

# Multiple Myeloma Presenting as Acute Kidney Failure Secondary to Lambda Light Chain Deposition

Marie-Eve Emond-Boisjoly<sup>1,\*</sup>, Emilie Lemieux-Blanchard<sup>1,2</sup>, Antonia Maietta<sup>3</sup> and Stéphanie Forté<sup>1,2</sup>

<sup>1</sup>Department of Medicine, University of Montréal, Montréal, Qc, Canada

<sup>2</sup>Division of Hematology and Medical Oncology, Centre Hospitalier de l'Université de Montréal, Montréal, Qc, Canada

<sup>3</sup>Department of Pathology and Cellular Biology, University of Montréal, Montréal, Qc, Canada

**Abstract:** Renal monoclonal immunoglobulin deposition disease (MIDD) is a rare disease defined by deposition of monoclonal light chains and/or heavy chains on basement membranes and vascular walls of the kidney. We describe a case of a 71-year-old woman with kidney failure secondary to monoclonal immunoglobulin deposition disease lambda in association with plasma cell dyscrasia. Her initial serum protein electrophoresis did not demonstrate a monoclonal protein, and classic cast nephropathy was absent on renal biopsy. However, lambda light chain deposits and associated changes confirmed MIDD. She achieved a very good partial response (VGRP) after 8 cycles of CyBORd (cyclophosphamide, bortezomib, dexamethasone) and her kidney function improved. This case highlights the importance of an early diagnostic with renal biopsy to prevent end-stage renal disease. A review of the existing literature and a discussion on the management of the disease is presented.

**Keywords:** Monoclonal immunoglobulin deposition disease, Light chain and heavy chain deposition disease, Plasma cell neoplasms, Light chain deposition disease, Multiple myeloma, Randall disease, Kidney failure.

## INTRODUCTION

Kidney disease is a common complication of monoclonal gammopathies. The range of renal complications is wide, and their classification relies on the type of paraprotein, the pattern of ultrastructural organization of immunoglobulin deposits and on the localization of renal lesions. Monoclonal immunoglobulin deposition disease (MIDD) is a rare disease defined by deposition of monoclonal light chains and/or heavy chains on tissue and causing organ dysfunction [1]. These non-amyloid deposits are neither fibrillar nor Congo red positive. Light chain deposition disease (LCDD) is the most prevalent with Kappa being the most dominant light chain [2]. Most patients with LCDD meet diagnostic criteria for multiple myeloma, and monoclonal gammopathy of renal significance (MGRS) is the second most common diagnosis [2]. Kidney involvement is the major manifestation in most patients and consists of nephrotic syndrome, microscopic hematuria and kidney failure. Extra-renal manifestations are probably underdiagnosed as they are usually asymptomatic. Tissue deposits can occur in a variety of organs, especially the liver, the myocardium or the nerve fibres [3]. The diagnosis requires demonstration of linear

deposits of the involved monoclonal immunoglobulin on an affected tissue, most commonly the kidney [4]. Treatment targets the underlying plasma cell clone with chemotherapy. We present a case of a 71-year-old woman with kidney failure secondary to monoclonal immunoglobulin deposition disease lambda.

## CASE REPORT

### Investigations

A 71-year-old female with no prior history of renal disease presented to emergency after routine blood work ordered by her primary care physician revealed new abnormal renal function. Her history was notable for severe obesity (BMI 53 kg/m<sup>2</sup>), gonarthrosis and hypertension for many years. She was taking antihypertensive medications in the form of calcium channel blockers and diuretics. She smoked one pack per day for 15 years before quitting 20 years ago. She did not consume alcohol. Family history was negative for any nephropathy or autoimmune processes. She had no specific complaint. At admission, she was in sinus rhythm, had a blood pressure of 120/65 and oxygen saturation on room air was 98%. There was no particular finding on physical examination.

Laboratory investigations revealed a serum creatinine and albumin levels of 360 µmol/L and 35 g/L, respectively. Urinalysis revealed 1+ protein, 11-100

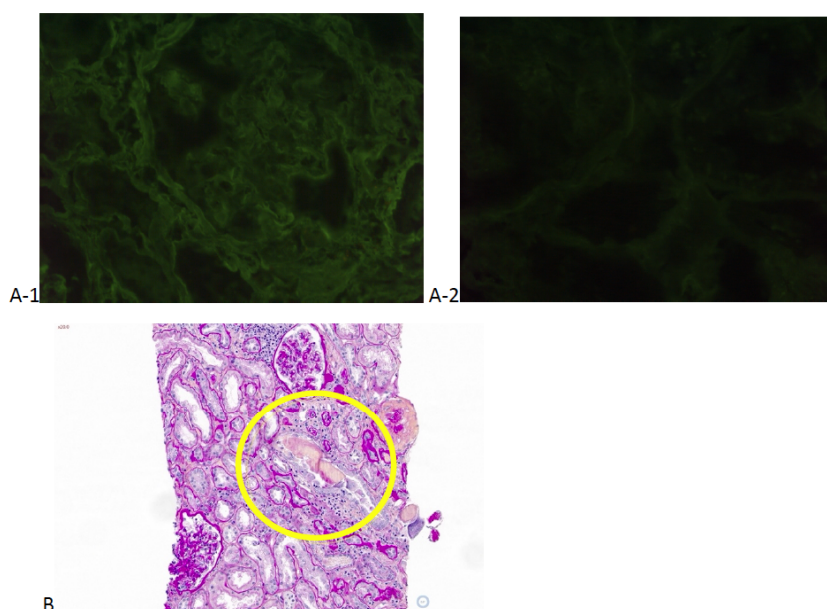
\*Address correspondence to this author at the Department of Medicine, University of Montréal, Montréal, Qc, Canada; Tel: +1 514-343-6111; E-mail: marie-eve.emond-boisjoly@umontreal.ca

WBCs, 3-5 red blood cells and no cast. Urine protein/creatinine ratio was 0.291 g/mmol. The 24 h urine protein excretion was 3.8 g. The extended electrolytes, including calcium (2.43 mmol/L), were normal. Ultrasound examination showed kidneys of normal size and echogenicity. The initial laboratory workup revealed a normocytic anemia (Hgb 80 g/L, MCV 94.2 fl, WBC  $10.7 \times 10^9/L$ , platelet  $417 \times 10^9/L$ ). Haptoglobin, Coombs test, iron panel, liver function tests, vitamin B12 and folate were all unremarkable. The serum protein electrophoresis did not identify a paraprotein. Autoimmune serology testing revealed a positive antinuclear antibody (ratio 1/2560) in anti-SP-100 pattern and a positive anti-RNP at a concentration of 4.7 AI (normal range 0-0.9 AI). All other autoantibodies (*i.e.*, anti-double stranded DNA antibodies, anti-Ro, anti-La, anti-cyclic citrullinated peptide (anti-CCP) antibodies and antineutrophil cytoplasmic antibodies (ANCA)) were negative. Complement components 3 and 4 (C3 and C4) were within the normal range. The consulted rheumatologist did not find any clinical and paraclinical features of connectivitis: renal injury secondary to autoimmune disease was considered unlikely. HIV, HBV and HCV infections were ruled out. There were no specific drug exposures suggestive of drug-induced nephropathy.

## Diagnosis

Since the etiology of the kidney failure was still unknown, she subsequently underwent renal biopsy which was exempt of classic cast nephropathy associated my multiple myeloma. However, the biopsy demonstrated monoclonal immunoglobulin deposition disease. On the renal biopsy, sixteen glomeruli exhibited diffuse mesangial expansion and thickening of tubular basement membranes. Immunofluorescence revealed lambda light chain deposition in tubular basement membranes and glomerular basement membranes but no evidence of cast nephropathy. Staining for IgG, IgA, IgM, C3, C1q were negative (Figure 1). There was only 1 cast with a fractured appearance and a variable staining pattern with Masson trichrome suggesting myeloma kidney (Figure 1). No features of vasculitis or microangiopathy were found. Red Congo staining was negative, indicating non-amyloid disease.

While waiting for the pathological diagnosis, serum free light chain results became available. Lambda light chains were extremely elevated (1010 mg/L) with a kappa/lambda ratio of 0.02. The immunofixation of the serum protein electrophoresis identified a small monoclonal IgA lambda M-protein at a concentration of



- A) Immunofluorescence (IF) staining features of the renal biopsy. The IF was positive for lambda chains (A-1) but not for kappa chains (A-2).  
B) Cast with a fractured appearance (yellow circle) with peripheral cellular reaction and polychromatic Masson trichrome staining.

**Figure 1:** Pathologic finding of the renal biopsy.

2 g/L. Immunoglobulin quantification showed lightly elevated IgA 3.67 g/L (normal range 0.56-3.60) with low IgM 0.20 g/L (normal range 0.35-2.85) and normal IgG 7.08 g/L (normal range 5.39-13.70). The presence of the monoclonal deposits and the increase in lambda free light chains warranted bone marrow examination. Bone marrow aspiration and biopsy revealed monoclonal plasma cell infiltration up to 30% (Figure 2). A whole-body CT scan did not detect osteolytic lesions.

The patient was diagnosed with multiple myeloma accompanied by lambda light chain deposition disease. The severity of the renal involvement warranted an interventionist approach. According to the International Staging System (ISS), she was diagnosed with stage III multiple myeloma as beta-2-microglobulin level was 10.12 mg/L, albumin level was 35 g/L and serum LDH were elevated. Unfortunately, no cytogenetic testing was done.

### Treatment

During her hospitalization, the patient received her first cycle of CyBorD (cyclophosphamide, bortezomib, dexamethasone) chemotherapy. Treatment was well tolerated. After the first cycle, the kidney function improved and she left the hospital with a creatinine of 204  $\mu\text{mol/L}$ .

### Follow-up and Outcomes

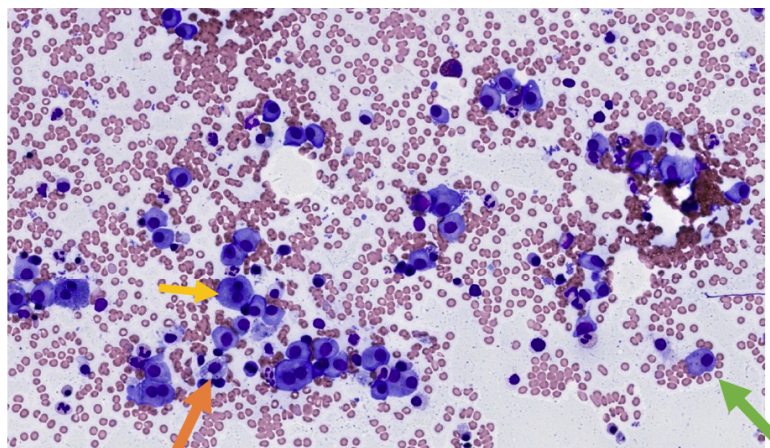
Six months after her diagnosis, the patient was hospitalized for acute hypoxemic respiratory failure secondary to severe COVID-19 infection. She

developed chronic hypoxemic respiratory failure and she was discharged with oxygen at home. Because of her hospital-associated deconditioning, a very good partial response (VGPR) with a reduction >90% of lambda light chain and the recovery of her kidney function and proteinuria, the chemotherapy was stopped after 8 cycles. Seventeen months after initial presentation, the patient is still in VGPR and her kidney function is stable.

### DISCUSSION

MIDD is defined by deposition of monoclonal immunoglobulin molecules in basement membranes and vascular walls [4]. The MIDD includes light chain deposition disease, in which the deposits are composed of monoclonal light chains only as illustrated in this report, heavy chain deposition disease (HCDD), in which the deposits are composed of monoclonal heavy chains only, and light and heavy chain deposition disease (LHCDD), in which the deposits are composed of both light and heavy chains. LCDD is the most prevalent with Kappa chains being the most dominant [2] light chains (90% in one case series). LCDD can coexist with myeloma cast nephropathy (MCN).

In a multicenter study with 63 cases of LCDD, Pozi and colleagues reported that the mean age at presentation was 58 years, with a male predominance [5]. Clinically, most patients with LCDD present with hypertension, kidney failure and proteinuria. Fifty-two percent of patients present with acute kidney insufficiency with a mean creatine level of 336  $\mu\text{mol/L}$ .



Infiltration of bone marrow by plasmacytes (in blue) is illustrated. Some plasmacytes are atypical showing binucleation (yellow arrow). Others exhibit prominent cytoplasmic vacuolization (orange arrow). Accumulation of amorphous cytoplasmic content is suspected in several plasmacytes with enlarged cytoplasm (green arrow).

**Figure 2:** Bone marrow aspirate with Wright stain.

Forty percent of patients have nephrotic proteinuria with a median proteinuria of 2.7 g/d but only 17% present with a full nephrotic syndrome [2]. Microscopic hematuria is also described. Patients with LCDD associated MCN have higher serum creatinine at presentation and lower incidence of nephrotic proteinuria.

Extra-renal manifestations of LCDD are probably underdiagnosed as they are usually asymptomatic. Tissue deposits can occur in a variety of organs especially the liver, the myocardium or the nerve fibres and cause hepatomegaly with abnormal liver test function, hypertrophic cardiomyopathy with impaired diastolic function or peripheral neuropathy, respectively [2]. Pulmonary light chain deposition disease is a rare disease presenting principally with nodular and cystic lesions [6].

The diagnosis of MIDD requires a renal biopsy. LCDD can produce nodular glomerulosclerosis in 50% of cases. At electronic microscopy, LCDD shows linear light chain deposits along the tubular basement membranes, the glomerular basement membranes, the arterial walls and the mesangium. These deposits are nonorganized and granular (not fibrillar). They show positive PAS staining and Congo-red negative [6]. The immunofluorescence is characterized by a single light chain isotype, usually kappa. The typical findings of combined LCDD & MCN are fractured and polychromatic casts associated with interstitial edema, inflammation, fibrosis and tubular degenerative changes. Immunofluorescence also reveals fractured casts with a single light chain component [2]. In our case, the renal histology did not perfectly match the description of LCDD & MCN as no cast was found on immunofluorescence.

In a study of 64 cases of MIDD patients, Nasr and colleagues reported that only 19% of patients were known to have a dysproteinemia before MIDD diagnosis [8]. By immunofixation, monoclonal protein was found in 70% of cases in serum and 78% in urine after renal biopsy. Serum free light chain ratio was abnormal for all patients. Patients with MIDD and LCDD are diagnosed with multiple myeloma in 20-40% and 65% respectively. The incidence of multiple myeloma in LCDD & MCN is around 90% [2]. The principal diagnosis associated with pure MIDD is MGRS.

The therapeutic approaches for pure MIDD or LCDD associated myeloma are similar to those used

for myeloma. However, there is currently no standardized treatment. Ziogas *et al*, in a study of 18 patients with MIDD treated with bortezomib-based regimens, reported that 61% achieved a hematological response and 33% achieved a complete or very good partial response [9].

In more recent series [5], the mean renal and overall survivals were 64 and 90 months respectively in MIDD. 30-40% of patients diagnosed with MIDD progressed to end-stage renal disease at follow-up. The most important predictor of renal prognosis is the initial serum creatinine at the time of the biopsy [2, 5]. Renal and overall survival prognosis is worst for patients diagnosed with MIDD with underlying myeloma [2]. As mentioned, LCDD & MCN tend to have more severe renal disease at presentation which probably contributes to the worst renal outcome. In a study of 63 patients with LCDD [5], age, coexisting multiple myeloma and evidence of extra-renal light chain depositions were independent factors of overall survival.

### Learning Points

In conclusion, our case highlights the importance of taking MIDD into account as a possible cause of kidney injury even when a paraprotein is not identified on the initial electrophoresis. Early kidney biopsy and serum light chains assay are primordial for the investigation of MGRS and multiple myeloma. Rapid treatments, based on the underlying clone, is crucial to prevent end-stage renal disease. Chemotherapy may lead to hematological remission and kidney dysfunction resolution.

### ACKNOWLEDGEMENT

We thank the patient for granting permission to publish this information. We like to acknowledge Dr François Gougeon, pathologist, for providing the images of the kidney biopsy.

### FINANCIAL DISCLOSURE

None to declare.

### CONFLICT OF INTEREST

The authors have no conflict of interest.

### INFORMED CONSENT

Consent obtained directly from the patient.

## AUTHOR CONTRIBUTIONS

Marie-Eve Emond-Boisjoly, Stéphanie Forté and Emilie Lemieux-Blanchard were involved in the care of the patient. Marie-Eve Emond-Boisjoly designed the case report and drafted the manuscript. Stephanie Forte and Antonio Maietta selected the images. All authors contributed to the revision of the manuscript.

## DATA AVAILABILITY

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

## ABBREVIATIONS AND ACRONYMS

BMI ; body mass index, HCDD ; heavy chain deposition disease, LCDD ; light chain deposition disease, LHCD ; light and heavy chain deposition disease, MCN; myeloma cast nephropathy, MGRS ; monoclonal gammopathy of renal significance , MIDD ; monoclonal immunoglobulin deposition disease, VGRP ; very good partial response.

## REFERENCES

- [1] Khoury JD, Solary E, Ablu O, Akkari Y, Alaggio R, Apperley JF, Bejar R, *et al.* The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia*. 2022; 36(7): 1703-1719. <https://doi.org/10.1038/s41375-022-01613-1>
- [2] Lin J, Markowitz GS, Valeri AM, Kambham N, Sherman WH, Appel GB, *et al.* Renal monoclonal immunoglobulin deposition disease: the disease spectrum. *J Am Soc Nephrol*. 2001; 12(7): 1482-1492. <https://doi.org/10.1681/ASN.V1271482>
- [3] Javaugue V, Bouteau I, Sirac C, Quellard N, Diolez J, Colombo A, Desport E, *et al.* Classification et prise en charge thérapeutique des gammopathies monoclonales de signification rénale, *La Revue de Médecine Interne* 2018; 39(3): 161-170. <https://doi.org/10.1016/j.revmed.2017.03.012>
- [4] Leung N, Bridoux F, Batuman V, Chaidois A, Cockwell P, D'Agati VD, Dispenzieri A, *et al.* The evaluation of monoclonal gammopathy of renal significance: a consensus report of the International Kidney and Monoclonal Gammopathy Research Group. *Nat Rev Nephrol* 2019; 15(1): 45-59. <https://doi.org/10.1038/s41581-018-0077-4>
- [5] Pozzi C, D'Amico M, Fogazzi GB, Curioni S, Ferrario F, Pasquali S, Quattrocchio G, *et al.* Light chain deposition disease with renal involvement: clinical characteristics and prognostic factors. *Am J Kidney Dis* 2003; 42(6): 1154-1163. <https://doi.org/10.1053/j.ajkd.2003.08.040>
- [6] D'Agati VD, Jennette JC, Silva FG. Glomerular Diseases with paraproteinemia or organized deposits In: D'Agati VD, Jennette JC, Silva FG, eds. *Atlas of nontumor pathology: Non-Neoplastic kidney diseases*. Washington, DC: American Registry of pathology, Armed Forces Institute of Pathology; 2005: 199-237.
- [7] Wei P, Tao R, Liu Y, Xie H, Jiang S, Yu D, Lu H, *et al.* Pulmonary light chain deposition disease: a case series and literature review. *Annals of translational medicine* 2020; 8(9): 588. <https://doi.org/10.21037/atm-20-2708>
- [8] Nasr SH, Valeri AM, Cornell LD, Fidler ME, Sethi S, D'Agati, Leung N. Renal monoclonal immunoglobulin deposition disease: a report of 64 patients from a single institution. *Clin J Am Soc Nephrol* 2012; 7(2): 231-239. <https://doi.org/10.2215/CJN.08640811>
- [9] Ziogas DC, Kastiris E, Terpos E, Roussou M, Migkou M, Gavriatopoulou M, Spanomichou D, *et al.* Hematologic and renal improvement of monoclonal immunoglobulin deposition disease after treatment with bortezomib-based regimens. *Leukemia & Lymphoma* 2017; 58(8): 1832-1839. <https://doi.org/10.1080/10428194.2016.1267349>

Received on 09-11-22

Accepted on 25-11-22

Published on 30-11-2022

DOI: <https://doi.org/10.12974/2312-5411.2022.09.03>

© 2022 Emond-Boisjoly *et al.*

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.