https://nephropathol.com DOI: 10.34172/jnp.2024.25550 J Nephropathol. 2024;13(4):e25550

Journal of Nephropathology

Light chain deposition disease as monoclonal gammopathy of renal significance-a rare disease with scarce therapy; a case report

Fereshteh Saddadi[1], Bahareh Marghoob[1*], Mohamadhasan Fallahkohan[2]

[1]Hashemi Nejad Kidney Center (HKC), Iran University of Medical Sciences (IUMS), Tehran, Iran
[2]Shahid Beheshti Medical University (SBMU), Tehran, Iran

ARTICLE INFO

Article type:
Case Report

Article history:
Received: 9 May 2024
Accepted: 6 Jul. 2024
Published online: 10 Aug. 2024

ABSTRACT

The kidneys are one of the main organs which involved in light chain deposition disease (LCDD). The usual renal presentations are renal failure with or without nephrotic range proteinuria and microscopic hematuria. There is not a standard therapy of kidney involvement in this disease which named as monoclonal gammopathy of renal significance (MGRS). The present case is focused on a new therapeutic strategy.

Keywords: Light chain deposition disease, Monoclonal gammopathy renal significance, Mycophenolate mofetil

Case Report

Implication for health policy/practice/research/medical education:
Monoclonal gammopathy of renal significance is a new diagnostic terminology which demonstrates patients with kidney disease due to monoclonal proteins whose clinical course does not fulfill the criteria for multiple myeloma.

Please cite this paper as: Saddadi F, Marghoob B, Fallahkohan M. Light chain deposition disease as monoclonal gammopathy of renal significance-a rare disease with scarce therapy; a case report. J Nephropathol. 2024;13(4):e25550. DOI: 10.34172/jnp.2024.25550.

Introduction

Monoclonal gammopathy is a rare cause of renal damage. The kidneys are one of the main organs which involved in light chain deposition disease (LCDD) (1). The usual renal presentations are renal failure with or without nephrotic range proteinuria and microscopic hematuria. Therefore, it can cause a variety of glomerular, tubulointerstitial, and vascular lesions within the kidney (2).

When the only organ involvement is kidney, it can be called as monoclonal gammopathy of renal significance (MGRS) which exhibits clonal disorder of B cells or plasma cells that does not meet the criteria for multiple myeloma but secrets a nephrotoxic light chain and leads to kidney injury (3-5).

When we can say multiple myeloma that the criteria of multiple myeloma diagnosis are present. It means involvement of bone marrow with more than 10% plasma cells or presence of mono-clonal spike more than 3 g/dl and evidences end-organ damage. CRAB criteria (C is hypercalcemia, R is renal injury, A is anemia, and B is bone lytic lesions) shows evidence of end-organ damage (6). Treatment is recommended in patients that fulfill the criteria for multiple myeloma; all others patients should have followed up observation. The diagnostic criteria are seen in most patients but in some situations the exact diagnosis is not clear and the treatment option is controversial. There may be no correlation between tumor size and kidney injury.

In patient presenting with monoclonal immunoglobulin deposition disease the diagnosis of multiple myeloma is depends to end-organ damage. Patients who have monoclonal gammopathy–related kidney with less than 10 percent of bone marrow involvement is called monoclonal gammopathy of undetermined significance (MGUS). However, clonal disorder may require treatment. Lack of clarity in diagnostic criteria has made treatment recommendations for such patients difficult (7).

MGRS-associated kidney injury has three features: 1- lack of response to immunosuppressive regimens used in the treatment of glomerulonephritis; 2 - risk of recurrence after kidney transplantation (more than 90%); and 3- high risk of progression to the corresponding hematologic malignancy (8).

MGRS-related kidney disease are proximal tubule

*Corresponding author: Bahareh Marghoob,
Email: baharehmarghoob@yahoo.com

involvement and glomerular disorders (5). MGRS lesions are consist of proteinuria (>1.5 g/d), and high serum free light-chain. In patients with the diagnosis of MGRS-related kidney disease, a hematologic evaluation with bone marrow aspiration and biopsy should be performed to identify the clonal involvement which secretes the pathogenic monoclonal immunoglobulin. For detection of monoclonal spike, serum and urine protein electrophoresis should be performed. If the monoclonal protein has not already been identified serum free light chain and immunofixation should be assessed to identify type of monoclonal immunoglobin.

Case Presentation

A 56-year-old female patient was admitted on March 2019 due to three months of lower extremities edema. Her past medical history was hypertension and diabetes type 2. Physical examinations were unremarkable except blood pressure of 180/100 mm Hg. Laboratory test results were: hemoglobin 9.7 g/L, erythrocyte sedimentation rate (ESR) 131, serum creatinine 3.6 mg/dL, estimated glomerular filtration rate (eGFR) 20 mL/min/1.73 m^2 (MDRD), serum potassium 5.2 mmol/L, sodium, 143.0 mmol/L, calcium 9.7 mg/dL, phosphorus 4.8 mg/dL and fasting blood glucose of 166 mg/dL.

Urine analysis showed, urine protein 1+, red blood cell 3–4 /HPF with white blood cells of 5-6/HPF. Moreover, 24 hours urine protein consisted of 3.1 g/L of serum protein. Immunofixation test showed gamma light chain monoclonal was positive. Meanwhile, bone marrow biopsy detected plasmacytes were less than 4%.

Serology for antineutrophil cytoplasmic antibodies (P and C), C3 complement and ANA and anti dsDNA levels were all normal. Additionally, hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV tests were negative. Renal ultrasound showed that both kidneys had normal in size (right =123 mm, left =129 mm parenchymal thickness 18 mm), with enhanced echogenicity in the parenchymal area. Besides, serum-free kappa/lambda light chain ratio was within normal range.

Kidney biopsy revealed the following morphologic lesions in light microscopy; increasing mesangial expansions, no endothelial cells hyperplasia, across with one mesangial nodule. Furthermore, interstitial fibrosis and tubular atrophy was 30% (Figures 1 and 2).

On immunofluorescence microscopy, there were 1+linear depositions of IgG, IgA and IgM along with light chain lambda 2+, while kappa chain was negative. Since bone marrow examination was normal, the final diagnosis was LCDD with kidney involvement (MGRS). According to oncology consultation no therapy recommended for this type of LCDD.

The patient was treated with mycophenolate mofetil 1500 mg daily and prednisolone 0.5 mg/kg daily. On 4 years follow-up, she has a good health; while her renal function is maintained as her first admission without need for renal replacing therapy.

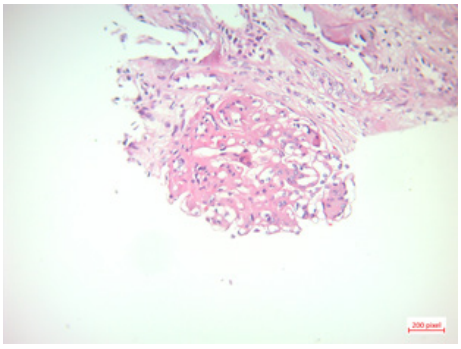

Figure 1. Hematoxylin and eosin section shows a glomerulus with mild increased mesangium and a nodule formation (×20).

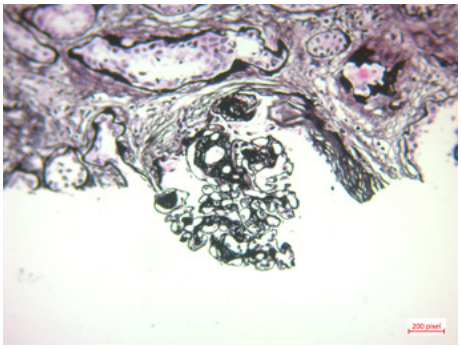

Figure 2. Jones staining shows a nodule formation (×20).

Results of laboratory tests

Her last lab data are as follows: WBC, 5.7 (1000/µL); hemoglobin, 9.8 (g/dL); platelets, 290 (1000/µL); blood urea nitrogen, 101.1 (mg/dL); serum creatinine, 3.85 (mg/dL); Na, 137 (mEq/L); serum potassium (K), 4.29 (mEq/L).

Discussion

Treatment decisions should be considered to risk and benefit of the drugs. While the clonal involvement of plasma cells is more than 10 percent treatment should be based on anti-multiple myeloma agents. Monoclonal gammopathy of clinical significance is a premalignant condition that can leads to any end-organ damage (9).

In our case because of absence of bone marrow clonal involvement, the indication of clonal directed therapy is not certain so we start immunosuppressive treatment and clinical response during follow-up was acceptable and lacking any disease progression.

Conclusion

Monoclonal gammopathy of renal significance is a new diagnostic terminology which demonstrates patients with kidney disease due to monoclonal proteins whose clinical course does not fulfill the criteria for multiple myeloma. Since the tumor burden is not high, the decision for prescription of chemotherapeutic agents is depends to experts' opinion and is different for patient to patient. MGRS and MGUS are both pathogenic manifestations of monoclonal proteins and may need anti-myeloma chemotherapeutic agents; therefore, understanding these two conditions lead to better treatment options with even fewer adverse effects.

Acknowledgments

The authors of this study would like to appreciations to the patient for her aid to publish this case report.

Authors' contribution

Data curation: Fereshteh Saddadi, Bahareh Marghoob.
Investigation: Fereshteh Saddadi.
Writing–original draft: Fereshteh Saddadi, Bahareh Marghoob.
Writing–review & editing: Mohamadhasan Fallahkoham, Bahareh Marghoob.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Ethical issues

This case report was conducted in accordance with the ethical principles outlined in the World Medical Association Declaration of Helsinki. The patient has provided written informed consent for publication as a case report. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Popov H, Stoyanov GS, Ghenev P. Light chain deposition disease: a morphological case report. Cureus. 2022 7;14:e26357. doi: 10.7759/cureus.26357.
2. Pozzi C, D'Amico M, Fogazzi GB, Curioni S, Ferrario F, Pasquali S, et al. Light chain deposition disease with renal involvement: clinical characteristics and prognostic factors. Am J Kidney Dis. 2003;42:1154-63. doi: 10.1053/j.ajkd.2003.08.040.
3. Nasr SH, Valeri AM, Cornell LD, Fidler ME, Sethi S, D'Agati VD, et al. Renal monoclonal immunoglobulin deposition disease: a report of 64 patients from a single institution. Clin J Am Soc Nephrol. 2012;7:231-9. doi: 10.2215/CJN.08640811.
4. Fermand JP, Bridoux F, Kyle RA, Kastritis E, Weiss BM, Cook MA, et al; International Kidney and Monoclonal Gammopathy Research Group. How I treat monoclonal gammopathy of renal significance (MGRS). Blood. 2013 Nov 21;122:3583-90. doi: 10.1182/blood-2013-05-495929.
5. Leung N, Bridoux F, Nasr SH. Monoclonal Gammopathy of Renal Significance. N Engl J Med. 2021 May 20;384:1931-1941. doi: 10.1056/NEJMra1810907.
6. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014;15:e538-48. doi: 10.1016/S1470-2045(14)70442-5.
7. Steiner N, Göbel G, Suchecki P, Prokop W, Neuwirt H, Gunsilius E. Monoclonal gammopathy of renal significance (MGRS) increases the risk for progression to multiple myeloma: an observational study of 2935 MGUS patients. Oncotarget. 2017;9:2344-2356. doi: 10.18632/oncotarget.23412.
8. Heilman RL, Velosa JA, Holley KE, Offord KP, Kyle RA. Long-term follow-up and response to chemotherapy in patients with light-chain deposition disease. Am J Kidney Dis. 1992;20:34-41. doi: 10.1016/s0272-6386(12)80314-3.
9. Fermand JP, Bridoux F, Dispenzieri A, Jaccard A, Kyle RA, Leung N, et al. Monoclonal gammopathy of clinical significance: a novel concept with therapeutic implications. Blood. 2018;132:1478-1485. doi: 10.1182/blood-2018-04-839480.