Primary glomerulonephritis with predominant mesangial immunoglobulin G deposits

Néphropathie glomérulaire primitive a dépôts mesangiaux d'IGG

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A R É S U M É

Introduction: Les dépôts glomérulaires sont une caractéristique pathologique majeure d'une large gamme de néphropathies glomérulaires et peuvent être situés dans les régions mésangiale, sous-épithéliale et sous-endothéliale. Des cas rares de glomérulopathies primitives définis par des dépôts mésangiaux exclusifs ou prédominants d'IgG ont été signalés.

Méthodes: Nous avons examiné les résultats de 848biopsies rénales pratiquées dans notre département entre 2007 et 2016, on a trouvé un seul cas de glomérulopathie primitive à dépôts mésangiaux d'IgG en l'absence de toute preuve de lupus érythémateux systémique, d'autres maladies systémiques ou d'infections.

Case report: Patient de sexe masculin âgé de 55 ans consulte pour des œdèmes. A la biologie, il avait un syndrome néphrotique avec hématurie. Le taux de créatinine était à 88 µmol/l. Il ne présentait pas de syndrome inflammatoire biologique. IL a bénéficié d'une ponction biopsie rénale concluant à des dépôts mésangiaux exclusifs d'IgG sans lésions prolifératives. Le bilan immunologique était sans anomalies durant toute la période de suivi. Les sérologies: HVB, HVC étaient négatives. Le patient était alors mis sous corticothérapie à pleine dose (1mg/Kg/j). L'évolution était marquée par une rémission complète atteinte après 3mois du début du traitement. Au cours du suivi, le patient a présenté 3 rechutes du syndrome néphrotique en 3 ans sans facteur de décompensation évident. La décision était alors de mettre le patient sous Mycophénolate mofétil (MMF) avec une rémission complète atteinte après 2 mois.

Conclusion: La néphropathie glomérulaire à dépôts mésangiaux d'IgG est un type de glomérulopathie primaire très rare mais distinct.

M o t s - c l é s

Néphropathie glomérulaire- ponction biopsie rénale- dépôts mésangiaux -IgG

S U M M A R Y

Introduction: Glomerular deposits are a major pathologic feature of a wide range of human glomerulonephritis and may be located in the mesangial, subepithelial, and subendothelial regions. Rare cases of primary glomerulonephritis definied by exclusive or predominant mesangial IgG deposits were reported.

Methods: We reviewed the pathologic findings for the 848 renal biopsies examined in our department between 2007 and 2016, one case of primary mesangial IgG glomerulonephritis (MIG) in the absence of any evidence of systemic lupus erythematous (SLE), of other systemic diseases or of Infections.

Reported case: Male patient aged 55 years consults for nephrotic syndrome (proteinuria=7g/1.73m2/day; Albuminemia=14g/L) with hematuria. The serum creatinine concentration was 88 µmol/l, and the creatinine clearance was on MDRD at 82 ml/min/1.73m2. He had a renal biopsy showing the absence of proliferative lesions and the presence of exclusive mesangial IgG deposit. CH50, C3 and C4 levels were normal and antinuclear antibody and anti-DNA antibody assays remained negative during the follow-up period. A full dose corticosteroid was initiated (1mg/Kg/day). The interval from onset of steroid therapy to remission was 2 months. During follow-up; the patient had developed 2 relapsing nephrotic syndrome episods. Then he was switched to Mycophenolate mofetil with remission after 2 months.

Conclusion:MIG is a very rare but distinct type of primary glomerulonephritis that is characterized by exclusive or predominant mesangial IgG deposits. Its renal prognosis may be less favorable than previously reported because of the possibility of steroids resistance of the nephrotic syndrome and the recurrence after renal transplantation.

K e y - w o r d s

Renal biopsy- glomerulonephritis- mesangial IgG deposits

Glomerular deposits are a major pathologic feature of a wide range of human glomerulonephritis and may be located in the mesangial, subepithelial, and subendothelial regions. Rare cases of primary glomerulonephritis defined by exclusive or predominant mesangial IgG deposits were reported.

AIM

We reviewed the pathologic findings for the 848 renal biopsies examined in our departement between 2007 and 2016, a case of primary mesangial IgG glomerulonephritis (MIG) in the absence of any evidence of systemic lupus erythematous (SLE), infections or other systemic disease was found.

REPORTED CASE

Male patient aged 50 years consults for nephrotic syndrome (proteinuria=7g/1.73m^2/ day, Albuminemia=14g/l, Protidemia=31g/l) with hematuria. The serum creatinine concentration was 88 µmol/l, and the creatinine clearance was on MDRD at 82 ml/min/1.73m2. The hemoglobin level was 12 g/dl. He had no inflammatory biological syndrome.

The results of the renal biopsy studies are as follows: (Figure 1), (Figure 2).

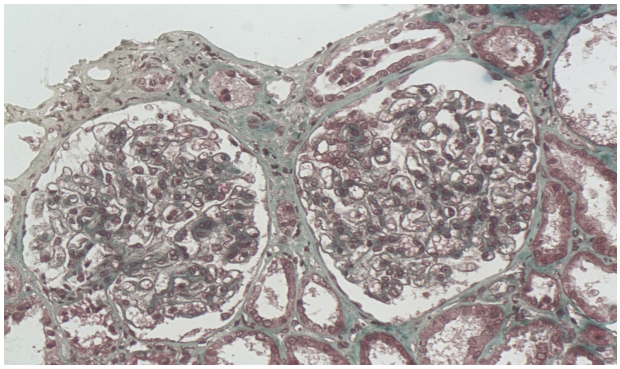

Figure 1: Mesangial proliferation

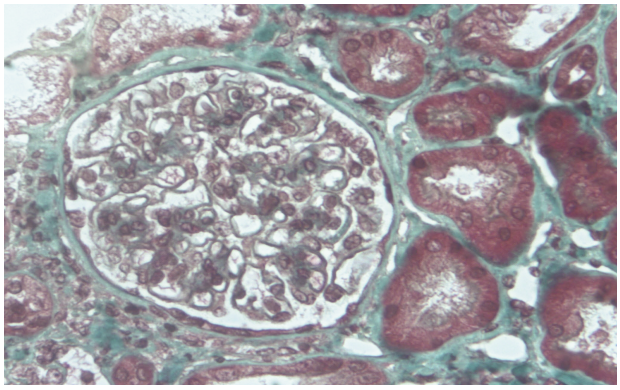

Figure 2 : Turgescent podocytes

Light microscopic examination: The glomeruli showed mild mesangial changes with variable degree of mesangial matrix expansion. The glomerular capillary wall was thickened with reduction of their light but without thrombosis. Immunofluorescence study showed in the glomeruli diffuse granular mesangial reaction predominantly with labeling for IgG.Very less intense mesangial reaction was demonstrated for C3. Negative results were obtained with labeling for IgA, IgM, and C1q. CH50, C3 and C4 levels were normal and antinuclear antibody and anti-DNA antibody assays remained negative during the follow-up period. A full dose corticosteroid was initiated (1mg/ Kg/ day). The interval from onset of steroid therapy to remission of nephrotic syndrome was 2 months. Later and during follow-up; the patient had developed 2 relapsing nephrotic syndrome episods without obvious decompensation factors. The first episode was at 12 months and treated by corticosteroid with remission after one month. The second episode of relapse was at 5 years after the diagnosis. The patient was switched to Mycophenolate mofetil with remission after 2 months. The duration of the total follow-up is 6 years.

DISCUSSION

Glomerular mesangial IgG deposition occurs in various types of primary and secondary glomerulonephritis, including lupus nephritis and mesangiocapillary nephropathy. In Immunoglobulin A (IgA) nephropathy, the most common type of primary glomerulonephritis, IgG (mainly IgG1 and IgG3) is codeposited with IgA in up to 40% of cases. In our case, there was no IgA deposit; so IgA nephropathy was eliminated.

The recognition of this disease as a new type of glomerulonephritis requires the careful exclusion of other types of glomerulonephritis. There was no marked mesangial cell proliferation in any case. No clinical or biologic features of ongoing infection were noted for any patient during extended follow-up monitoring. Marked mesangial proliferation and low complement levels, two main features of postinfectious glomerulonephritis, were absent in our case.

Although the number of cases with MIG reported in the literature is small (Table 1), comparison of patients' results from different parts of the world demonstrated some differences in the clinical presentation and behavior of the disease. The distribution of the reported cases seems to be concentrated in Japan from where most studies are published like in the report of Yoshikawa (2) concerning 10 pediatric cases of MIG and in the report of Sato (1) concerning adult cases of MIG. In the Japanese studies, the patients' followup indicated that most MIG cases have a benign clinical course with a relatively benign course of MIG after a median follow-up period of 4.9 years. On the contrary, fewer cases of MIG were reported from France

and most of these patients developed chronic renal disease (3). Then was reported the largest series of MIG cases to date by Fadi Fakhouri at Hôpital Necker, including 14 cases in wich the course of MIG was far from benign, in as much as chronic renal failure occurred in one-half of the patients. Treatment was purely supportive and consisted of an antihypertensive and/or antiproteinuric regimen in 5 patients. Moreover, symptomatic recurrence of MIG in allograft kidneys has been reported in two patients in two different studies; this finding was an additional evidence to prove that MIG is a specific and distinct entity. In the report by Yoshikawa *et al. (2*, four children with MIG, nephrotic syndrome, and normal renal function were treated with a corticosteroid regimen, with complete or partial remission in two cases. In a case report, nephrotic syndrome related to MIG may be resistant to corticosteroid and cyclophosphamide (5).
The evolution of our patient is different from that reported in the literature; he initially received a full dose corticosteroid. As he had developed 2 relapsing nephrotic syndrome episods, he was switched to Mycophenolate mofetil with remission after 2 months. No clinical kidney disease was noted after a total follow up of 6 years.

Table 1: Mesangial IgG glomerulonephritis: Reports in the literature

Author	Year	Nb of patients	Age (years)	Country
Sato M et al (1)	1993	6	6- 52	Japan
Yoshikawa N et al (2)	1994	10	Children	Japan
Kano K et al (4)	1996	1	8	Japan
Sepandj F (5)	1998	1	48	Canada
Onitsuka et al (6)	2000	1	48	Japan
Fakhouri F et al (3)	2002	14	13-47	France
Assadi FK (7)	2004	1	17	USA
Sawsan M Jalalah (8)	2009	2	4-16	Saudi Arabia
Present study	2017	1	50	Tunisia

CONCLUSION

In conclusion, there is sufficient evidence currently to support that MIG is a distinct type of GN. This entity is very rare; however, nephrologists and pathologists should be aware of its existence especially because some reports indicate that it may carry a less favorable course and prognosis. Recognition of larger number of cases with longer duration of follow-up is needed to understand the pathogenesis of MIG and help in designing the management for this group of patients.

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