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Case Report

Idiopathic Fibrillary Glomerulonephritis Confirmed by Immunofluorescence Staining for DNAJB9

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Abstract

Background: Fibrillary Glomerulonephritis (FGN) is a rare pathology that has been identified as an immune complex-mediated glomerulonephritis. While some cases of FGN are attributed to malignancy and other diseases, often they are idiopathic and must be differentiated from amyloid nephropathy. These differentiations can be confirmed by ultrastructural and light microscopy. **Case Report:** The patient is a 64-year-old woman presented to an outside facility with right lower quadrant pain that was worsening and associated with nausea and vomiting. She had no known medical history due to lack of primary care. She was diagnosed with acute diverticulitis with abscess leading to her transfer. Worsening renal function despite good urine output was noted during the hospitalization. Initial workup was negative for common co-morbidities associated FGN including hepatitis, human immunodeficiency virus (HIV), and malignancy. Renal biopsy confirmed FGN with endocapillary proliferation via positive staining for DNA J homolog subfamily B member 9 (DNAJB9). She was discharged home after having placement of a perm-cath and arrangement with outpatient dialysis. **Discussion:** Fibrillary Glomerulonephritis is a rare glomerulopathy which can manifest as nephrotic syndrome with an unclear pathogenetic mechanism. Due to the rare nature of this disease, a lack of evidence supporting a standard treatment exists. While some studies have suggested that immunomodulators such as Rituximab may be beneficial, there is not enough data to support this claim. This case highlights the importance of including FGN in a wide differential in the case of unrelenting nephrotic syndromes, even if the patient has no clear associated comorbidities.

Keywords: Renal failure; Fibrillary glomerulonephritis; Immunofluorescence; DNA J homolog subfamily B member 9; DNAJB9; Electron microscopy; Case report

Introduction

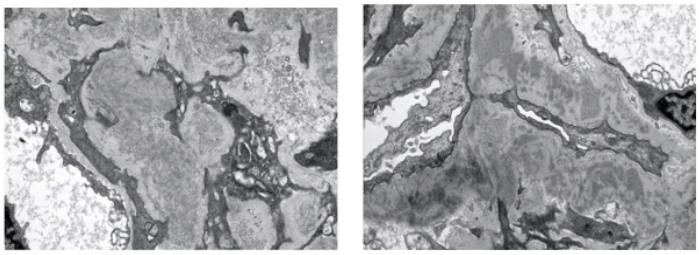
Fibrillary Glomerulonephritis (FGN) is a rare pathology that has been identified as an immune complex-mediated glomerulopathy. While diagnoses such as amyloidosis or immunotactoid glomerulopathy can both reveal 20nm fibrils haphazardly arranged within the mesangium and/or the glomerular basement membranes via electron microscopy, specialized staining must set the diagnoses apart [1]. For instance, renal amyloidosis is ruled out with Congo Red staining [2]. Recently, advances were made using Laser Microdissection-Assisted Liquid Chromatography-Tandem Mass Spectrometry (LMD/MS-MS) to discover a highly specific and sensitive immunomarker for FGN, DNA J homolog subfamily B member 9 (DNAJB9), part of the molecular chaperone gene family [1]. While the aetiology of FGN remains unclear, there appears to be an association within the literature with concurrent autoimmune disease, malignant neoplasm, monoclonal gammopathies, or hepatitis C viral infections [1,3]. In a multi-institutional cohort study by Andeen, et al. (2019), 176 of 266 patients who were diagnosed with FGN had a standing diagnosis of a systemic disease [4,5]. The overall prognosis is poor

and there are no management guidelines. Renal function has been noted to be stabilized in patients given immunosuppressors such as rituximab, cyclophosphamide, or corticosteroids, but progression to End-Stage Renal Disease (ESRD) occurs within a few years [6]. We present here a case of idiopathic FGN in a 64-year-old woman, confirmed by electron microscopy and positive glomerular staining of DNAJB9.

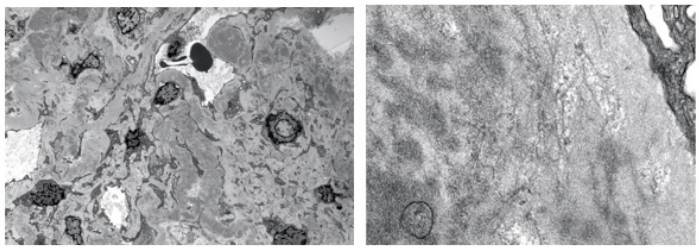
Case Presentation

A 64-year-old woman, with no known previous medical history, presented to an outside facility with right lower quadrant abdominal pain that had been worsening with associated nausea and vomiting. She was diagnosed with acute diverticulitis with abscess. Three days after admission to the initial facility, she was transferred to our facility for further testing and potential surgical management due to refractory pain and persistently elevated White Blood Cell counts (WBC). Upon admission to our facility, she was hypertensive (219/95 mmHg), with a creatinine of 3.87mg/dL (n: 0.84-1.21mg/dL), despite good urine output. Urinalysis showed 7 red blood cells per high power field, 3+ proteinuria, and 5 hyaline casts per low power field. Renal ultrasound was performed at the transferring facility with only finding being signs of chronic kidney disease. Further workup revealed a protein clearance of 3,607g/day (n: <150mg/day), moderate microscopic hematuria, and a hemoglobin of 11.6g/dL (n: 12.0-15.5g/dL, women). The initial thought was that poor renal function was due to a possible hypoperfusion etiology in the setting of sepsis, but the patient continued to have poor renal function despite adequate sepsis management. Serology workup for Hepatitis A, B and C, as well as Human Immunodeficiency Virus (HIV), and Anti-Nuclear Antibodies (ANA) were found to be negative and complement levels were within normal limits. Serum free light chains revealed Ig Kappa free light chain of 14.6mg/dL and Ig Lambda Free Light Chain of 7.67mg/dL giving a light chain ratio of 1.90 consistent with chronic kidney disease. A kidney biopsy was then performed to determine possible etiologies for the persistently elevated creatinine. The patient was started on hemodialysis within the first week of her hospital admission given her worsening renal function which she remained on throughout the hospital course.

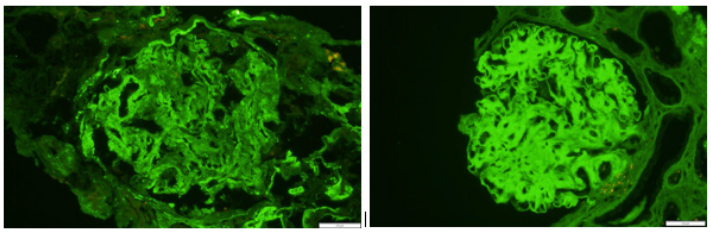
Biopsy results of the kidney resulted in findings of FGN with endocapillary proliferation. Further, immunofluorescence was positive for DNAJB9, excluding other fibrillary glomerulonephropathies such as amyloidosis (Table 1). Light microscopy demonstrated a combination of globally sclerotic damage to glomeruli, mesangial expansion, endocapillary hypercellularity, interstitial fibrosis, and tubular atrophy noted. Immunofluorescence demonstrated sclerotic damage and DNAJB9 as seen in Figures 5-6. Electron microscopy continued to show sclerotic damage and fibrils globally including the mesangial areas and glomerular basement membranes along with 90% effacement of the podocytes of the peripheral capillary surface area, seen in Figures 1-4. There was concern that the renal pathology was driving the patient's leukocytosis given the association of FGN and malignancy. Given concern for possible malignancy, a peripheral blood smear was performed demonstrating leukocytosis and thrombocytosis. Flow cytometry was negative for leukemia and lymphoma. Staining for fusion genes BCR-ABL and JAK2 were negative. CT imaging of the chest revealed a 0.3mm nodule along the inferior aspect of the lingula and emphysematous changes. No concurrent malignancy or obvious inciting factor was found. The patient was ultimately discharged on long term hemodialysis.



Figures 1 and 2: Electron Microscopy with fibrils noted throughout and global sclerosis, 2. Electron Microscopy with fibrils and scattered sclerosis noted.



Figures 3 and 4: Electron Microscopy with fibrils noted within the mesangium.



Figures 5 and 6: Immunofluorescence staining of C3 showing positive deposition within the glomerulus 6. Immunofluorescence staining of DNAJB9 showing positive deposition within the glomerulus.

Day	Creatinine	GFR	Serum Albumin
1	3.87	11.6	2
2	3.95	11.3	2
3	4.22	10.5	1.7
4	4.39	10	1.6
5	4.53	9.6	1.6
6 (Post first session of HD)	3.23	14.5	1.7
7	3.84	11.7	1.6

Table 1: Initial kidney functions upon arrival.

Discussion

This case report provides insight into the need for a thorough work-up in the case of renal failure, and the importance of the discovery of DNAJB9 as the immunomarker for the diagnosis of FGN. While it is an extremely rare glomerulopathy with an unclear pathogenetic mechanism, it has been speculated that DNAJB9 is misfolded and deposited in the glomeruli which then may trigger an autoimmune response [4]. The glomerular pattern of injury varies and are characterized based on light microscopy, electron microscopy, and immunofluorescence [1]. As discussed previously, many cases are associated with at least one co-morbidity such as malignancy, autoimmune disorder, Hepatitis C, or monoclonal gammopathy [5]. While our patient had a thorough work-up that returned pan-negative results, biopsy and immunohistochemical staining was performed to give the diagnosis of FGN endocapillary proliferative type, as seen in Figure 3, with the worst prognosis. She was discharged on thrice weekly hemodialysis due to the nonrecovery of her renal function. Unfortunately, there exists a lack of evidence supporting a standard management plan. While some studies have suggested that immunomodulators such as Rituximab may be beneficial, there is not enough data to support this claim [3,5]. This case highlights the importance of a thorough renal workup in the cases of glomerulonephropathies, which includes immunomarker DNAJB9 staining.

Conclusions

In cases of idiopathic renal failure, full workup should be conducted to determine the etiology of the renal failure. This report has demonstrated the role of electron microscopy and immunofluorescence for DNAJB9 in the diagnosis of FGN.

Acknowledgements

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