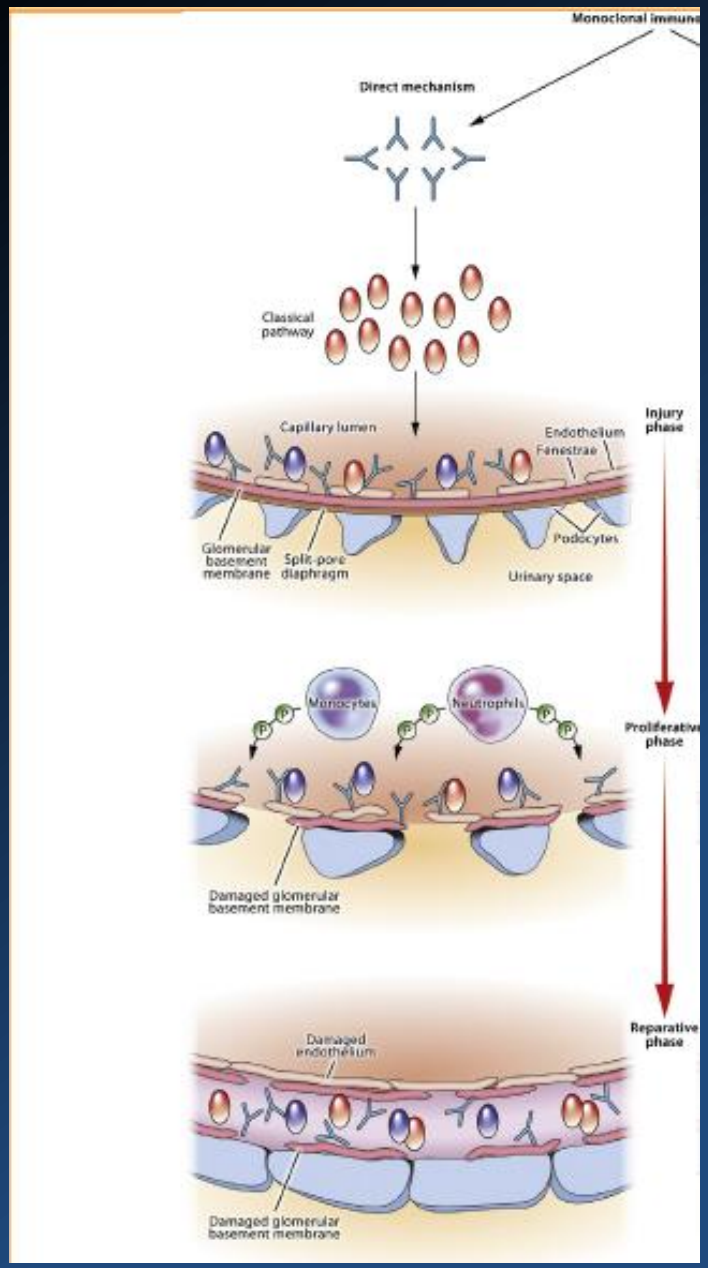
Table 6. Clinical follow-up (32 patients)

Parameter	Value
Duration of follow-up (mo; mean [range])	30.3 (1.0 to 114.0)
Treatment	
none	5 (15.6)
RAS blockade alone	9 (28.1)
IM	18 (56.3)
steroids	11
cyclophosphamide	3
cyclosporine	2
mycophenolate mofetil	5
rituximab	4
chlorambucil	1
thalidomide	2
bortezomib (Velcade)	1
Outcome[a]	
CR	4 (12.5)
PR	8 (25.0)
PRD	12 (37.5)
Persistent hematuria (with normal creatinine and no proteinuria)	1 (3.1)
ESRD	7 (21.9)
Death	5 (15.6)

2 Complete Remission,
2 Partial Remission
4 Persistent Renal Dysfunction
1 ESRD

2 Complete Remission,
6 Partial Remission
7 Persistent Renal Dysfunction
3 ESRD

Patogenesi



Proliferazione di uno o più cloni B cellulari in corso di risposta immunitaria ad antigene estrinseco o intrinseco, produce IgG monoclonali (in particolare IgG3) in grado di:

- **aggregare,**
- **depositarsi nei glomeruli per intrappolamento e/o interazione con cariche negative glomerulari**
- **attivare il complemento attraverso la via classica.**

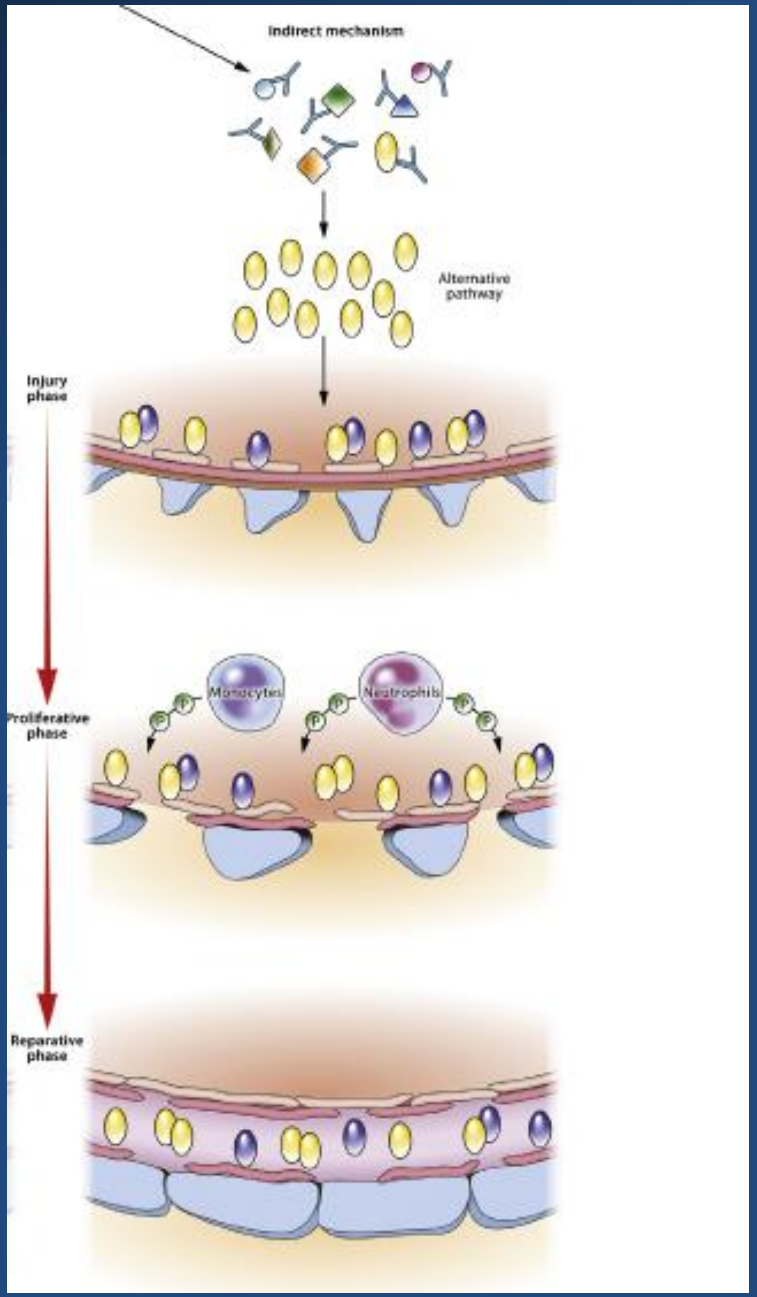
Sethi S. Mayo Clin Proc. 2013;88(11):1284-1293

Ig monoclonale può attivare
la via alternativa del complemento
agendo da auto-Ab verso
le proteine regolatrici del complemento
o la C3 convertasi
con deposito di fattori complementari a livello mesangiale e subendoteliale

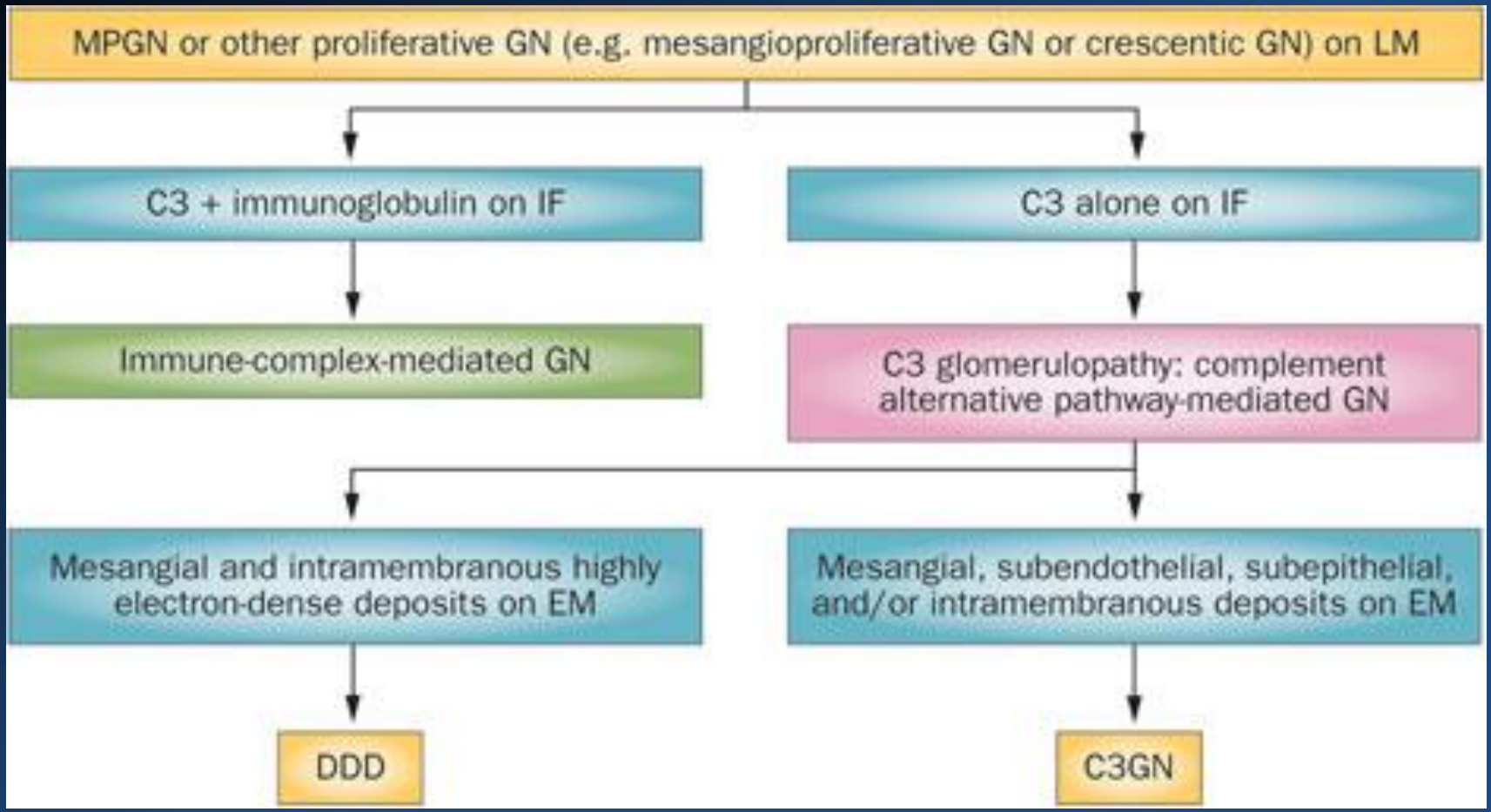
C3 glomerulopathy

C3 glomerulonephritis

Depot Dense Disease



C3 GLOMERULOPATHY ASSOCIATA A GAMMOPATIA MONOCLONALE



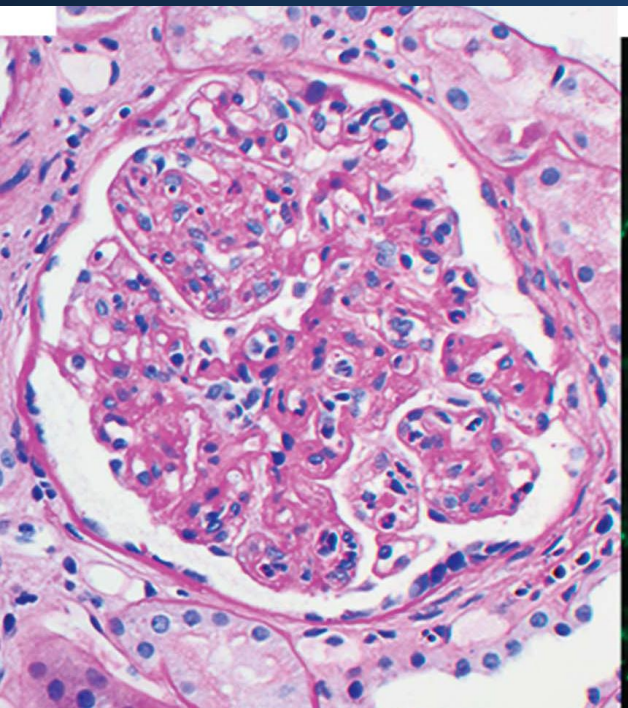
Nat. Rev. Nephrol. 8, 634–642 (2012)

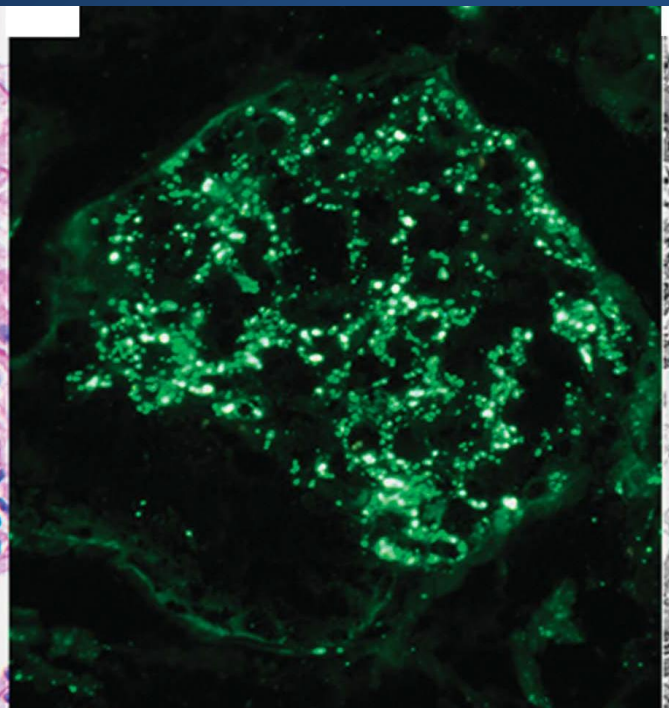
C3 glomerulonephritis

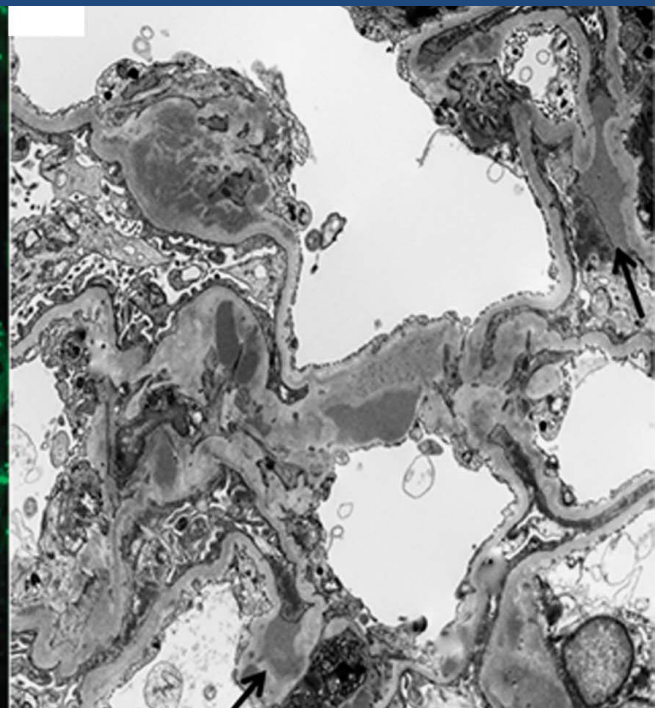
Ipercellularità mesangale ed endocapillare con infiltrato linfo/monocitaria intracepiallare

IF: depositi granulari di C3 a livello mesangiale e della parete dei capillari glomerulari

ME: depositi elettrondensi mesangiali e subendoteliali.







Glomerulonephritis With Isolated C3 Deposits and Monoclonal Gammopathy: A Fortuitous Association?

Clin J Am Soc Nephrol 6: 2165–2174, 2011

Table 1. Renal presentation at baseline and clinical outcome

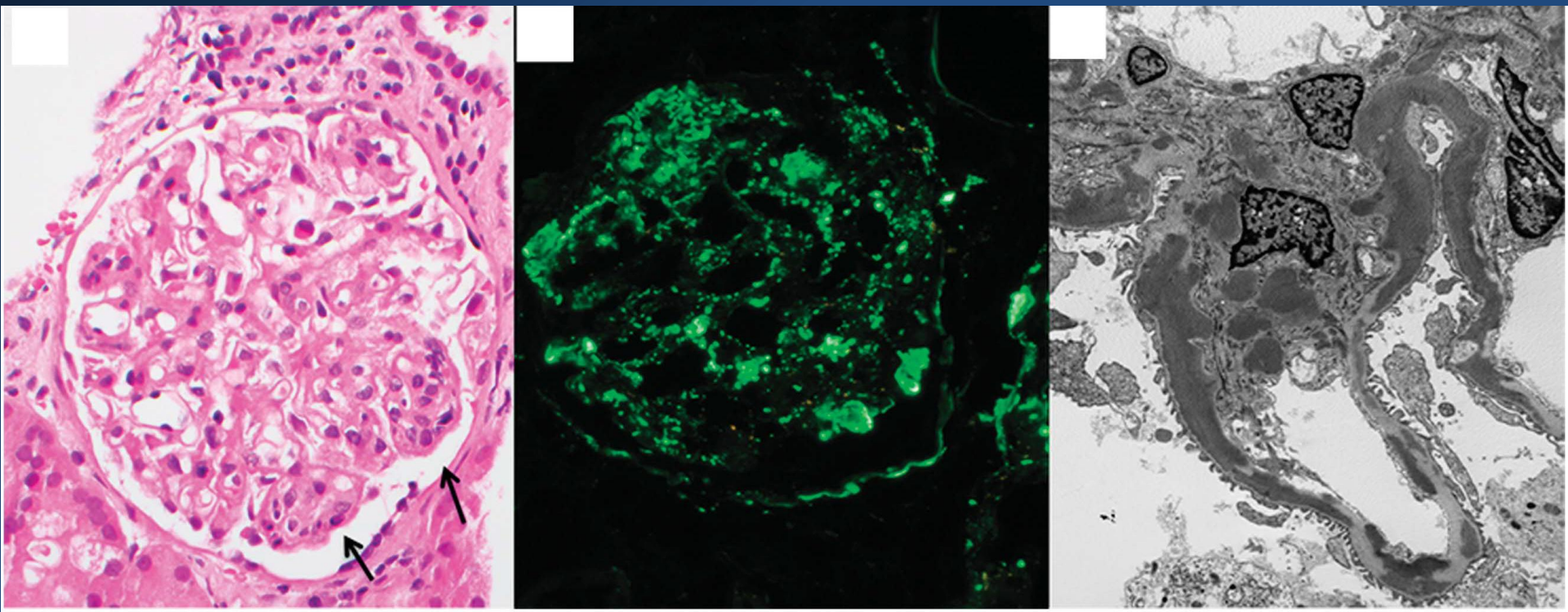
Patient No.	1	2	3	4	5	6
Baseline characteristics						
age (years)/gender (M/F)	40/F	59/M	74/M	71/F	73/F	64/M
hypertension	No	Yes	Yes	Yes	Yes	Yes
serum creatinine (μmol/L)	70	150	150	298	130	280
GFR ml/min per 1.73 m^2	85	44	42	14	37	21
protids/albumin (g/L)	75/32	60/34	66/28	69/35	57/24	64/29
proteinuria (g/24 h)/ Nephrotic syndrome	0.5/No	2/No	3.3/Yes	2.5/No	5.1/Yes	3.5/Yes
haematuria	Yes[a]	Yes	Yes	Yes	Yes[a]	Yes
serum monoclonal Ig	IgG1κ	IgG1λ	IgGκ	IgGκ	IgGκ	IgGλ
MIg concentration (g/L)	30	7	16	18.9	21.3	4
serum FLC (mg/L)	NA	988 (λ)	NA	525 (κ)	102 (κ)	NA
kappa/lambda ratio	NA	0.03	NA	53.2	5.0	NA
LC proteinuria	κ (U + S)	λ (U + S)	κ (U)	κ (U)	κ (U + S)	No
bone marrow PC (%)	4	< 5	3 (dystrophic)	7.5	5	3
Treatment						
time from diagnosis (months)		47	36	7	20	
serum creatinine (μmol/L)		450	180	500	250	
GFR (ml/min per 1.73 m^2) at the onset of treatment		12	34	8	17	
chemotherapy regimen	No treatment	Dex	Mel + Dex	CYC + Dex	Bortezomib + Dex	No treatment
Outcome						
ESRD (months from diagnosis)	Yes (90)	Yes (55)	Yes (48)	Yes (12)	Yes (23)	No
serum Cr (μmol/L)						290
serum monoclonal IgG (g/l)	23	17	27	14	NA	6
serum FLC (mg/L)	8800 (κ)	NA	NA	653 (κ)	559 (κ)	NA
kappa/lambda ratio	1392.4	NA	NA	31.4	36.3	NA
death	Yes	No	No	No	No	No
follow-up time (months)	162	94	60	25	36	4

Depot Dense Disease

Ipercellularità mesangiale ed endocapillare con ispessimento segmentale di GBM

IF: depositi granulari/semilineari di C3 a livello mesangiale e della parete dei capillari glomerulari

ME: depositi elettrondensi intramembranosi



Dense Deposit Disease Associated With Monoclonal Gammopathy of Undetermined Significance

Sanjeev Sethi, MD, PhD,[1] William R. Sukov, MD,[1] Yuzhou Zhang, PhD,[2] Fernando C. Fervenza, MD, PhD,[3] Donna J. Lager, MD,[1] Dylan V. Miller, MD,[1] Lynn D. Cornell, MD,[1] Srivilliputtur G. Santhana Krishnan, MD,[4] and Richard J. H. Smith, MD[2,5]

AJKD 2010

Table 2. Clinical and Pathologic Features and Laboratory Findings Associated With 10 Patients With an Established Diagnosis of MGUS Diagnosed With DDD on Kidney Biopsy

Case No.	Sex	Age (y)	Presentation	Serum M Protein	Light Microscopy	C3[a]	Follow-up
1	F	77	Hematuria	IgG κ	MPGN	3+	ESRD, dialysis, no myeloma at 44 mo
2	F	58	Nephrotic syndrome	IgG λ	MPGN	3+	ESRD, recurrence in transplant at 1 mo with eventual transplant failure
3	F	63	Proteinuria	IgG κ	MPGN	3+	ESRD, dialysis at 24 mo; no myeloma at 72 mo
4	M	60	Anemia, proteinuria	IgG λ	Nodular glomerulosclerosis	2+	ESRD, dialysis; myeloma at 120 mo
5	F	60	Kidney failure & proteinuria	IgG κ	Mesangioproliferative changes	2+	Chronic kidney failure, no myeloma at 4 mo
6	M	74	Kidney failure & proteinuria	IgG & IgA λ	Nodular mesangioproliferative changes	2+	Chronic kidney failure, plasma cell proliferative disorder at 22 mo
7	F	61	Kidney failure	IgG λ	FSGS with fibrous crescents	3+	Recent diagnosis, chronic kidney failure
8	F	52	Proteinuria	IgG κ	MPGN, exudative	3+	Recent diagnosis, normal kidney function
9[b]	F	58	Hematuria, acute kidney failure	IgG κ	MPGN with crescents	3+	Recent diagnosis, presented with SCr level of 7.4 mg/dL
10	F	49	Kidney failure & proteinuria	IgG κ	MPGN	3+	Recent diagnosis, presented with SCr level of 1.8 mg/dL and protein excretion of 500 mg/d

CONCLUSIONI

Il coinvolgimento renale in corso di gammopatie monoclonali può avvenire anche in presenza di patologie a bassa massa.

La gestione di questi pazienti richiede una stretta collaborazione tra ematologo, nefrologo e anatomo-patologo, al fine di arrivare precocemente alla diagnosi.

Compito del nefrologo e del patologo è porre tempestivamente diagnosi di patologia linfoproliferativa, in presenza di quadro clinico aspecifico caratterizzato da anomalie urinarie, ipertensione e/o insufficienza renale.

Compito dell'ematologo è indirizzare al nefrologo i pazienti con anomalie urinarie isolate o insufficienza renale anche lieve, per valutare eventuale indicazione nefrobioptica.

GRAZIE PER LA CORTESE ATTENZIONE