Hyperchloremic or Normal Anion Gap Metabolic Acidosis

Hyperchloremic (normal anion gap) metabolic acidosis can have a renal or extrarenal origin. Metabolic acidosis of renal origin is the result of abnormalities in tubular H^+ transport. Metabolic acidosis of extrarenal origin is most commonly caused by gastrointestinal losses of HCO_3^-. Other causes include the external loss of biliary and pancreatic secretions and ureteral diversion procedures. Figure 27-7 provides a clinical approach to metabolic acidosis of renal origin.

Renal Origin of Metabolic Acidosis

Proximal Renal Tubular Acidosis

The diagnosis of proximal renal tubular acidosis (type II RTA) is suspected in a patient with a normal anion gap acidosis, hypokalemia, and an intact ability to acidify the urine to a pH of less than 5.5 while in a steady state. In the steady state, the serum HCO_3^- concentration is usually in the range of 16 to 18 mmol/L. Proximal RTA can be an isolated finding but most commonly is accompanied by generalized dysfunction of the proximal tubule (i.e., Fanconi's syndrome). The UAG is normal.

Proximal RTA is not associated with nephrolithiasis or nephrocalcinosis. However, osteomalacia can develop as a result of chronic hypophosphatemia or deficiency of the active form of vitamin D. Osteopenia may occur as a result of acidosis-induced demineralization of bone.

Treatment of patients with proximal RTA is difficult. Correction of the acidosis is often not possible, even with large amounts of HCO_3^- (3 to 5 mmol/kg/day), because exogenous alkali is rapidly excreted in the urine. This therapy also leads to accelerated renal K^+ losses. Use of a thiazide diuretic to induce sufficient volume depletion to lower the GFR and decrease the filtered load of HCO_3^- may increase the effectiveness of alkali therapy. Potassium-sparing diuretics may limit the degree of renal K^+ wasting. After therapy is initiated, close monitoring is required to guard against severe electrolyte derangements. Topiramate can cause metabolic acidosis due to its inhibitory effects on carbonic anhydrase.

Hypokalemic Distal Renal Tubular Acidosis

The diagnosis of hypokalemic distal RTA (type I RTA) should be considered in a patient with hyperchloremic or normal anion gap acidosis, hypokalemia, and an inability to lower the urine pH maximally. A urine pH greater than 5.5 in the setting of systemic acidosis is consistent with distal RTA. The UAG value is positive. The systemic acidosis tends to be more severe than in patients with a proximal RTA with serum HCO_3^- concentrations as low as 10 mmol/L.

Hypokalemia can be severe and cause musculoskeletal weakness and symptoms of nephrogenic diabetes insipidus. Patients frequently have nephrolithiasis and nephrocalcinosis. The predisposition to renal calcification results from the combined effects of increased urinary calcium ion (Ca^{2+}) excretion due to acidosis-induced bone mineral dissolution, a persistently alkaline urine pH, and low rate of urinary citrate excretion.

Correction of the metabolic acidosis in distal RTA can be achieved by administration of alkali in an amount equal to daily acid production (usually 1 to 2 mmol/kg/day). In patients with severe K^+ deficits, correction of the acidosis with HCO_3^- can transiently cause further lowering of the extracellular K^+ concentration and result in symptomatic hypokalemia. In this setting, the K^+ deficit should be corrected before correcting the acidosis. Potassium citrate is the preferred form of alkali for patients with persistent hypokalemia or with calcium stone disease.

Hyperkalemic Distal Renal Tubular Acidosis

Hyperkalemic distal RTA (type IV RTA) should be suspected in a patient with a normal anion gap (hyperchloremic) metabolic acidosis associated with hyperkalemia. The UAG is slightly positive, indicating little to no NH_4^+ excretion in the urine. Patients in which the disorder is caused by a defect in mineralocorticoid activity typically have a urine pH of less than 5.5, reflecting a

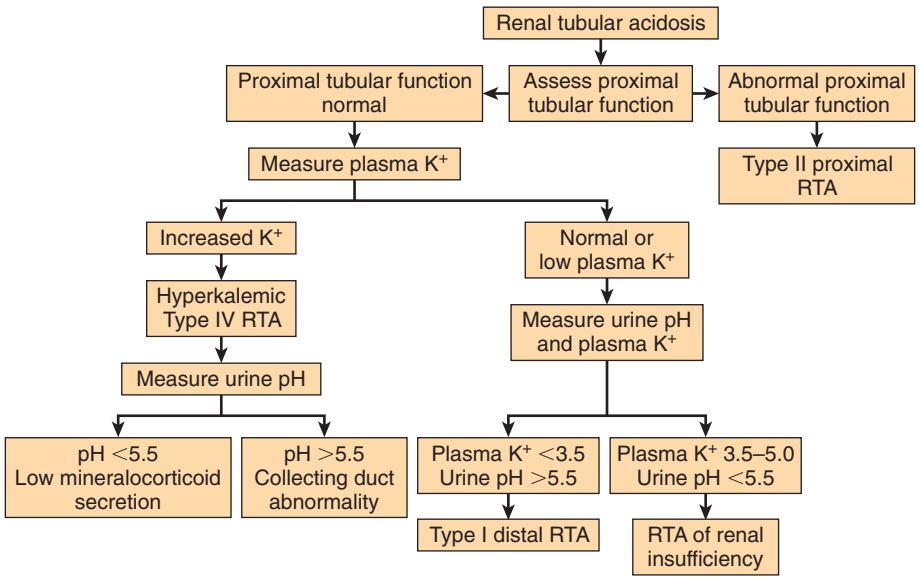

FIGURE 27-7 Approach to the patient with acidosis of renal origin. K^+, Potassium ion; RTA, renal tubular acidosis.