Lack of H-ATPase in distal nephron causing hypokalaemic distal RTA in a patient with Sjögren’s syndrome

Sir,

In a recent report in this journal [1] a young woman was described with hypokalaemic paralysis due to distal renal tubular acidosis (dRTA) as the presenting manifestation of primary Sjögren’s syndrome. The patient had a profound hypokalaemic hyperchloraemic non-anion gap metabolic acidosis with inappropriate alkaluria and a positive urinary anion gap, all suggestive of a classic hypokalaemic dRTA. Moreover, the patient’s proximal tubular functions were normal with no evidence of glucosuria or aminoaciduria.

Immunological investigations had revealed a positive rheumatoid factor (RF), a high titre of ANA (speckled pattern), and a positive anti-Ro (SSA) antibody titre suggestive of primary Sjögren’s syndrome. Labial and kidney biopsies had both shown focal lymphocytic infiltrate, confirming the diagnosis.

We have subsequently stained the kidney biopsy of the patient with a monoclonal antibody raised against the 31 kDa subunit of bovine H-ATPase as described before [2]. We found brush-border membrane staining for H-ATPase in the proximal tubules; however, several collecting ducts present in the section did not show any H-ATPase staining (Figure 1). Furthermore, biopsy sections stained with rabbit sera raised against the 56 kDa H-ATPase kidney specific isoform subunit [3] and mouse red blood cell Cl:HCO₃ anion exchanger (band-3 protein) [4] showed no staining. This was in contrast to normal human kidney, where the former antibody showed prominent staining in the apical pole (data not shown) and the latter antibody in the basal membrane (Figure 2) of the intercalated cells in the collecting ducts.

The distal nephron is responsible for net acid excretion which is accomplished by the intercalated cells present in the collecting duct. The intercalated cells are specialized cells that have dense arrays of the vacuolar type H-ATPase in their plasma membrane, in a polarized distribution, and are responsible for net acid secretion. Normal distal acidification requires an adequate rate of hydrogen ion secretion by the intercalated cells of the cortical and medullary collecting ducts, an impermeant luminal membrane that can sustain large pH gradients, and a lumen-negative potential difference in the cortical collecting ducts which would support electrogenic proton secretion.

Fig. 1. Immunofluorescent staining of the patient’s kidney biopsy using a monoclonal antibody to the 31 kDa subunit of the H-ATPase. In panel A several proximal convoluted tubules (P) are shown with apical brush border membrane staining, and there is a long cortical collecting duct (C) which shows no staining in any cell. In panel B the bright field view of the same section, there is a mild mononuclear cell infiltrate in the interstitium adjacent to the cortical collecting duct.
Our findings suggest that lack of H-ATPase in the distal nephron, as evidenced by the absence of two of its subunits tested, is responsible for dRTA in this patient. The additional finding of lack of staining for band-3 protein in any collecting duct cells suggests either absence of the intercalated cells or failure of intercalated cells to express both the H^+ATPase and the anion exchanger. This case, together with two previous reports [5,6] from our laboratory, of patients with primary Sjögren's syndrome and classic hypokalaemic dRTA of secretory defect variety, would indicate that lack of H-ATPase in the intercalated cells of the collecting duct may be the cellular mechanism responsible for the distal acidification defect in this clinical setting. This is in contrast to two cases of hyperkalaemic dRTA of the voltage defect variety in which intercalated cells were shown to have intense staining for the H-ATPase [7]. Altogether, these cases shed light on the pathophysiological basis, at the cellular level, of the proton secretory defect and voltage defect dRTAs. In the former there is total absence of the H-ATPase in the intercalated cells. In the latter the pump may be rendered non-functional due to the lack of appropriate lumen-negative voltage to support proton secretion.

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Infected intracardiac thrombi: complication of vascular access in haemodialysis patients

Sir,
We read with interest the description of an infected right atrial thrombus due to haemodialysis vascular access, as described by Korzets et al. [1]. We have recently seen two cases of infected intracardiac thrombi in patients on haemodialysis, cannulated for vascular access. The first patient was a 74-year-old female with polycystic kidney disease, on haemodialysis since September 1993 for end-stage renal failure. Mid September 1994 she developed high fever and chills, caused by a generalized tunnel infection of a right subclavian vein temporary dialysis catheter. The