## Diagnosing Oxalate Nephropathy on Kidney Biopsy Specimens

Kenji Yamada, Mari Ikeda, Yoshinori Koyama, Kurumi Seki, Atsuro Kawaji, Tomohiko Inoue, and Tomo Suzuki

man in his 70s with a history of total gastrectomy and ARoux-en-Y reconstruction 13 years prior presented with increasing malaise and anorexia over the past 6 months. He had a history of hypertension, and his medications included an angiotensin receptor blocker and a calcium channel blocker. He had a serum creatinine level of 3.82 mg/dL (estimated glomerular filtration rate  $13 \text{ mL/min}/1.73 \text{ m}^2$ ) and no edema. Eight months earlier, his kidney function was normal. His urine proteinto-creatinine ratio was 3.5 g/g, with no hematuria on urinalysis. A kidney biopsy revealed round and square crystals under light microscopy before formalin fixation (Fig 1A). After fixation, hematoxylin and eosin staining revealed an acute tubular injury with numerous intratubular calcium oxalate crystals (Fig 1B). The histological diagnosis was oxalate nephropathy. Additionally, a high 24-hour urine oxalate excretion of 59.6 mg/day was observed.

Diagnosing oxalate nephropathy can be challenging,<sup>1</sup> and its prevalence may be underestimated<sup>2</sup> despite a poor prognosis.<sup>1,2</sup> One reason is that calcium oxalate crystals can be difficult to visualize without polarized light microscopy.<sup>3</sup> Oxalate nephropathy can be diagnosed easily with polarized light microscopy. However, it is challenging to suspect oxalate nephropathy without clinical information or confirmation of crystals using kidney biopsy. We visualized crystals using hematoxylin and eosin staining with Carazzi hematoxylin. For further examination, we stained with Carazzi hematoxylin and Mayer's hematoxylin, both of which allowed observation of the crystals (Fig S1A and S1B). However, crystals

were difficult to visualize with Meyer's stain after periodate treatment (Fig S1C). Although it is unclear why crystals were visible with hematoxylin and eosin staining, these results suggest that crystals may have been dissolved during staining. Furthermore, the contribution to the diagnosis of kidney biopsy is generally enhanced with periodic acid-Schiff and periodic acid-methenamine silver staining, whereas hematoxylin and eosin staining offers relatively lower diagnostic value. This difference may explain why oxalate nephropathy can be missed following kidney biopsy.

When sectioning for immunofluorescence and electron microscopy, kidney specimens are commonly observed using light microscopy before formalin fixation. Our image highlights the importance of actively searching for oxalate crystals before formalin fixation to facilitate an accurate diagnosis.

#### SUPPLEMENTARY MATERIALS

Supplementary File (PDF) Figure S1: Crystal by different hematoxylin stainings.

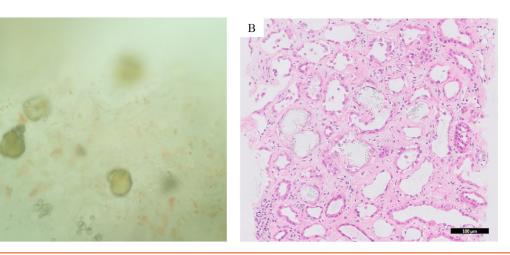
#### **ARTICLE INFORMATION**

Authors' Full Names and Academic Degrees: Kenji Yamada, MD, Mari Ikeda, MD, Yoshinori Koyama, MT, Kurumi Seki, MD, Atsuro Kawaji, MD, Tomohiko Inoue, MD, PhD, and Tomo Suzuki, MD, PhD Authors' Affiliations: Department of Nephrology (KY, MI, AK, TI, TS), Kameda Medical Center, Chiba, Japan; and Department of Pathology (YK, KS), Kameda Medical Center, Chiba, Japan.

Address for Correspondence: Tomo Suzuki, MD, PhD, Department of Nephrology, Kameda Medical Center, Chiba, Japan 296-8602,

Figure 1. (A) Kidney biopsy performed before formalin fixation. (B) Hematoxylin and eosin staining.

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929, Higashicho, Kamogawa, Chiba, Japan. Email: suzuki.tomo@kameda.jp

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