

## CLINICAL IMAGE

## Lysozyme nephropathy in chronic myelomonocytic leukemia

Ami B. Patel<sup>1</sup>  | Rodney R. Miles<sup>2</sup> | Michael W. Deininger<sup>1</sup><sup>1</sup>Division of Hematology and Hematologic Malignancies, University of Utah, Salt Lake City, Utah<sup>2</sup>Department of Pathology, ARUP Laboratories, University of Utah, Salt Lake City, Utah

## Correspondence

Ami B. Patel, 2000 Circle of Hope, Huntsman Cancer Institute, The University of Utah, Salt Lake City 84112, UT. Email: ami.patel@hci.utah.edu

## Abstract

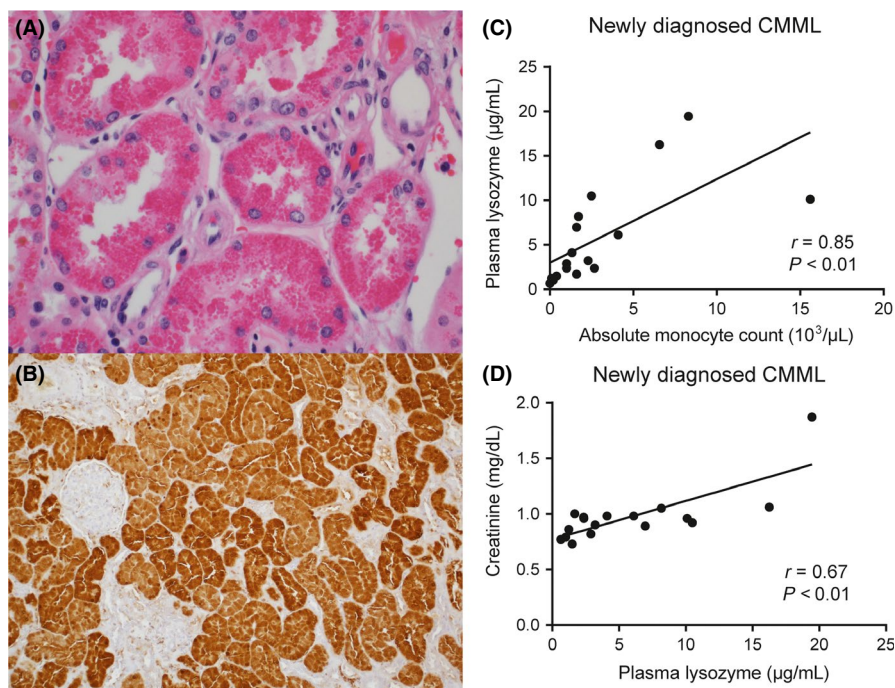
Lysozyme nephropathy is a frequently unrecognized cause of renal disease in chronic myelomonocytic leukemia and may serve as a novel indication for treatment in this patient population. We demonstrate that in newly diagnosed CMML patients, plasma lysozyme levels are positively correlated with both absolute monocyte count and serum creatinine.

## KEYWORDS

hematology, nephrology, oncology

A 60-year-old woman with white blood cell count of  $70 \times 10^3/\mu\text{L}$  with monocytosis, hemoglobin 11.2 g/dL, platelets  $89 \times 10^3/\mu\text{L}$ , and creatinine 1.41 mg/dL had bone marrow biopsy demonstrating chronic myelomonocytic leukemia (CMML). Subsequent nephrectomy revealed renal cell carcinoma (RCC). Proximal tubules uninvolved by RCC contained

abundant eosinophilic droplets confirmed as lysozyme (Figure 1A,B). Serum and urine lysozyme concentrations were  $>10 \mu\text{g/mL}$ . She received 5-azacitidine with reduction in monocytosis and serum lysozyme and creatinine, with complete normalization of these parameters following allogeneic stem cell transplant.



**FIGURE 1** Lysozyme nephropathy in CMML. A, H&E stain demonstrating bright eosinophilic cytoplasmic granules within renal proximal tubule cells. B, Lysozyme immunohistochemical stain highlighting cytoplasmic droplets within the proximal tubule. C, Correlation of absolute monocyte count of newly diagnosed CMML patients with plasma lysozyme levels. D, Correlation of plasma lysozyme levels with concurrent serum creatinine measurements

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2019 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.

Lysozyme is a bacteriolytic enzyme detectable in monocytes. Lysozyme is reabsorbed by renal proximal tubule cells until concentrations exceed 45  $\mu\text{g/mL}$  and urinary excretion is observed.<sup>1</sup> Increased serum and urine lysozyme are seen in diseases characterized by monocytic proliferation, including myeloid leukemia.<sup>1</sup>

We measured plasma lysozyme in CMML patients at diagnosis (N = 18), on therapy with hypomethylating agents (N = 10), and in healthy controls (N = 6). Median concentrations were highest at diagnosis (7.5  $\mu\text{g/mL}$ ) and correlated with monocyte count and serum creatinine (Figure 1C,D). Treatment reduced concentrations (1.59  $\mu\text{g/mL}$ ), without reaching those of controls (0.68  $\mu\text{g/mL}$ ).

Renal impairment in CMML may reflect age-related comorbidities. However, intravenous lysozyme causes tubular damage in rats, arguing that monocyte-derived lysozyme could cause renal injury in CMML that is amenable to reversal with cytoreduction.<sup>2</sup>

### CONFLICT OF INTEREST

None declared.

### AUTHOR CONTRIBUTION

ABP: wrote the initial draft of this manuscript. MWD: edited the manuscript and participated in clinical care. RRM:

provided histologic images. All authors reviewed the final draft of the manuscript and approved its submission. ABP: is supported by an American Society of Hematology RTAF award.

### ORCID

Ami B. Patel  <https://orcid.org/0000-0002-5374-3831>

### REFERENCES

1. Hayslett JP, Perillie PE, Finch SC. Urinary muramidase and renal disease. Correlation with renal histology and implication for the mechanism of enzymuria. *N Engl J Med.* 1968;279:506-512.
2. Cojocel C, Dociu N, Baumann K. Early nephrotoxicity at high plasma concentrations of lysozyme in the rat. *Lab Invest.* 1982;46:149-157.

**How to cite this article:** Patel AB, Miles RR, Deininger MW. Lysozyme nephropathy in chronic myelomonocytic leukemia. *Clin Case Rep.* 2019;7:1263–1264. <https://doi.org/10.1002/ccr3.2188>