Hypokalaemia in leukaemia

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Summary

Five cases are presented which demonstrate the various factors contributing to the development of hypokalaemia and the relevant literature is briefly reviewed. Hypokalaemia is a common finding in leukaemia. Proper evaluation, adequate replacement of potassium and careful follow-up are necessary for prevention of potential dangers related to hypokalaemia.

Introduction

Leukaemia is a common cause of hypokalaemia in a hospital population (Lawson *et al.*, 1979). The pathogenesis of hypokalaemia is multifactorial and not completely understood. Five cases which demonstrate this multifactorial aetiology are presented.

Case histories

No. 1

A 48-year-old male with chronic lymphocytic leukaemia was admitted with fever, hypotension and tachycardia. Vital signs at admission were: BP 100/50 mmHg; pulse 115/min; respiration 22/min; temperature 40.2°C; blood cultures were drawn and antibiotic therapy was initiated. This included cloxacillin sodium (1 g/6 hr), gentamicin sulphate (80 mg/8 hr) and ticarcillin sodium (3 g/4 hr). Figure 1 shows the serum and urine potassium values in chronological sequence. The patient complained of weakness of his lower limbs on the third day after admission. Despite receiving 160 mmol/l of potassium chloride i.v., the patient remained hypokalaemic. Withdrawal of ticarcillin on the seventh day resulted in hyperkalaemia.

No. 2

A 38-year-old male with previously diagnosed acute myeloblastic leukaemia was admitted to hospital for evaluation of unexplained episodes of fever, and chest pain. A diagnosis of pulmonary aspergillosis was eventually arrived at and the patient was started on amphotericin B (50 mg daily).

Initial admission electrolytes were sodium 141

mmol/l, potassium 4.6 mmol/l, chloride 105 mmol/l, total carbon dioxide 27 mmol/l. Serum BUN and creatinine were normal. Sixteen days after starting treatment with amphotericin B the patient's serum potassium was 2.8 mmol/l. Urine potassium assayed at the same time was 48 mmol/24 hr, an inappropriately high urine potassium for the hypokalaemia.

FIG. 1. Serial serum and urine potassium concentrations in case no. 1.

No. 3

A 49-year-old woman with previously diagnosed acute myelomonocytic leukaemia presented with a week-long history of malaise, weight loss and easy bruising. Laboratory investigations included Hb 7.3 g/dl, WBC $99 \times 10^9/l$ of which more than 60% were monocytes. Admission electrolytes were sodium 134 mmol/l, potassium 2.7 mmol/l, chloride 94 mmol/l and total carbon dioxide 29 mmol/l. A urine protein electrophoresis showed the presence of a cathodally moving band consistent with presence of lysozyme (Fig. 2).

No. 4

A 68-year-old man presented with a 6-week history

of night sweats, weight loss and cervical lymphadenopathy. He was also found to have enlargement of the liver and spleen. Bone marrow examination and a peripheral blood smear confirmed the diagnosis of chronic lymphocytic leukaemia. Laboratory testing revealed a serum potassium of 2.8 mmol/l, a total serum calcium of 3.6 mmol/l, serum phosphorus of 1.5 mmol/l and an elevated alkaline phosphatase of 237 i.u./l. Urine potassium was 42 mmol/24 hr. A bone scan revealed scattered uptake of the isotope in the rib cage. The hypercalcaemia showed a rapid response to i.v. saline and frusemide. Adequate potassium supplementation was given i.v.

FIG. 2. Urine protein electrophoresis (case no. 2).

No. 5

A 49-year-old female with chronic granulocytic leukaemia was in good health until 2 weeks before admission when she developed an influenza-like syndrome.

The laboratory data at admission was: Hb 6.3 gm/dl; white blood cell count $265 \times 10^9/l$ with 48% blast cells. Bone marrow examination showed the presence of 36% myeloblasts. Electrolyte values were sodium 137 mmol/l, potassium 2.6 mmol/l, chloride 104 mmol/l and total carbon dioxide 23 mmol/l. Urine potassium was 18 mmol/24 hr. The patient denied any vomiting or diarrhoea.

With treatment the serum potassium returned towards normal without any potassium supplementation. She developed several bouts of Gram-negative septicaemia while in hospital and died 3 months after admission.

Discussion

The factors responsible for hypokalaemia in leukaemia are shown in Table 1. The pathogenesis of the hypokalaemia is not always completely understood and is in some cases controversial.

Anorexia, related to the malignancy and its treatment, occurs commonly in patients with cancer and occasionally reaches such a degree of severity that spontaneous nutrition is almost impossible.

TABLE 1. Causes of hypokalaemia in leukaemia

I. Inadequate dietary intake:	
(a) related to malignancy	
(b) related to treatment	
II. Gastrointestinal losses:	
(a) vomiting	
(b) diarrhoea	
III. Renal losses:	
(a) antibiotics:	(i) Antibacterial: carbenicillin, nafcillin, ticarcillin, penicillin, gentamicin, polymyxin B, cephalothin
	(ii) antifungal: amphotericin B
(b) lysozymuria	
(c) corticosteroids	
(d) damage to renal tubular cells by leukaemic infiltrates	
(e) hypercalcaemia	
(f) starvation	
IV. Cellular shift:	
(a) blast crisis	
(b) ? antibiotic therapy	
(c) ? presence of membrane inhibitory factor	

Increased kaliuresis may also be responsible for the hypokalaemia in starvation. It has been suggested that this is due to organic anion excretion (Sigler, 1975). Vomiting and diarrhoea which are common complications of chemotherapy for malignant disease are associated with gastrointestinal losses of potassium. Except in gastric alkalosis, the urine potassium is generally less than 10 mmol/24 hr (Nardone, McDonald and Girard, 1978).

Case 1 demonstrates the association of hypokalaemia with antibacterial antibiotic therapy. Hypokalaemia has been associated with massive intravenous doses of penicillin (Brunner and Frick, 1968), carbenicillin (Lipner *et al.*, 1975) and nafcillin (Mohr *et al.*, 1979). Patient no. 1 was receiving ticarcillin sodium. These antibiotics behave as non-reabsorbable anions. The potassium depletion in patients receiving these drugs can be attributed to the increased electrical negativity of the tubular lumen with subsequent enhancement of potassium secretion. A strong stimulus for distal sodium reabsorption is thought to be necessary for the non-permeant anion effect (Bank and Schwartz, 1960). Gentamicin also increases urinary losses of potassium but the mechanism is unclear (Holmes, Hesling and Wilson, 1970). Another type of antibiotic, amphotericin B, also causes hypokalaemia, but by a different mechanism. It is thought to be directly toxic to the distal tubular epithelium. This in some way alters cellular permeability and leads to excessive potassium loss (McCurdy, Frederic and Elkinton, 1968). The association between lysozymuria and hypokalaemia is controversial (Muggia, Heinneman and Farhangi, 1969; Pickering and Catovsky, 1973; Mir, Brabin and Tang, 1975).

Some workers report no association between the degree of hypokalaemia and urine of serum lysozyme concentrations, whilst other studies show that only prolonged elevations in serum lysozyme produce detectable lysozymuria and hypokalaemia. Lysozyme, a product of abnormal cellular proliferation and destruction is thought to cause hypokalaemia by proximal renal tubular damage, thus decreasing potassium reabsorption.

The occurrence of concomitant hypokalaemia in the presence of hypercalcaemia in malignancy, as in the case of patient no. 4, has been reported previously (Aldinger and Samaan, 1977). The mechanism involved is probably augmented renal losses of potassium (Sanderson, 1967). The importance of this finding is related to the possible development of arrhythmias in a patient with hypokalaemia and hypercalcaemia who may also be receiving potentially cardiotoxic drugs such as adriamycin and daunorubicin. Furthermore, care needs to be exercised in the treatment of hypercalcaemia with vigorous diuresis. Other postulated causes of renal potassium loss in leukaemia are treatment with corticosteroids and tubular damage due to renal leukaemic infiltrates which are a common finding at post-mortem (Boggs, Wintrobe and Cartwright, 1962). Corticosteroids predispose to potassium wasting by improving glomerular filtration rate, by increasing catabolic activity and exerting a mild mineralocorticoid effect at the distal tubular sodium-potassium exchange site (Nardone *et al.*, 1978).

Hypokalaemia in the acute blast crisis of chronic granulocytic leukaemia, as in case of patient no. 5, has been reported previously (Yeung and Trowbridge, 1976). Rapid cellular uptake of potassium by rapidly dividing cells as seen in the initiation of therapy of B_{12} deficiency anaemia (Lawson, Murray and Parker, 1972) is a probable factor. Treatment resulting in the resolution of the blast crisis would be expected to return the potassium to normal. It has also been postulated that antibiotic treatment would enhance the intracellular shift of potassium (Fisher, 1977). Other work has suggested that inhibitory factors produced by leukaemic cells may impair Na/K transport in the renal tubule, resulting in hypokalaemia (Mir and Robinski, 1975).

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