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Original article

Fibrillary glomerulonephritis: clinicopathological characteristics and treatment in a spanish tertiary center

Glomerulonefritis fibrilar: características clínico-patológicas y tratamiento en un centro terciario Español

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ABSTRACT

Introduction: Fibrillary glomerulonephritis (FGN) has a poor prognosis and lacks standardized treatment. In this study, we describe clinicopathological characteristics, clinical course, and management of patients with FGN at our center.

Materials and methods: A retrospective cohort study of 13 patients diagnosed with FGN by positive DNAJB9 at kidney biopsy between 2019 and 2024. Demographic data, comorbidities, laboratory values, histopathological findings, and treatments were collected, Complete remission was defined as proteinuria <500 mg/g with normal renal function; partial remission as $>50\%$ reduction in proteinuria to <2000 mg/g with stable renal function; and no remission as absence of improvement, progression to end-stage kidney disease (ESKD), or death.

Results: The mean age was 61.4 years, 69,2% male, median proteinuria of 2318 mg/g (38% nephrotic range) and serum creatinine 1.64 mg/dL, Histopathological findings: 29% global glomerulosclerosis. The most frequent pattern was membranoproliferative (61.6%), followed by mesangial (30.8%) and membranous in 1 patient (7.7%), Hypoalbuminemia (<3 g/dL) was associated with worse prognosis (HR 6.52, $p = 0.04$); proteinuria >3500 mg/g and creatinine showed non-significant trends. Immunosuppression was given in 84.6% of patients: rituximab (RTX) (61.5%), RTX + mycophenolate (7.7%), sequential RTX followed by ocrelizumab and obinutuzumab (7.7%), and corticosteroids alone (7.7%). Partial remission was achieved in 30.8%, all within the exclusive RTX group, A total of 38.4% progressed to ESKD or death.

Conclusions: In our study, FGN showed poor prognosis and partial response to rituximab. FGN with hypoalbuminemia had worse outcomes. Prospective studies and larger cohorts are needed to validate these findings and optimize its management.

Palabras clave:
Glomerulonefritis fibrilar
Rituximab
DNAJB9

RESUMEN

Introducción: La glomerulonefritis fibrilar (GNF) tiene un mal pronóstico y carece de tratamiento estandarizado.

Materiales y métodos: En este estudio analizamos las características clínicas y patológicas, evolución y manejo de 13 pacientes diagnosticados con GNF mediante biopsia renal positiva para DNAJB9 entre 2019 y 2024 en nuestro centro. Se recogieron datos demográficos, comorbilidades, valores de laboratorio, hallazgos histopatológicos y tratamientos. Se definió remisión completa como proteinuria <500 mg/g con función renal

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normal; remisión parcial como reducción >50% de proteinuria a <2000 mg/g con función renal estable; y sin remisión como ausencia de mejora, progresión a enfermedad renal crónica (ERC) estadio 5 o muerte.
Resultados: La media de edad fue 61,4 años, 69,2% hombres, con una proteinuria mediana de 2318 mg/g (38% en rango nefrótico) y creatinina sérica mediana de 1,64 mg/dL. Resultados de biopsia renal: el 29% de los glomérulos estaba esclerosado. El patrón histológico más frecuente fue el membranoproliferativo (61,6%), seguido del mesangial (30,8%) y membranosa (7,7%). La hipoalbuminemia (<3 g/dL) se asoció a peor pronóstico (HR 6,52, p = 0,04). La proteinuria >3500 mg/g y creatinina mostraron tendencias no significativas. El 84,6% recibió inmunosupresión: rituximab (RTX) (61,5%), RTX + micofenolato (7,7%), RTX seguido de ocrelizumab y obinutuzumab (7,7%), y corticoides en monoterapia (7,7%). Se consiguió remisión parcial en 30,8%, todos tratados con RTX en monoterapia. Un 38,4% progresó a ERC estadio 5 o falleció.
Conclusión: La GNF mostró mal pronóstico y respuesta parcial a RTX. La GNF con hipoalbuminemia presentó peor pronóstico. Se necesitan estudios prospectivos con mayores cohortes para confirmar estos hallazgos y optimizar su manejo.

Introduction

Fibrillary glomerulonephritis (FGN) is a rare disease that is identified in 0.5–1% of renal biopsies.[1,2] It is characterized by the presence of nonamyloid fibrils, typically of 10–30 nm in diameter, lacking a hollow center, located in the glomerulus, particularly the mesangium and the glomerular basement membrane. They stain intensely for IgG, kappa, lambda and C3 and are usually negative for Congo red.[1–4]

FGN has been associated with various autoimmune diseases, monoclonal gammopathy, neoplasia and infections, notably hepatitis C. However, in more than half of cases, the cause remains unidentified, suggesting that the pathogenic mechanisms underlying FGN are not yet understood.[5,6] Clinically, it usually manifests at approximately 60 years of age nonspecifically; up to 70% of patients have renal failure, hematuria and proteinuria, the last of which is frequently in the nephrotic range. In 15–36% of cases, the disease may begin as a pure nephrotic syndrome.[1,2,6,7]

Recently, it was shown that the DNAJB9 protein, which under physiological conditions can be found at low levels in tubular cells, podocytes, mesangial cells and renal endothelial cells, is located exclusively as extracellular deposits in the glomeruli in FGN. This finding has transformed the diagnosis of the disease, allowing it to be identified with a sensitivity of 98% and a specificity greater than 99%, eliminating the need for ultrastructural analysis, the classic diagnostic method.[8–11]

To date, patients experience unfavorable outcomes, as more than half will progress to stage 5 chronic kidney disease (CKD) within 5 years after diagnosis.[6] Evidence on optimal treatment remains limited, and immunosuppressive management, including mainly steroids, cyclophosphamide, mycophenolate and rituximab (RTX), has shown variable results in different cohorts.[1,6] Recent studies have suggested that RTX can slow disease progression; however, evidence on its efficacy is scarce.[12,13]

In the current study, we described the main clinicopathological characteristics of patients diagnosed with FGN in our hospital, analyzed the risk factors associated with its progression and explored the impact of treatment on its course.

Materials and methods

We conducted a retrospective cohort study that included 13 patients diagnosed with FGN by renal biopsy, followed by DNAJB9 testing for confirmation, in our center between 2019 and 2024.

Demographic data, body mass index (BMI), comorbidities associated with the diagnosis of FGN, laboratory results (both at baseline and at follow-up), treatments used (both supportive and immunosuppressive) and characteristics of the renal biopsy were collected from a review of the medical records. Due to its prognostic relevance, proteinuria was included as an additional baseline clinical variable and classified into 2 categories: less than or greater than 3.500 mg/g. With respect to the renal biopsy, the number of glomeruli per biopsy, the percentage of sclerosed glomeruli, the lesion pattern on optical microscopy and the location of the fibrils on electron microscopy were recorded, if available. Inflammation and tubular atrophy were categorized as absent (0%), mild (1–25%), moderate (25–50%) or severe (>50%).

Information, including proteinuria levels and their changes, albumin levels and changes in renal function was collected at follow-up visits at 3, 6 and 12 months and subsequently annually until censoring or the end of the study period. Patients were classified into groups according to the treatments received (supportive, immunosuppressive or their combination) and analyzed according to their outcomes. The outcomes of the study included complete remission, defined as a reduction in proteinuria to less than 500 mg/g and normal renal function; partial remission, defined as a reduction in proteinuria by more than 50% with respect to baseline to lower than 2.000 mg/g and stable renal function (no increase greater than 20% with respect to baseline); and no remission, which included patients who did not achieve complete or partial remission, as well as those who progressed to stage 5 CKD or died during follow-up.

Statistical analysis was performed using Python (version 3.13). Categorical variables are described as frequencies and percentages, while the continuous variables are expressed as means ± standard deviations (SDs) or medians with interquartile ranges (IQRs), according to the nature of the distribution as evaluated by the Shapiro–Wilk normality test; given the small number of patients, cases with missing values were excluded from the corresponding analysis. For survival analyses, univariable Cox proportional hazards regression models were applied to identify risk factors for progression to stage 5 CKD or death, considering the time from diagnosis until the event (stage 5 CKD, death) or censoring. The proportionality of the risks was evaluated using the Schoenfeld test, and sensitivity analyses were performed to verify the robustness of the findings after adjusting for different hypoalbuminemia thresholds (<3 vs. <2.5 g/dL) and proteinuria (median 2.318 mg/g). No multivariable analysis was performed because of the limited sample size. Statistical significance was defined if $p < 0.05$.

Results

Clinical and analytical characteristics

During the study period, 13 patients were diagnosed with FGN at our hospital. The mean age of the patients was 61.4 years, and most were male (69.2%) and of white ethnicity (92%). The most frequent comorbidity was arterial hypertension, which was observed in 92% of the patients, followed by diabetes mellitus, in 23.1%. A patient with

Table 1
Demographic and baseline clinical characteristics.

Variable	Value
Sex	Male: 9 (69.2%)
Ethnicity	White: 12 (92.3%)
	Hispanic: 1 (7.7%)
Age (years)	61.4 ± 5.51
IMC (kg/m^2)	27.58 ± 8.98
Systolic blood pressure (SBP, mmHg)	130.69 ± 16.29
Diastolic blood pressure (DBP, mmHg)	72.08 ± 9.71
Diabetes mellitus	3 (23.1%)
Malignancy	0 (0%)
Autoimmune disease	0 (0%)
Hepatitis C	1 (7.7%)
Cardiovascular disease	3 (23.1%)
Arterial hypertension (AHT)	12 (92.3%)

BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure.

hepatitis C virus infection was included, but no cases of FGN associated with autoimmune diseases or neoplasms were detected (Table 1).

In terms of laboratory analysis, the patients presented a median serum creatinine (sCr) concentration of 1.64 mg/dL and a median estimated glomerular filtration rate of 31 ml/min/1.73 m^2. At the time of renal biopsy, all the patients exhibited proteinuria, with a median urine protein/creatinine ratio (UPCR) of 2.318 mg/g; this value reached the nephrotic range in 38% of the patients. Three patients had serum albumin concentrations lower than 3 g/dL, and hematuria was observed in 38.5% of the patients. Five patients had positive antinuclear antibodies (ANAs), with titers of 1/80 in 3 patients, 1/160 in 1 patient and 1/320 in another patient. Complement levels were normal in all the patients, and cryoglobulins, which were evaluated in 9 patients, were negative (Table 2).

Indications of kidney biopsy

Among 13 renal biopsies performed, the main indication was the presence of proteinuria with deterioration of renal function, representing 9 patients (69.2%). This was followed by proteinuria with preserved renal function, which was observed in 3 patients (23.1%). The final patient (7.7%) underwent biopsy due to an acute kidney injury. The median time from the first observation of altered kidney function to the completion of the biopsy was 224 days [38–316 days].

Table 2
Laboratory findings at the time of diagnosis in patients with fibrillary glomerulonephritis.

Variable	Value
Serum creatinine (mg/dL)	1.64 [1.31–2.27]
Glomerular filtration (ml/min/1.73 m^2)	31 [27–58.5]
UPCR (mg/g)	2.318 [1.114.7–5.952.6]
UACR (mg/g)	1072 [604.5–4396.9]
Cholesterol (mg/dL)	182.69 ± 57.09
Hemoglobin (g/dL)	12.33 ± 2.64
HbA1c (%)	5.65 [5.43–5.88]
Albumin (g/dL)	3.66 ± 0.71
C3 (mg/dL)	120.79 ± 23.85
C4 (mg/dL)	31.75 ± 9.45
Proteinuria, n (%)	13 (100%)
Nephrotic range (>3.5 g/24 h), n (%)	5 (38%)
Hypoalbuminemia (<3 g/dL), n (%)	3 (23.1%)
Hematuria, n (%)	5 (38.5%)
Leukocyturia, n (%)	5 (38.5%)
ANA positivity, n (%)	5 (38.5%)
1/80 titer, n	3
1/160 titer, n	1
1/320 titer, n	1
Negative cryoglobulins, n/tested	9/9 (100%)

ANA: antinuclear antibodies; C3: complement 3; C4: complement 4; HbA1c: glycosylated hemoglobin; UACR: urinary albumin/creatinine ratio; UPCR: urinary protein/creatinine ratio.

Histopathological characteristics

Regarding the characteristics of the kidney biopsy samples, an average of 23 glomeruli were identified per biopsy. An average of 29% of the glomeruli showed global sclerosis. The most frequent histopathological pattern was membranoproliferative, which was observed in 8 patients (61.6%), followed by the mesangial pattern in 4 patients (Fig. 1A and B) (30.8%) and a membranous pattern in one patient (Fig. 1C) (7.7%). No crescentic lesions were identified in any patient. Regarding tubular atrophy, mild atrophy was observed in 5 patients (38.5%), moderate atrophy was observed in 7 (53.8%) and severe atrophy was observed in 1 (7.7%). A total of 76.9% of the patients showed interstitial inflammation, 70% of whom presented mild and focal inflammation. Two patients exhibited concomitant diseases: one with diabetic nephropathy and another with acute interstitial nephritis associated with diabetic nephropathy (Table 3).

Regarding the immunofluorescence results, 9 patients (69.2%) were positive for IgG, with a mean intensity of 2.5+ (Fig. 1D). Six patients (46.2%) were positive for IgA, with a mean intensity of 1+, and another 6 (46.2%) were positive for IgM, with an average intensity of 0.2+. Four patients (30.8%) were positive for C1q, with an average intensity of 1.1+. Similarly, 10 patients (76.9%) were positive for kappa light chains, with an average intensity of 2.1+; for lambda, with an average intensity of 2.05+; and for C3, with an average intensity of 2+ (Table 3).

Among 6 patients, electron microscopy revealed the presence of fibrils exclusively in the mesangium in one patient, in the glomerular wall in a second, and at both sites in the remaining 4 patients. All six patients were positive for DNAJB9 (Fig. 1E and F).

Treatment and progression

Regarding treatment, 10 of the 13 patients received antiproteinuric therapy, most commonly involving a combination of SGLT2 inhibitors (SGLT2i) and renin–angiotensin–aldosterone system blockers (RASb) (n = 7), followed by SGLT2 monotherapy (n = 2) and monotherapy with RASb (n = 1). A total of 11 of the 13 patients received immunosuppressants: monotherapy with RTX (n = 8), RTX combined with mycophenolate (n = 1), and bolus corticosteroid monotherapy (n = 1). The duration from diagnosis to the start of immunosuppressive therapy was 54.5 days [32.3–151.5 days]. Of the 9 patients treated with RTX, 7 received the standard schedule of 2 doses of 1 g separated by 2 weeks, and one patient received a single dose of 1 g. In addition, one of these patients was retreated with RTX at 18 months because of progressive deterioration of renal function and increased proteinuria, but no clinical improvement was observed at the end of the follow-up period. Another patient who started treatment with RTX (1 g in 2 doses) received sequential treatment with other anti-CD20 antibodies —first ocrelizumab, followed by obinutuzumab—, owing to the progressive deterioration of renal function and persistence of proteinuria. At the end of the follow-up period, 24 months after the administration of obinutuzumab, the patient had an sCr concentration of 3.21 mg/dL and proteinuria of 2.300 mg/g. The remaining 2 patients did not receive immunosuppressants. All treatments were administered at the discretion of the treating physician.

During a median follow-up period of 2.0 years [0.9–3.9 years], 5 events, namely, progression to stage 5 CKD or death, were recorded. Four patients (30.8%), all of whom were treated with RTX alone, achieved partial remission, and no patient achieved complete remission. Patients with partial remission had similar baseline median UPCRs (3,940.5 vs. 4,205.9 mg/g) and sCr concentrations (1.48 vs. 1.64 mg/dL) to patients who did not achieve remission.

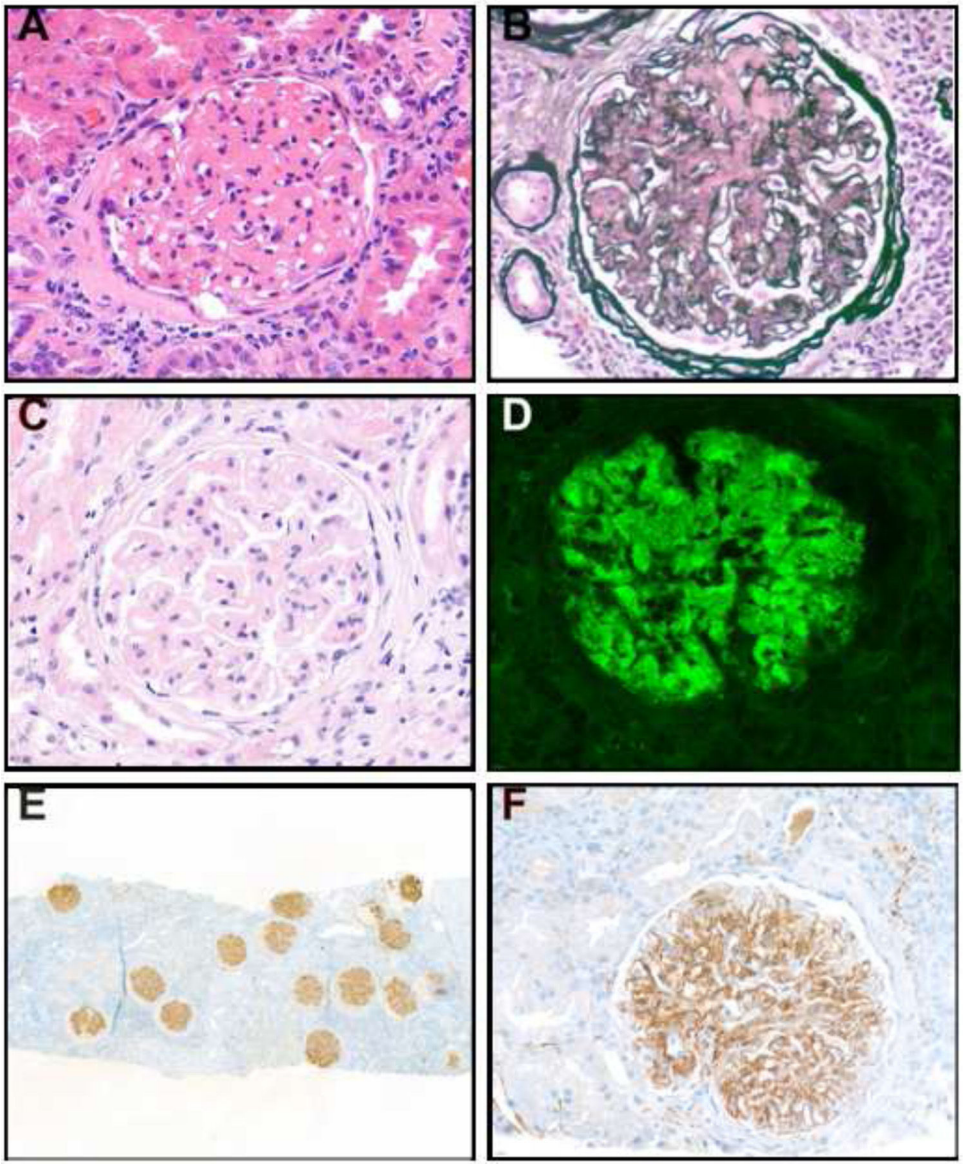

Figure 1. (A–F) Kidney biopsy images: (A) Significant mesangial expansion revealed by hematoxylin and eosin (H&E) staining of eosinophilic material deposits; (B) Expanded mesangial areas revealed by silver staining of nonargyrophilic deposits; (C) Marked thickening of the basal membranes revealed by H&E staining of eosinophilic material deposits; (D) Mesangial and capillary loop IgG deposits revealed by immunofluorescence staining; (E) Immunohistochemical staining of DNAJB9, especially in the capillary loops; (F) Mesangial and capillary loop DNAJB9 deposits.

Patients who achieved partial remission experienced a mean 63% reduction in proteinuria. Among patients who did not achieve remission, one patient with an associated diagnosis of acute interstitial nephritis had severe renal failure on admission, requiring the initiation of renal replacement therapy, and died during hospitalization. Another 3 patients progressed to stage 5 CKD and started renal replacement therapy during a median follow-up of 2 years; of these, 2 underwent transplantation, and at the end of the follow-up, no evidence of recurrence of FGN was detected. The third patient experienced kidney disease progression, which was treated with conservative management; died during follow-up due to complications associated with multiple comorbidities (Table 4).

Factors associated with a poor outcomes

In this cohort, potential associations were observed between several clinical characteristics and the risk of progression to stage 5 CKD or death. According to the univariable Cox regression analysis, the presence of hypoalbuminemia (<3 g/dL) at the time of renal biopsy was associated with an increased risk of the composite outcome (HR: 6.52; 95% CI: 1.06–40.02; $p = 0.04$). Nonsignificant trends were also observed in patients with proteinuria $>3{,}500$ mg/g (HR: 6.65; 95% CI: 0.73–60.11; $p = 0.09$) and in those with elevated sCr at diagnosis (HR: 6.8; 95% CI: 0.64–72.9; $p = 0.11$). Similarly, the membranoproliferative histological pattern, although frequent among patients who experienced progression to stage 5 CKD, was not significantly associated with the outcome (HR: 1.56; 95% CI: 0.17–14.04; $p = 0.69$). Owing to the small sample size, low number of events, and wide confidence intervals, the results of these univariable Cox regression analyses are considered exploratory.

The results of the sensitivity analysis on the association between hypoalbuminemia and the composite event at the stricter threshold (<2.5 g/dL; HR: 2.08; 95% CI: 0.23–18.84; $p = 0.51$) was consistent with that of the full analysis (HR: 6.52; $p = 0.04$); however, the association was not significant, probably because of the scarcity of such low levels. For proteinuria, we attempted a sensitivity analysis

Table 3
Histopathological characteristics and immunofluorescence findings of kidney biopsies in patients with fibrillary glomerulonephritis.

Characteristic	Value
Number of glomeruli	23.38 ± 10.82
Sclerotic glomeruli, %	28.96 ± 20.46
Histopathological pattern, n (%)	
Mesangial	4 (30.8)
Membranoproliferative	8 (61.6)
Membranous	1 (7.69)
Crescentic lesions, n (%)	0 (0)
Interstitial inflammation, n (%)	
None	3 (23.08)
Mild	7 (53.85)
Moderate	2 (15.38)
Severe	1 (7.69)
Tubular atrophy, n (%)	
Mild	5 (38.46)
Moderate	7 (53.85)
Severe	1 (7.69)
Hyaline arteriosclerosis, n (%)	
None	3 (23.08)
Mild	5 (38.46)
Moderate	3 (23.08)
Severe	2 (15.38)
SM localization of fibrils, n (%)	6
Mesangial	1 (7.69)
Glomerular wall	1 (7.69)
Mesangial and glomerular wall	4 (30.77)
Other glomerular diseases, n (%)	
None	11 (84.62)
Diabetic nephropathy + ATN	1 (7.69)
Diabetic nephropathy	1 (7.69)
DNAJB9, n (%)	13 (100)
IgG IF (mean intensity, positive), n (%)	9 (69.23) (2.5 +)
IgA IF (mean intensity, positive), n (%)	2 (15.38) (0.75 +)
IgM IF (mean intensity, positive), n (%)	3 (23.08) (2.05 +)
C3 IF (mean intensity, positive), n (%)	10 (76.92) (2 +)
C1q IF (mean intensity, positive), n (%)	4 (30.77) (1.125 +)
Kappa IF (mean intensity, positive), n (%)	10 (76.92) (2.1 +)
Lambda IF (mean intensity, positives), n (%)	10 (76.92) (2.05 +)

IF: immunofluorescence; EM: electron microscopy; ATN: acute tubulointerstitial nephritis.

with the median UPCR (2.318 mg/g) as the threshold, but this was not possible because the relationship between this cutoff point and the data in our cohort was too strong. Therefore, we opted for a clinical threshold of 3,500 mg/g in the main analysis, given its established prognostic value and its relevance in glomerular diseases. The assumption of proportional hazards was evaluated using the Schoenfeld test, and no significant violations were detected ($p > 0.05$ implicit for all variables).

Discussion

In this study, we described the clinical characteristics, management and outcomes of patients diagnosed with FGN at our center. Our cohort, with a mean age of 61 years, was predominantly male, which interestingly, contrasts the results of other published series, which usually reported a higher proportion of women.[14,15] The majority of our patients had arterial hypertension and diabetes mellitus, denoting a relevant comorbidity profile; however, we found no association of FGN with malignancies or autoimmune diseases, in contrast to the findings in the literature, where these conditions are present in 5–10% and 5–15% of patients, respectively.[1,6,9] This interesting finding could suggest that our population may be uniquely characterized and further explored in larger studies.

Similar to what has been reported in other studies, our patients had impaired renal function at the time of diagnosis, along with significant proteinuria, which in 38% of the patients reached the nephrotic range, highlighting the severity of FGN at the time of diagnosis. However, unlike what has been described in the literature, only 38% of our patients had hematuria at the time of diagnosis of the disease, which is lower than what is usually reported.[1,6,9]

In our cohort, the most common histopathological pattern was membranoproliferative, followed by mesangial. In agreement with other series, patients with a membranoproliferative pattern tended to progress to kidney failure; however, in our study, this trend did not reach statistical significance.[2,15,16] In addition, one patient in our cohort exhibited a membranous pattern and a slow disease course, marked by significant renal disease progression and death due to multiple comorbidities, an outcome that aligns with the findings of several case reports in the literature that have described an unfavorable disease course in patients with this pattern.[17,18] Our patients presented an immunofluorescence pattern characterized primarily by IgG, kappa, lambda and C3 positivity that coincided with that described in other cohorts.[1,9,15] All our patients also had positive for DNAJB9, highlighting the importance of this marker in the diagnosis of the disease.[3,8,10,11]

Table 4
Summary of treatments and outcomes in patients with fibrillary glomerulonephritis (n = 13).

Category	Characteristic	N (%) or description
Antiproteinuric treatment	Total patients treated	10/13 (76.9)
	Combination SGLT2i + RAASi	7/10 (70)
	SGLT2i only	2/10 (20)
	RASb only	1/10 (10)
Immunosuppression	Total patients treated	11/13 (84.6)
	Rituximab alone	8/11 (72.7)
	RTX + mycophenolate	1/11 (9.1)
	Corticosteroids alone	1/11 (9.1)
	Sequence: RTX → ocrelizumab → obinutuzumab	1/11 (9.1)
	No immunosuppression	2/13 (15.4)
Remission	Partial remission	4/13 (30.8)
	- Partial remission among patients receiving RTX	4/10 (40)
	- Average reduction of proteinuria	63
	Complete remission	0/13 (0)
Progression/outcome	Death	2/13 (15.3)
	Progression to CKD stage 5 and initiation of RRT	3/13 (23.1)
	- Transplantation (without recurrence at study closure)	2/3
	- Median time to CKD stage 5	2 years
	Severe renal failure on admission (acute interstitial nephritis)	1/13 (7.7)
	Progression to stage 5 CKD with conservative management	1/13 (7.7)
Follow-up	Median duration	2 years

Percentages reflect the proportion within each subcategory or of the total.
RASb: renin–angiotensin system blocker; CKD: chronic kidney disease; SGLT2i: SGLT2 inhibitor; RTX: rituximab; RRT: renal replacement therapy.

The patient outcomes reflect the severity of FGN in our cohort, with progression to kidney failure or death reported for 38.4% of the patients, a finding that aligns with the most numerous international cohorts, highlighting the poor outcomes of this disease.[1,6] The presence of hypoalbuminemia was associated with a worse outcome in this cohort. In addition, proteinuria greater than 3.500 mg/g and decline in kidney function at the time of diagnosis tended to be associated with an increased risk of a poor outcome, although the associations were not significant. Notably, proteinuria has presented variable results in other cohorts[9,15,19] and has been identified as a risk factor in some studies but not in a multicenter cohort by Andeen et al.,[6] which adds complexity to the interpretation of these findings. However, the results related to the degree of deterioration of renal function at the time of diagnosis are consistent with those reported in other cohort studies[1,6,9] as well as with those observed in other glomerulopathies.[20,21] Kidney biopsy data, such as the degree of tubular atrophy, the percentage of glomerular sclerosis and the histopathological patterns, were not significantly related to patient outcomes.

In our center, the most commonly used immunosuppressive strategy is RTX treatment, which is generally used as a single therapy, but in some cases is combined with another immunosuppressant. Partial remission was observed in 4 of the 13 patients (30.8%), exclusively in those treated with RTX alone. These results are consistent with findings from other studies,[6,8,12] which have associated RTX with a greater probability of remission and a slowing of disease progression, although larger studies are needed to confirm the efficacy of this treatment.

Our study has several limitations. The small size of our cohort results in limited statistical power in detecting significant associations, as observed for proteinuria and renal function. Therefore, all the findings should be considered exploratory and hypothesis-generating, and extrapolations or causal interpretations should be avoided. Furthermore, residual confounding cannot be ruled out; thus, caution is recommended in the interpretation of the observed associations. In addition, as this was a retrospective study of the data from a single center, selection bias and variability in clinical management could have influenced the outcomes. The heterogeneity in the treatments, the absence of a control group and the lack of a multivariable analysis for adjusting for confounding factors also limit our conclusions.

In conclusion, our findings reflect the notable severity of FGN, with rates of kidney disease progression and mortality consistent with those reported in other cohorts, highlighting the relevance of the identified risk factors and the limited therapeutic potential of RTX, despite our limited sample size. These results emphasize the need for multicenter prospective studies, new therapeutic strategies and larger populations to validate our findings and improve the management of this disease.

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Declaration of competing interest

MJS declares receiving personal fees from NovoNordisk, Jansen, AstraZeneca, Esteve, Fresenius, Ingelheim Lilly, Vifor, ICU, Pfizer, Bayer, Travere Therapeutics, Emerald, and GE Healthcare, as well as grants and personal fees from Boehringer Ingelheim, outside the scope of the present review. The other authors have no conflicts of interest.

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