Clinical Note

A young man with reversible quadriparesis

Sir,

Carbonic anhydrase II deficiency is a rare disorder associated with osteopetrosis, renal tubular acidosis, cerebral calcification, some degree of mental retardation and growth failure.[1-3] Hypokalemia is an important cause of generalized weakness of the muscles.[4] The total amount of potassium is approximately 4000 mmol/l in the body. Of the total, 98% is intracellular.[5] Serum potassium is a poor indicator of the body content, but it is the change in the concentration that affects the neuromuscular activity and cardiac function. The renal causes of hypokalemia and the clinical features of hypokalemia are given in Table 1.

Renal Tubular Acidosis (RTA) is an important cause of hypokalemia. Renal Tubular Acidosis may be distal (classical or type I) or proximal (type II). In both conditions the ability to form acid urine is lost, but more in the distal type and urine pH cannot be reduced to less than 5.3 even in the presence of severe systemic acidosis. The defect is due to failure of the collecting ducts to secrete hydrogen ion. There is hypersecretion of potassium by the tubules.[6]

In proximal RTA (type II) Na+/H+ exchange is impaired resulting in decreased bicarbonate reabsorption, large losses of bicarbonate in the urine, and a marked reduction in plasma bicarbonate. Once the bicarbonates have fallen to about 12 mmol/l, the reduced filtered load can be reabsorbed and the amount reaching the distal tubules is minute. In these circumstances, the distal tubules can secrete hydrogen ions against the gradient so that the urine pH falls below 5.3.

Carbonic anhydrase deficiency can cause either type of RTA. Osteopetrosis (Marble Bone Disease) is clinically, biochemically and genetically heterogeneous. Although osteopetrosis has many causes, a defect in bone resorption is always the mechanism. Infantile osteopetrosis is an autosomal recessive trait that is manifested in utero and progresses after birth with anemia, hepatosplenomegaly, hydrocephalous, cranial nerve palsies and death due to infections Less fulminant forms of osteopetrosis occur in older children and adults. Anemia is not severe, neurological abnormalities are not frequent, and recurrent fractures are the main features. It may be discovered accidentally.

An intermediate form has been described in which skeletal abnormality is associated with RTA and cerebral calcification. The form is compatible with long survival and is associated with impairment of one of the isoenzymes of carbonic anhydrase (carbonic anhydrase II). Carbonic anhydrase creates an acid environment around osteoclasts necessary for bone resorption and deficiency of carbonic anhydrase impairs bone resorption.[7]

We present a case who we think has carbonic anhydrase II deficiency. A 20-year-old Saudi gentleman was admitted on 10-07-1420H with a history of weakness of all 4 limbs of a few days duration. He noticed the weakness after waking up from sleep. There was no history of trauma to the head or spine, no history of urinary or bowel symptoms, no history of loss of consciousness or convulsion, no history of ingestion of heavy carbohydrate meals, and no family history of similar illness. The patient was suffering from osteopetrosis and was admitted with fracture of right femur in 1416H and was admitted again the following year

Table 1 - Clinical features and renal causes of hypokalemia.

Clinical features of hypokalemia[8]	**Renal causes of hypokalemia**[9]
Tiredness	**Enhanced Na+/K+ Exchange:**
Muscular weakness	Secondary hyeraldosteronism Cushing's syndrome
Inability to climb upstairs	Ectopic ACTH secretion Steroid therapy
Tingling in the fingers	Barter's syndrome
Apathy	**Excess Na+ available for exchange:**
Paralysis	Diuretic therapy
Coma in extreme cases	**Decreased Na+/H+ exchange:**
Cardiac arrhythmia	Carbonic anhydrase deficiency Renal tubular acidosis
Longstanding hypokalemia can cause nephrogenic diabetes insipidus	**Impaired proximal tubular reabsorption:**
Paralytic ileus	Renal tubular dysfunction Fanconi syndrome

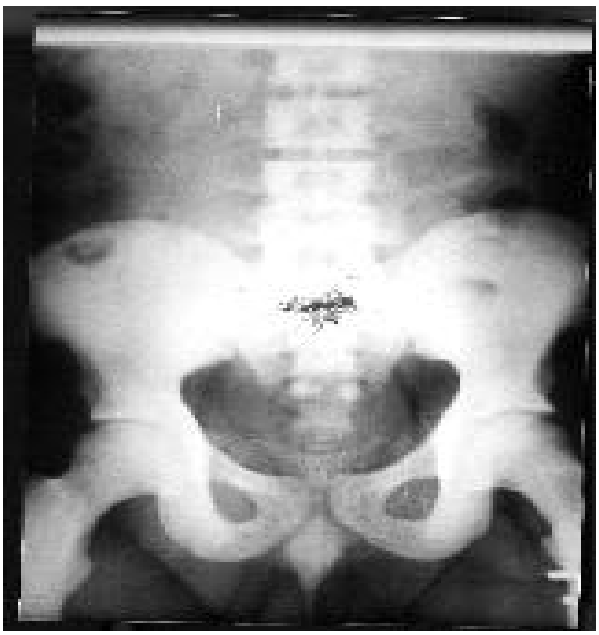

Figure 1 - X-ray of the pelvis shows increased bone density typical of osteopetrosis and evidence of fracture of left femur.

with history of fracture of left femur. Both fractures followed after a history of fall and were almost transverse radiologically, a typical finding in fractures due to osteopetrosis (Figure 1). Two months ago, he had similar episodes of body weakness but did not seek medical advice.

Physical examination. Revealed a young, mildly obese man with some mental retardation. He was fully conscious and well orientated. Speech was normal, he had no facial weakness or asymmetry, he has normal eyeball movement. Motor system examination revealed no abnormal movement. Tone was decreased in all 4 limbs. Power was 2/5 in both upper limbs and 1/5 in both lower limbs. All tendon reflexes were diminished. Both plantar were equivocal. Sensory system was grossly intact. Patient was hemodynamically stable. Heart sounds were normal. He was not breathless and his chest examination was unremarkable.

Investigations. Biochemistry revealed serum potassium of 1.3 mmol/l, serum sodium 137 mmol/l, creatinine 90 micromol/l, random blood glucose 6.5 mmol/l serum calcium 2.226 mmol/l, phosphate 0.7 mmol/l, total serum proteins 81.1 gm/l, serum albumin 46.8 gm/l. Serum cortisol was 296 ng/l (165-744 ng/l) arterial blood gas analysis revealed pH 7.309, PCO_2 37.4mmHg, PO_2 84.7 mmHg, HCO_3 18.4 and O_2 saturation was 95%. Urinary spot electrolytes were sodium 66.0 mmol/l and potassium 22.5/l and urinary pH 6.0. Electrocardiogram (ECG) showed prominent U wave due to hypokalemia.

Hospital course and management. The patient was given potassium chloride in infusion form for the first 2 days and then put on oral potassium supplement. Also, he was given sodium bicarbonate orally for his metabolic acidosis. Gradually, the power in his extremeties improved and on the 4th day of the admission, the patient was able to walk independently. His potassium was 4.0 mmol/l. Arterial Blood Gasses (ABG) showed pH 7.32, $PC_2$40.1, PO_2 92.6, $HC0_3$ 20. He was discharged on 12-07-1420H in good condition with potassium of 3.4 mmol/l. He was discharged on syrup potassium chloride 10 ml 3 times daily (TID) and tablet sodium bicarbonate 375mg twice a day (BD).

This case illustrates severe hypokalemia manifested as severe generalised weakness of the extremities in a patient who had osteopetrosis. His ABG at the time of admission showed mild metabolic acidosis. We think this is a case of carbonic anhydrase deficiency though we do not have the facility to measure the activity of the enzyme. But based on clinical and biochemical findings it fits well into the diagnosis of carbonic anhydrase deficiency, causing osteopetrosis and hypokalemia due to RTA.

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