Editorials

1707 A Blueprint for Assessing Affordability of SGLT2 Inhibitors in the United States: The Cost-Effectiveness of Dapagliflozin in Three European Countries
Annika Khine and Eugene Lin
See related article on page 1730.

1710 Toward Guideline-Directed Medical Therapy in Nephrology: Lifetime Benefit of RAAS and SGLT2 Inhibition in Nondiabetic Kidney Disease
Evan M. Zeitler and Amy K. Mottl
See related article on page 1754.

1713 Bardoxolone Methyl for Alport Syndrome: Opportunities and Challenges
Catherine Quinlan and Kushani Jayasinghe
See related article on page 1763.

1716 Reproductive Health in Women with Kidney Disease
Ramnika Gumber and Silvi Shah
See related article on page 1742.

Original Articles

Chronic Kidney Disease

1719 Symptom Burden before and after Dialysis Initiation in Older Patients
Esther N.M. de Rooij, Yvette Meuleman, Johan W. de Fijter, Kitty J. Jager, Nicholas C. Chesnaye, Marie Evans, Fergus J. Caskey, Claudia Torino, Gaetana Porto, Maciej Szymczak, Christiane Drechsler, Christoph Wanner, Friedo W. Dekker, and Ellen K. Hoogeveen, on behalf of the EQUAL study investigators

1730 Cost-Effectiveness of Dapagliflozin as a Treatment for Chronic Kidney Disease: A Health-Economic Analysis of DAPA-CKD
Phil McEwan, Oliver Darlington, Ryan Miller, John J.V. McMurray, David C. Wheeler, Hiddo J.L. Heerspink, Andrew Briggs, Klas Bergenheim, and Juan Jose Garcia Sanchez
See related editorial on page 1707.

1742 Menstrual Abnormalities and Reproductive Lifespan in Females with CKD: A Systematic Review and Meta-Analysis
Chantal L. Rytz, Golasa Samedi Kochaksaraei, Leslie Skeith, Paul E. Ronksley, Sandra M. Dumanski, Magali Robert, and Sofia B. Ahmed
See related editorial on page 1716.

1754 Estimated Lifetime Benefit of Combined RAAS and SGLT2 Inhibitor Therapy in Patients with Albuminuric CKD without Diabetes
See related editorial on page 1710.
Effects of Bardoxolone Methyl in Alport Syndrome
See related editorial on page 1713.

Nephrology Program Director Protected Time for Program Administration in the United States
Christina M. Yuan, Brian Y. Young, Maura A. Watson, and Amy N. Sussman

Development and Validation of a Lifetime Risk Model for Kidney Failure and Treatment Benefit in Type 2 Diabetes: 10-Year and Lifetime Risk Prediction Models
Helena Bleken Østergaard, Stephanie H. Read, Naveed Sattar, Stefan Franzén, Nyokke Halbesma, Jannick A.N. Dorresteijn, Jan Westerink, Frank L.J. Visseren, Sarah H. Wild, Björn Eliasson, and Joep van der Leeuw

A Survey of Environmental Sustainability Practices in Dialysis Facilities in Australia and New Zealand
Benjamin Talbot, Katherine Barraclough, Matthew Sypek, Pedro Gois, Leila Arnold, Stephen McDonald, and John Knight

Effect of Furosemide on Proximal Tubular Secretion of Organic Solutes in Patients Receiving Hemodialysis
Tammy L. Sirich, Thomas H. Hostetter, and Jennifer E. Flythe

Correction: Use and Outcomes of Induction Therapy in Well-Matched Kidney Transplant Recipients

Overview of the Medical Management of the Critically Ill Patient
Rebecca H. Martinez, Kathleen D. Liu, and J. Matthew Aldrich

How I Treat Focal Segmental Glomerulosclerosis
Adrian Liew and Keisha L. Gibson

Obesity in CKD: A Promising Path Forward
Allon N. Friedman

Community Houses to Increase Access to Home Dialysis
Rachael Walker and Suetonia Palmer

The Immune System and Idiopathic Nephrotic Syndrome
Ruth E. Campbell and Joshua M. Thurman
On the Cover
What is the Diagnosis?

An 85-year-old man with type 2 diabetes and hypertension was initially evaluated for proteinuria (1 g/day), of which only 200 mg was albuminuria. Serum protein electrophoresis showed an IgA-lambda monoclonal protein and an elevated serum kappa/lambda ratio at 5.71. Urine protein electrophoresis showed free kappa monoclonal protein (8% of total urine protein). A bone marrow biopsy workup revealed chronic myelomonocytic leukemia (CMML). His plasma lysozyme level taken shortly after was greater than 10.8 μg/ml (reference range: 2.6–6.0 μg/ml) with concurrent monocytosis (7.2 billion/L). His serum creatinine increased to 2.25 mg/dl from a baseline serum creatinine at 1.70 mg/dl. A kidney biopsy was then performed.

Image Description:
Light microscopy (left image) showed an unremarkable glomerulus (G) but dilated proximal tubules (blue arrows) with granular and strongly eosinophilic cytoplasm on hematoxylin and eosin-stained sections. Immunohistochemical staining for lysozyme (pre-diluted polyclonal antibody, Cell Marque, Rocklin, CA) was strongly positive (green arrows) in the cytoplasm and nuclei of the proximal tubules (middle image). Lysozyme staining was negative in the glomerulus (G), serving as an internal control. Electron microscopy (right image) showed expanded lysosomes in the proximal tubular cytoplasm with rounded, dense dots in a chocolate chip cookie pattern indicated with orange arrows (scale bar =1.5 μm), as demonstrated previously (1). No monoclonal protein was detected by immunofluorescent stains in the kidney biopsy.

Teaching Points:
Lysozyme nephropathy is a rare etiology of AKI in patients with chronic myelomonocytic leukemia (1,2). Lysozymes are small cationic proteins produced by monocytes that can be freely filtered through glomerular basement membranes and reabsorbed by proximal tubules. Overproduction of lysozyme in patients with CMML leads to over-reabsorption and retention within the proximal tubule lysosomes, which can be confirmed ultra-structurally and immunohistochemically. After the kidney biopsy, our patient was treated with azacitidine for 1 week and his serum creatinine improved to 1.67 mg/dl after a 1-month follow-up. Further work with larger patient cohorts will be needed to better understand the pathophysiology and outcomes of lysozyme nephropathy, in addition to investigating whether serum creatinine and proteinuria in patients with CMML should be closely monitored for early targeted therapy, as with monoclonal gammopathy of renal significance (3).

References:
(Text and images provided by Vasudevan D. Mahalingam, Beaumont Health, Department of Pathology, Royal Oak, Michigan; Jamal Abukhaled, Beaumont Health, Department of Nephrology, Royal Oak, Michigan; and Ping L. Zhang, Beaumont Health, Department of Pathology, Royal Oak, Michigan)