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Fibrillary inclusions in light chain proximal tubulopathy associated with myeloma

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A 66-year-old retired librarian was referred to the nephrology clinic for evaluation of a recent onset of asymptomatic proteinuria identified at a routine hypertension check-up. She had a 15-year history of hypertension and was treated with ramipril and bendrofluomethazide with no history of diabetes. The urinary protein–creatinine ratio was elevated at 819 mg/mmol, with no evidence of glycosuria, hypoalbuminaemia, acidaemia or impaired renal function (serum creatinine 78 μmol/L). Serum electrophoresis identified a monoclonal IgG kappa band quantified at 20 g/L with associated immunoparesis. Urinary immunofixation demonstrated kappa free light chains.

On renal biopsy (Figure 1), there was marked vacuolation of tubular epithelial cells and electron microscopy demonstrated filaments 6 nm in diameter in these cells (Figures 2 and 3). Congo red staining for amyloid was negative. Immunoflorescence for light chains was negative on frozen sections but protease-digested paraffin sections showed kappa but not lambda light chain deposition in tubular epithelial cells. These findings are consistent with a proximal tubulopathy with fibrillary inclusions related to a kappa light chain plasma cell dyscrasia.

Subsequent bone marrow was hypercellular with 61% plasma cells, which were kappa light chain restricted; she was started on a CTD (cyclophosphamide, thalidomide and dexamethasone) chemotherapeutic regime and has preserved her renal function but has continuing proteinuria.

Light chain proximal tubulopathy is an increasingly recognized though still uncommon renal complication of myeloma almost exclusively related to light chain kappa [1]. Some individuals may manifest an associated Fanconi syndrome that was not seen in this woman. Diagnosis can be difficult with frequently non-specific light microscopy findings; on ultrastructural examination, crystalloid inclusions are frequently seen but occasionally may be fibrillary in nature

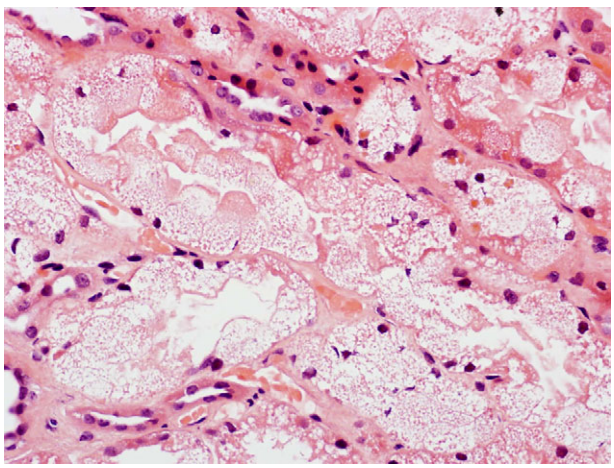

Fig. 1. Light microscopy demonstrating vacuolation of tubular epithelial cells.

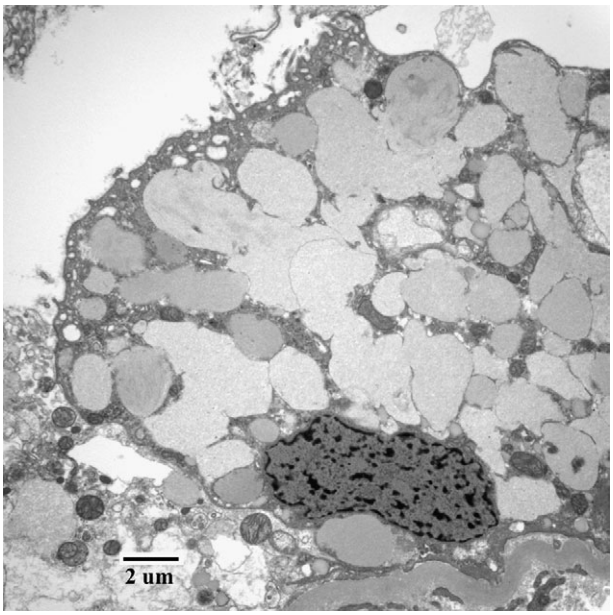

Fig. 2. Electron micrograph of a tubular epithelial cell showing numerous vacuoles in the cytoplasm.

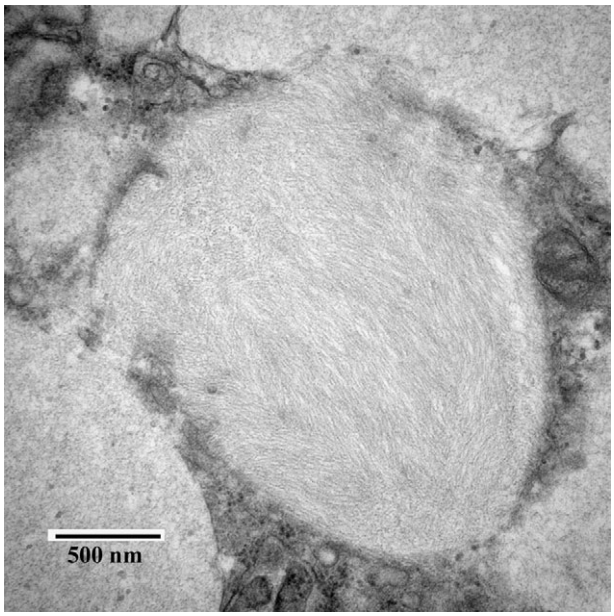

Fig. 3. Higher power view of cytoplasmic vacuole showing numerous closely packed filaments 6 nm in diameter.

[2]. Crystalloid deposition is thought to occur due to a resistance of the light chain-variable region to lysosymal proteolysis in the proximal tubule [3]. The unusual fibrillary appearances seen here may relate to the physicochemical properties determined by the amino acid sequence in the variable region.

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Conflict of interest statement. None declared.

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