Case Description
A 59-year-old woman with low-risk myelodysplastic syndrome (MDS), classified according to the World Health Organization classification-based prognostic scoring system 11 years ago, was admitted to the nephrology department after AKI. She presented with epigastric pain and nausea lasting for 6 days, acute diarrhea, and dark-colored morning urine. Her blood pressure was 136/84 mm Hg. Laboratory investigations showed a serum creatinine level of 10.19 mg/dl (reference range 0.65–1.07 mg/dl), serum lactate dehydrogenase of 1637 IU/L (reference range 124–222), and hemoglobin of 7.6 g/dl (reference range 13.7–16.8 g/dl). Urinalysis showed low-grade proteinuria and hematuria. Computed tomography revealed bilateral kidney enlargement. Nine days before admission, she had visited a regular outpatient clinic, and her laboratory tests had revealed a serum creatinine level of 0.5 mg/dl, serum lactate dehydrogenase of 658 IU/L, and hemoglobin of 10 g/dl. We suspected hemolytic-uremic syndrome and AKI. However, there were no findings of schistocyte or thrombocytopenia. Kidney biopsy revealed normal glomeruli and diffuse acute tubular injury with golden-brown pigmentation in the proximal tubular epithelial cells (Figure 1, A and B). The Prussian blue staining confirmed that the pigmentation indicated hemosiderosis (Figure 1C). Her renal function gradually improved without RRT. Flow cytometric detection of CD55 and CD59 surface proteins on blood cells confirmed paroxysmal nocturnal hemoglobinuria (PNH).

Discussion
Intravascular hemolysis can be caused by hematologic disorders, infectious diseases (malaria, sepsis), cardiac and vascular surgery, and ABO-incompatible blood transfusion, resulting in acute tubular injury via heme and iron-induced immune responses (1). PNH is a hematologic condition characterized by intravascular hemolysis and is a rare, acquired, chronic, and life-threatening disorder associated with hemolytic anemia, bone marrow failure, and thrombosis. Diagnosis of PNH is often delayed because of its nonspecific clinical features and variable clinical presentations. Patients with PNH usually have a prior hematologic disorder. A previous report showed that 38% and 5% of patients with PNH had been diagnosed with aplastic anemia and MDS in Japan, respectively (2). PNH hematopoietic stem cells are characterized by a reduction or absence of glycosylphosphatidylinositol-anchored

Figure 1. | Light microscopic findings of kidney histology. (A) Diffuse tubular injury without tubulitis. Few proximal tubules are detached from the basement membrane. Periodic acid–Schiff staining, ×200. (B) Proximal tubular epithelial cells have lost their brush border and pigments ranging from brown to gold are seen. Periodic acid–Schiff staining, ×400. (C) Numerous hemosiderin deposits are seen in the proximal tubular epithelial cells. Prussian blue staining, ×200.

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proteins, including CD55 (decay-accelerating factor) and CD59 (membrane inhibitor of reactive lysis), making them vulnerable to hemolysis by complement activation. The international PNH Registry revealed that 14% of patients with PNH had a history of impaired renal function (3). CKD in PNH is associated with chronic hemolysis and/or microvascular thrombosis. In a 16-year observational period, the incidence of AKI in patients with PNH was reported as 43% (4). The potentially curative therapy for PNH is allogeneic bone marrow transplantation; however, the morbidity and mortality associated with the procedure make it inappropriate for most patients. Eculizumab, a humanized monoclonal antibody that inhibits terminal complement activation, is another therapeutic option that improves hemolysis and renal impairment (5).

Teaching points
- PNH is one of the important causes of hemolysis-induced AKI, and a kidney biopsy helps diagnose hemosiderosis.
- Timely diagnosis of PNH and intervention with eculizumab will improve the patient’s renal condition and survival outcomes.

Disclosures
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Author Contributions
S. Isobe wrote the original draft of the manuscript. N. Ohashi and H. Yasuda reviewed and edited the manuscript.

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