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Low Efficacy of Chromogranin A Elimination by Therapeutic Plasma Exchange for Treatment of Chromogranin A Tubulopathy

To the Editor: Previous seminal work has revealed that chromogranin A (CgA) can mediate tubular injury, by either intraluminal precipitation with cast formation or excessive tubular CgA uptake.[1] We report an additional case of kidney injury in the context of CgA tubulopathy and explored the efficacy of CgA elimination by therapeutic plasma exchange (PEX). A 69-year-old white man with a medical history of pancreatic neuroendocrine neoplasm presented to our department with progressive worsening of kidney function for 2 years and proteinuria (741.6 mg/g creatinine). The patient had stable disease treated with somatostatin analogs for 2 years, CgA serum levels were elevated (147.9 μg/l, reference: <100 μg/l). Kidney biopsy result revealed tubular cell injury with intracytoplasmic granules reactive for CgA (Figure 1a–d). On the basis of the diagnosis of CgA tubulopathy, we performed a total number of 6 PEX treatments (plasma volume: 3000 ml) with low efficacy of CgA elimination (Figure 1e). As expected, we observed a decrease in serum creatinine during PEX treatment but no improvement thereafter (Figure 1f). CgA has an estimated molecular weight of 48 kilodaltons with a half-life of 18.4 minutes and is filtered by the glomerulus, thereby detectable in corresponding urines.[2–4] Because CgA tubulopathy is a rare but important complication directly attributed to tubular CgA precipitates, eliminating serum CgA could provide a therapeutic approach.[1] Although PEX might remove serum CgA, its low efficacy in this case suggests that the combination of a large volume of distribution and high CgA synthetic rate exceeds its clearance capacity by PEX.

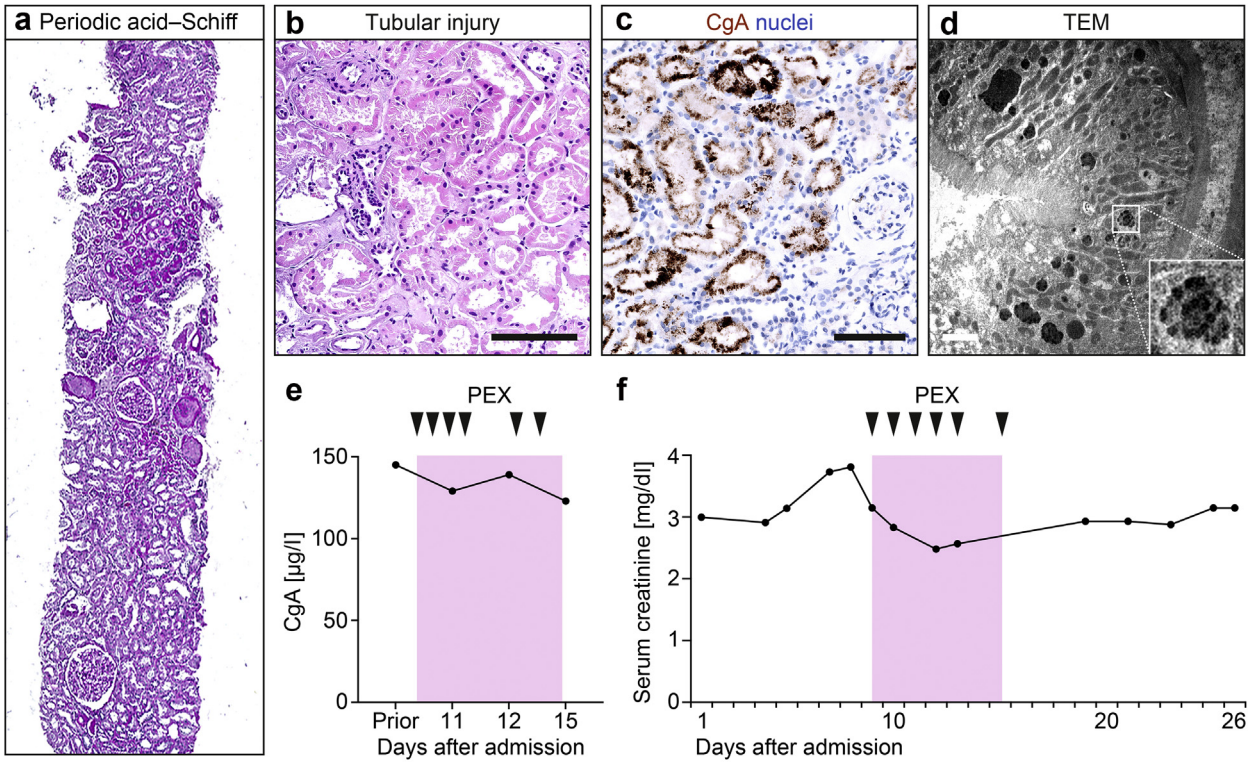

Figure 1. Kidney biopsy result confirming CgA tubulopathy and efficacy of CgA elimination by using PEX. (a) Kidney biopsy core stained with periodic acid–Schiff. (b) Tubules engorged with resorption eosinophilic granules on hematoxylin and eosin staining, tubular injury with flattening of the tubular epithelium, focal loss of the brush border, and regenerative changes with occasional apoptotic nuclei (bar = 100 μm). (c) As confirmed by immunoperoxidase staining, intracytoplasmic granules are reactive for CgA (bar = 100 μm). (d) TEM results revealed tubules containing numerous intracytoplasmic lysosomes with electron-dense, ring-shaped material (inset, bar = 2000 nm). (e) CgA serum levels measured directly before a total number of 6 PEX treatments (depicted by arrowheads). (f) Serum creatinine levels during the disease course. CgA, chromogranin A; PEX, plasma exchange; TEM, transmission electron microscopy.

DISCLOSURE

All the authors declared no competing interests.

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