Glomerulonephritis with non-organized non-Randall monoclonal Ig deposits (PGNMID): French experience of 71 patients

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Disclosures

None
Previous studies

A clone-directed approach may improve diagnosis and treatment of proliferative glomerulonephritis with monoclonal immunoglobulin deposits.


The clinicopathologic characteristics of kidney diseases related to monotypic IgA deposits.


Proliferative glomerulonephritis with monoclonal IgG deposits recurs in the allograft.


Kidney diseases associated with monoclonal immunoglobulin M-secreting B-cell lymphoproliferative disorders: a case series of 35 patients.

Chevallier D, Bidoux L, Ecobichon D, Javavane V, Singh S, Aruffo A, Teyssier A, Quettard M, Niel S, Bender S, Gousin JM, Jacob A, Ferrarri AP, Rouchou G.


More than 20 case reports and small series
Inclusion criteria

- Patients with monotypic glomerular deposits (1993-2018)
- Granular electron-dense deposits by EM, resembling immune complex GN
- No clinical and biological evidence of cryoglobulinemia

71 patients

Symptomatic treatment
- n=21

Immunosuppressive therapy
- n=15

Chemotherapy
- n=35
  - Detected B-cell clone
    - n=15
  - Undetected B-cell clone
    - n=20
Clinical characteristics at presentation

- Mean age: 59 years (range: 24-86 years)
- Renal presentation:
  - Renal insufficiency: 73% (CKD stage 3 = 50%, stage 4 = 33%, stage 5 = 17%)
  - Proteinuria: 100% (mean = 4.8 g/24h)
  - Nephrotic syndrome: 59%
  - Hematuria: 85%
  - Hypertension: 79%
- Hypocomplementemia: 18% (low C3 +/- C4)
- No extra-renal manifestation
Pathological findings (LM)

75%

14%

11%
Pathological findings (IF)

- IgGκ: 77%
- IgGλ: 10%
- IgMκ: 6%
- IgMλ: 7%
- IgAκ: 6%
- κ: 0%
- λ: 83%

**IgG-PGNMID (n=55)**

- γ3: 13%
- κ: 4%
- λ: 0%
Pathological findings (EM)
Hematological characteristics at presentation

- **IgM-PGMID (n=7)**
  - IFE+FLC: 86%
  - IFE: 100%
  - Abnormal FLC: 100%
  - Subtypes: Lymphoplasmacytic (n=4), MZL (n=3)

- **LC-PGMID (n=5)**
  - IFE+FLC: 80%
  - IFE: 80%
  - Abnormal FLC: 80%
  - Subtypes: Symptomatic MM (n=2), Indolent MM (n=2), Unknown (n=1)

- **IgA-PGMID (n=4)**
  - IFE+FLC: 75%
  - IFE: 75%
  - Abnormal FLC: 75%
  - Subtypes: Symptomatic MM (n=1), Plasmacytic (n=2), Unknown (n=1)

- **IgG-PGMID (n=55)**
  - IFE+FLC: 29%
  - IFE: 15%
  - Abnormal FLC: 15%
  - Subtypes: Plasmacytic (n=4), CLL (n=2), MZL (n=2), Unknown (n=47)

The detection rate and the nature of the B-cell clone differ according to the subtype of PGNMID.
Treatment and outcome

Whole cohort

Chemotherapy
IS therapy
Symptomatic

Cloned detected with clone-directed therapy n=15
No clone detected with empirical therapy n=20
- CyBorD n=13 IgG-PGNMID
- RTX-CYC-D n=4 IgG-PGNMID
- RTX-BorD n=3 IgG-PGNMID

Rituximab n=4 IgG-PGNMID
CYC +/- Pred n=4 (IgG-PGNMID, n=3; LC-PGNMID, n=1)
MMF n=3 IgG-PGNMID
Prednisone n=4 (IgG-PGNMID, n=3; IgA-PGNMID, n=1)

Proven or suspected clone-directed approach seems effective

Clone detected n=15
No clone detected n=20

IgG3k-PGNMID n=18/20
IgG3k-PGNMID: clone detection?

Only patients with negative immunofixation and normal FLC at baseline

**Serum immunoblot**
(n=20)

IgG3k detectable in 11 cases

**Immunoglobulin Repertoire Sequencing**
(n=12)
RepSeq analysis (1 patient)

M-spike (IgGk) was detectable at one-year follow-up

Sensitivity of immunofixation?
RepSeq analysis (11 patients)

Is it really monoclonal in all cases: oligoclonal?

In progress...
Conclusion

- Renal limited disorder with constant proteinuria
- Nature and rate of detection of B-cell clone varying according to the subtype of PGNMID
- Clone-directed approach seems effective to improve renal outcome
- Physiopathology of IgG3k-PGNMID is still unknown

RepSeq analysis (bone marrow) vs. Proteomic analysis (kidney)
Thank you

Collaborators

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