Immunoglobulin A Heavy Chain Deposition Disease: A Case Report

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Monoclonal immunoglobulin deposition disease (MIDD) is a rare disease characterized by the non-fibrous deposition of monoclonal immunoglobulin molecules along the glomerular or tubular basement membrane in kidney. We report herein the details of one case of heavy chain deposition disease (HCDD) diagnosed by renal biopsy, a relatively rare subtype of MIDD.

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Case Report

INTRODUCTION

Few cases of HCDD have been reported globally, and the pathogenesis was considered to be related to the loss of heavy chain CH1 functional areas and the activation of the complement system by monoclonal heavy chain.[1] The report of this case provides a guide for doctors to understand HCDD. Early diagnosis and treatment could improve the prognosis.

CASE REPORT

A 47-year-old Chinese woman was referred to us for the treatment of uncontrolled hypertension and repeated pedal edema. Her past medical history was unremarkable except hypertension. On admission, physical examination showed a blood pressure of 180/90 mmHg with pedal edema. Blood analyses revealed anemia (hemoglobin 91 g/L), marked elevation of serum creatinine (535 umol/L), hypogammaglobulinemia (IgG = 3.67 g (normal: 7.51 to 15.60g/L), IgA = 0.94 g/L (normal: 0.82 to 4.53 g/L), IgM = 0.24 g/L (normal: 0.46 to 3.04 g/L). Serological studies confirmed positive anti-nuclear antibodies and hypocomplementemia (C3 = 0.71 g/L (normal: 0.79 to 1.52 g/L), C4 = 0.15 g/L (normal: 0.16 to 0.38 g/L). Urinalysis demonstrated 3+ urine protein and urine protein was 3990 mg/d. The urine and blood Bence-Jones were negative. The immunofixation electrophoresis showed positive IgAλ M proteins and λ-light chain M proteins, negative heavy chain M proteins.

Kidney biopsy showed the nodular glomerulosclerosis by light microscopy (Figure 1, A-D), negative staining of IgG, marked positive staining of IgA, negative staining of α heavy chain, unapparent positive staining of IgM by immunofluorescence (Figure 2, A-C), granular electron-dense material deposits along the tubular and glomerular basement membrane by electron microscopy (Figure 2, D-F).

Taken together, these discoveries confirmed the diagnosis of α-HCDD of the kidney. For some reasons, the patient refused chemotherapy or hematopoietic stem cell transplantation, she was started on hemodialysis treatment instead.

DISCUSSION

In contrast with other renal diseases, MIDD has rarely been reported which account for less than 1% in the histopathological diagnosis of renal biopsy.[2] HCDD can be γ chain (IgG), α chain (IgA) or μ chain (IgM),[3] it is a rare subtype of the group of MIDD which includes the other two groups of light chain deposition disease (LCDD), both light and heavy chain deposition disease(L/HCDD). Studies have shown that the loss of CH1 functional

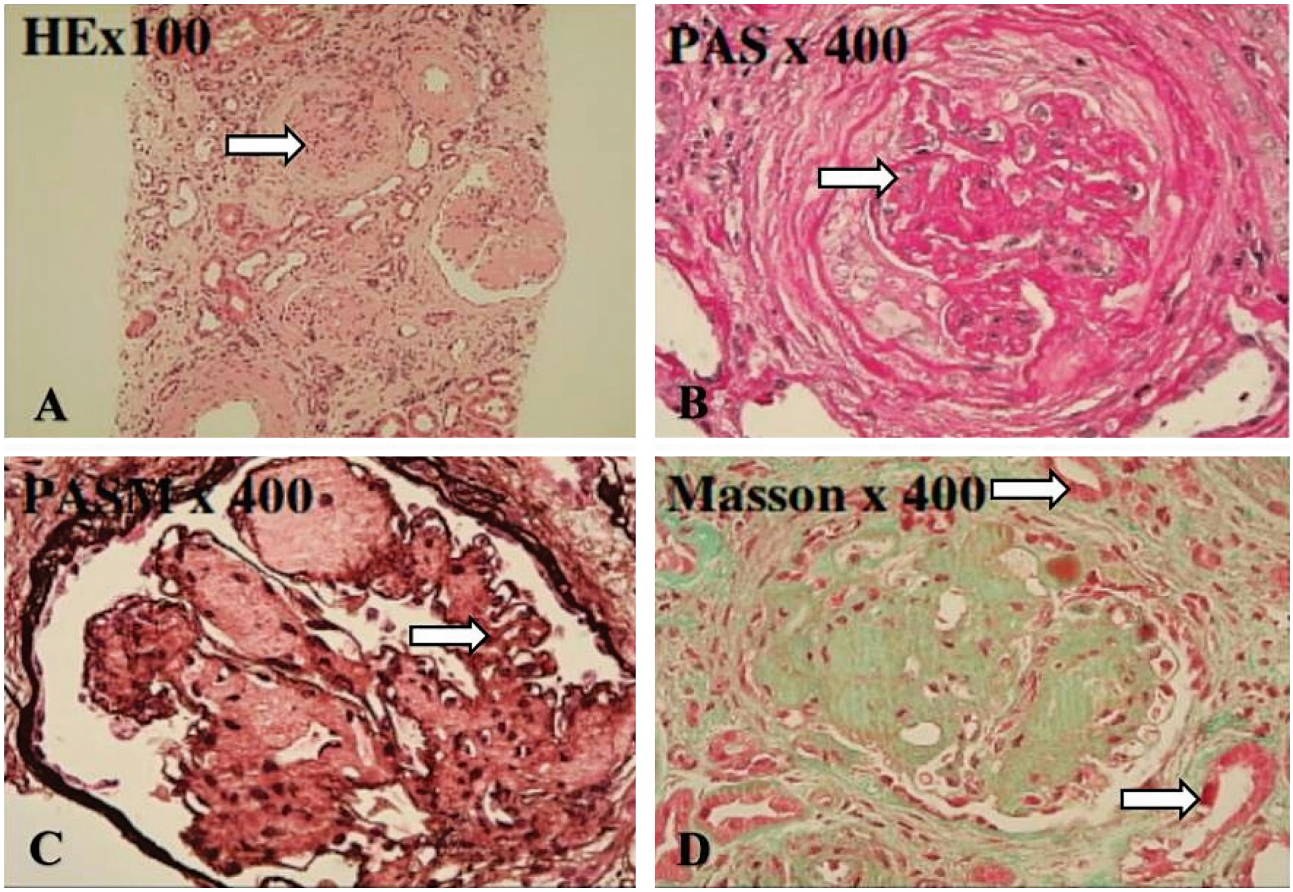

Figure 1. A, There are six glomerular sclerosis (Magnification, ×200). B, The mesangial cells and stroma of the glomerulus were moderately to severely proliferated with nodular changes. The nodules are periodic acid-Schiff (PAS) positive (Magnification, ×400). C, Stenosis and occlusion of capillary lumen, thickening of basement membrane, segmental mesangial insertion and bioracular formation were observed (Magnification, ×400). D, Multifocal and flaky infiltration of inflammatory cells in renal interstitium with fibrosis, thickening of arterioles, hyperplasia of intimal fibrous tissue, hyaline changes, and lumen stenosis were observed (Magnification, ×400).

areas is present in all described γ 1 cases of HCDD which potentially participates in the pathogenesis of HCDD.[4]

The age of HCDD patients ranged from 29 to 73 years old, with an average age of 53 years old and no gender or ethnic difference.[5] HCDD patients usually with renal function impaired, the clinical manifestations were mostly nonspecific such as nephrotic syndrome, proteinuria, microscopic hematuria and hypertension. The HCDD case we admitted which was a 47 years old woman characterized by hypertension and repeated pedal edema. The laboratory findings such as M proteinemia and the increase of free single chain had a certain guiding effect on the diagnosis, multiple myeloma could be ruled out by bone marrow biopsy results, kidney biopsy showed the nodular glomerulosclerosis, marked positive staining of IgA, negative staining of α heavy chain.

The diagnosis of HCDD mainly depends on the pathological examination of renal biopsy, especially by immunopathological light and heavy chain staining and electron microscopy. It is not clear now why the α-heavy chain immunostaining in this patient was negative. We guess that may be related to the indirect mechanism of complement activation or endothelial injury induced by monoclonal immunoglobulin (MIG) in a few cases of renal disease, so there was no MIG deposition in renal tissue.[6] It may also be related to certain errors or severe deterioration of renal function. A multi-center study should be conducted to collect more cases for further discussion.

Currently, there are no unified guidelines for the treatment of HCDD, and generally referred to the international treatment schemes for multiple myeloma and monoclonal light amyloidosis,[7] which used chemotherapy and autologous

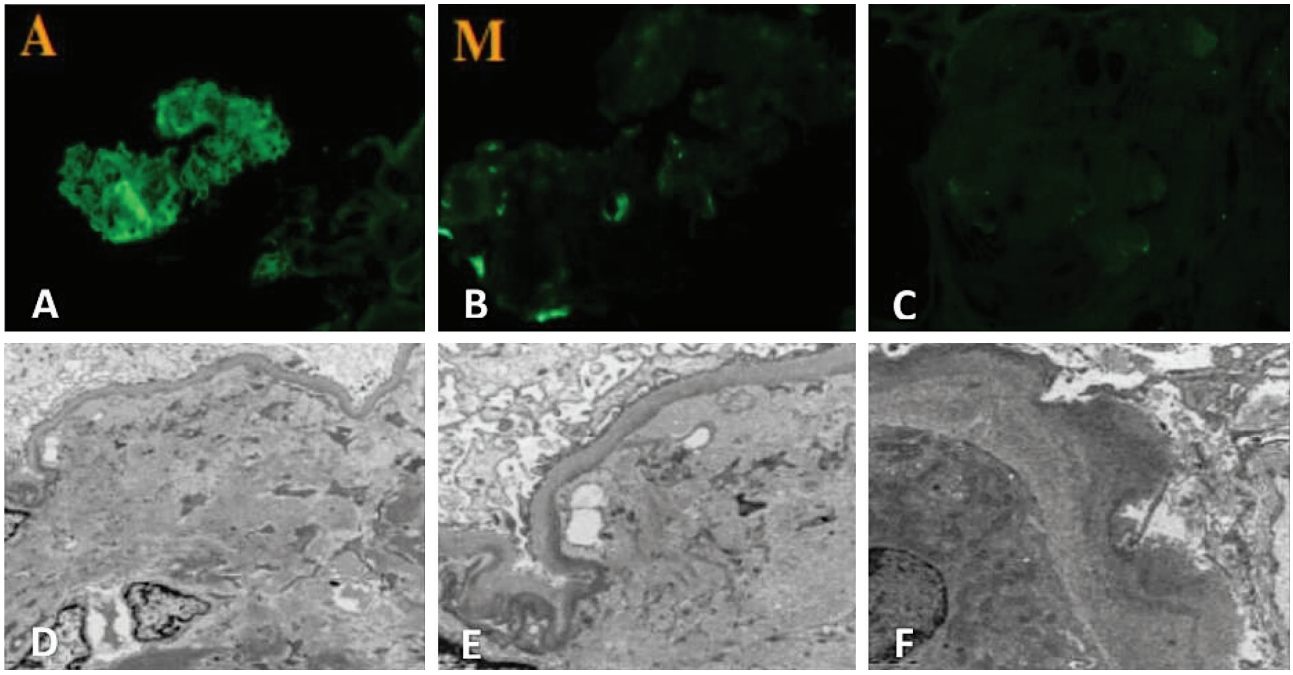

Figure 2. A, Immunofluorescence deposition of IgA was observed in the glomerulus, capillary loops and mesangial areas, and renal tubular epithelium. B, IgM Chain Suspiciously Positive. C, α heavy chain fluorescence staining was negative. D-F, The mesangial area, the medial basement membrane of the glomerulus, the lateral wall of the baumann's bursa, the lateral basement membrane of the renal tubule and the arterioles showed a lot of granular amorphous electron density.

hematopoietic stem cell transplantation. Literature have revealed that chemotherapy could improve patient outcomes especially among individuals in an early stage of disease.[8] Regrettably was the patient refused chemotherapy or hematopoietic stem cell transplantation, started on hemodialysis treatment instead, and the therapeutic effect after chemotherapy could not be followed up.

CONCLUSION

Taken together, we report herein one case of HCDD whose clinical scenario are not peculiar. We deem that prompt serological tests and biopsy led to the exact diagnosis; prompt treatment led to better prognosis.

DECLARATIONS

We have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

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Nil.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Cohen Camille, El-Karoui Khalil, Alyanakian Marie-Alexandra, et al. Light and heavy chain deposition disease associated with CH1 deletion[J].Clin kindey J, 2015, 8(2): 237-239.
2. Michael T, Anna C, Claire W, etal. Heavy chain deposition disease presenting with raised anti-GBM antibody levels;a case report[J]. BMC Nephrology, 2020, 21(1): 231-239.
3. Oe Y, Soma J, Sato H, et al. Heavy chain deposition disease: an overview[J].Clin Exp Nephrol, 2013, 17(6): 771-778.
4. Moulin B, Deret S, Mariette X et al. Nodular glomerulosclerosis with deposition of monoclonal immunoglobulin heavy chains lacking C(H)1[J].J Am Soc Nephrol,1999,10: 519–528.
5. Nasr SH, Valeri AM, Cornell LD, et al.Renal monoclonal immunoglobulin deposition disease: a report of 64 patients from a single institution[J]. Clin J Am Soc Nephrol, 2012, 7(2): 231-239.
6. Sethi Sanjeev,Rajkumar S Vincent, D'Agati Vivette D. The Complexity and Heterogeneity of Monoclonal Immunoglobulin-Associated Renal Diseases.[J].Journal of the American Society of Nephrology:JASN,2018, 29(7): 1810-1823.
7. Varga C, Titus SE, Toskic D, et al. Use of novel therapies in the treatment of light chain amyloidosis[J]. Blood Reviews, 2019, 37.

8. Oe Y, Nakaya I, Yahata M, et al. A case of gamma1-heavy chain deposition disease successfully treated with melphalan and predniso-lone therapy[J]. Intern Med, 2010, 49(14): 1411-1415.

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