Hypokalaemia of Unknown Aetiology Complicating Hodgkin’s Disease

In the following case Hodgkin’s disease was associated with abnormal urinary potassium loss of unknown pathogenesis.

Case Report

A woman of 23 was diagnosed as suffering from Hodgkin’s disease in November 1962. Lymphadenopathy was confined to the abdomen; at laparotomy biopsy specimens were taken from a large mass in the mesentery and around the coeliac axis. Her general condition improved after irradiation to the abdomen, but she continued to have mild systemic symptoms, and several months later developed enlarged glands in the neck and mediastinum, treated by cobalt beam; a large new abdominal mass was also irradiated in September 1963. Cytotoxic therapy was not given.

In November 1963 she was admitted to hospital, complaining of weakness, paraesthesiae, and intermittent vomiting of about a month’s duration. Muscle power, tone, and reflexes were normal; there were no signs of Cushings’s syndrome. Her blood-pressure was 130/80 mm. Hg, plasma potassium 1.5 mEq/l, and bicarbonate 35 mEq/l. E.C.G. showed the changes of hypokalaemia.

Initially she was given 150 to 240 mEq of potassium daily, of which 160 mEq was administered intravenously in the first three days. By the fourth day her plasma potassium had risen to 4.1 mEq/l, and the bicarbonate had fallen to 29 mEq/l (see Chart). The urinary pH was 6.0 on admission, and subsequently varied between 5.6 and 6.5.

Vomiting and diarrhoea ceased, but hypokalaemic alkalosis recurring immediately when supplemental potassium was reduced to 30 mEq on the fifth day. From the 12th day the daily urinary output was between 75 and 175 mEq, when her plasma potassium was around 2.5 mEq/l. Administration of ammonium chloride, at first orally and then intravenously, in a dosage of up to 9 g. daily, did not decrease the plasma bicarbonate concentration, while spironolactone did not significantly alter the plasma potassium concentration; urinary potassium loss continued at around 100 mEq/day. When both drugs had been given for four days the plasma potassium was 1.5 mEq/l, in spite of daily potassium supplements of 160 mEq. Gastro-intestinal loss was still occurring, and it seemed likely that urinary potassium excretion roughly equalled that absorbed from the gut.

The total exchangeable body potassium measured after injection of 30 μc. of 42K on the 24th day was 1,400 mEq, or 28 mEq/kg, of body-weight, a low figure for a thin, non-oedematous female—normal mean for females about 40 mEq/kg. (Moore et al., 1954). The 24-hour aldosterone excretion on the seventh day was 8.6 μg.

From the 25th day between 116 and 216 mEq of potassium was administered intravenously each day. This resulted in some reten-
of potassium, the plasma concentration increasing to 4 mEq/l, though urinary loss continued at a rate of 75 to 190 mEq/day. The plasma bicarbonate concentration fell spontaneously at the same time. Reduction of this massive intravenous dose resulted in a precipitous fall in plasma potassium and recurrence of alkalosis; high urinary loss continued. The patient received a short course of mustine (22.5 mg.) during the second week.

She deteriorated and developed mechanical intestinal obstruction, dying six weeks after admission. During this time her plasma potassium had risen above 4 mEq/l on only two occasions, and her blood urea had been normal throughout; the creatinine clearance was 65 ml/min. on the 21st day and 53 ml/min. on the 32nd day.

Necropsy (Professor W. A. J. Crane) showed that the intestine was obstructed by Hodgkin's tissue in several places. The kidneys were macroscopically and microscopically normal; no vacuolization of tubular epithelium was noted. The adrenals were of normal size and microscopical appearance except for the presence of a minute cortical nodule 1 mm. in diameter; this was lost in preparation and its histological appearance is therefore not known.

**COMMENT**

None of the recognized causes of hypokalaemia accounts for the findings in this patient. Although gastro-intestinal losses of potassium were occurring, the main problem was the high rate of renal excretion in the face of hypokalaemia. The recognized causes of this are hyperaldosteronism, Cushing's disease, renal tubular damage, alkalosis, and the effects of various drugs.

Aldosterone excretion was not increased, potassium excretion was not reduced by spironolactone, and the patient was excreting considerable amounts of urinary sodium in spite of a plasma sodium concentration at the lower limit of normal (see Table). It is therefore most unlikely that she suffered from hyperaldosteronism, or that the tiny adrenal adenoma was the cause of her hypokalaemia.

### Plasma and Urinary Concentrations of Electrolytes on Admission (Day 2), Before and After Treatment with Ammonium Chloride and Spironolactone (Days 11 and 22), and After Treatment with Large Parenteral Doses of Potassium (Day 30)

<table>
<thead>
<tr>
<th>Day</th>
<th>Day 2</th>
<th>Day 11</th>
<th>Day 22</th>
<th>Day 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K⁺ (mEq/l)</td>
<td>1.9</td>
<td>2.7</td>
<td>2.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Na⁺</td>
<td>135</td>
<td>131</td>
<td>129</td>
<td>130</td>
</tr>
<tr>
<td>HCO⁻³</td>
<td>35</td>
<td>30</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>83</td>
<td>83</td>
<td>94</td>
<td>94</td>
</tr>
<tr>
<td>Volume (mL)</td>
<td>1,400</td>
<td>1,700</td>
<td>2,010</td>
<td>2,500</td>
</tr>
<tr>
<td>K⁺ (mEq/l)</td>
<td>114</td>
<td>96</td>
<td>51</td>
<td>72</td>
</tr>
<tr>
<td>Na⁺</td>
<td>78</td>
<td>86</td>
<td>102</td>
<td>124</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>80</td>
<td>170</td>
<td>164</td>
<td>164</td>
</tr>
</tbody>
</table>

There was no evidence of radiation nephritis (Luxton, 1953) or pyelonephritis, and she was not hypertensive; the kidneys were not involved by Hodgkin's tissue, though this is a well-recognized cause of electrolyte disturbance (Wintrobe, 1961) or renal failure (Mitchell et al., 1965). Drugs cannot be incriminated. There is normally a reciprocal relation between amounts of hydron and potassium secreted by the distal renal tubule. Alkalosis per se, due to extra renal loss of hydron, may be associated with hypokalaemia because renal conservation of hydron leads to increased potassium secretion; the urine is alkaline. Conversely, hypochloremic alkalosis is an almost invariable result of potassium depletion because hydrogen ions migrate into potassium-depleted cells. Urinary potassium excretion is low, and the urine remains acid (de Wardener, 1961). However, our patient was excreting much potassium in an acid urine. Attempts to rectify the alkalosis with ammonium chloride were unsuccessful, whereas spontaneous reduction of the plasma bicarbonate occurred on partial correction of the potassium deficit. It thus seems that the alkalosis was a *result* rather than a *cause* of the urinary potassium loss; possibly the increased excretion represented a failure to reabsorb potassium from the glomerular filtrate rather than increased secretion by the distal tubule. The potassium in the urine represented about 75 % of the filtered load.

It is well known that extra-adrenal tumours may produce the picture of Cushing's syndrome (Brown, 1928; Thorne, 1952; Allott and Skelton, 1960; Thompson et al., 1962); many of the reports have involved bronchial carcinoma, though other tumours have been incriminated (Bagshawe, 1960; Edmunds et al., 1961). In most cases there was adrenal cortical hyperplasia, but this was not invariable, the tumour itself elaborating a hormone with corticosteroid activity. There have often been clinical stigmata of Cushing's syndrome; our patient showed none. Nevertheless, cases of carcinoma of the bronchus are described which present with a “biochemical” Cushing's syndrome without the usual clinical signs (Muller and O'Connor, 1958; Prunty et al., 1963; Ross, 1964); they have a severe hypokalaemic alkalosis, and usually glycosuria; while their aldosterone secretion is low, the glucocorticoid excretion is much increased (Massachusetts General Hospital, 1958; Meador et al., 1962). It is suggested that clinical features of Cushing's disease may not develop in patients with cachectic malignant disease. Our patient was hypokalaemic for at least six weeks, and, when one recalls how rapidly Cushingoid features develop in patients on corticosteroid therapy, it is difficult to believe that she was producing excess glucocorticoids. Unfortunately the corticosteroid excretion was not measured, but she did not have glycosuria. It is suggested that the Hodgkin's tissue was producing a substance other than aldosterone or glucocorticoids which increased potassium excretion.

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**REFERENCES**