Hypercalcaemia as complication of accelerated chronic granulocytic leukaemia

Hypercalcaemia is a well-recognised, potentially lethal complication of certain non-endocrine neoplasms but rarely occurs in leukaemia. This is especially true in the case of chronic granulocytic leukaemia (CGL), few such instances having been reported.\(^1\)\(^-\)\(^3\) We therefore describe three patients with CGL who developed hypercalcaemia while in the accelerated phase of the disease. Two also had complicating encephalopathy.

Case reports

Case 1—A 19-year-old girl was diagnosed as a case of Philadelphia-chromosome-positive CGL in October 1972. Treatment with hydroxyurea was initially successful but in February 1973 blastic transformation occurred with 60\(^\circ\) myeloblasts in the bone marrow. Blood chemistry was normal. Haematological remission was obtained but in June she relapsed and was found to have a serum calcium concentration of 3.7 mmol/l (14.6 mg/100 ml). Blood urea, serum phosphorus, and alkaline phosphatase concentrations were normal. Radiography showed generalised lytic lesions and extensive blood vessel calcification (see figure). There were no symptoms referable to either bone lesions or hypercalcaemia. Prednisone and intravenous phosphates failed to reduce the serum calcium but a combination of intravenous mithramycin 2 mg and calcitonin 160 MRC units eight-hourly was rapidly effective. Subsequent episodes of hypercalcaemia were treated with mithramycin alone. Antileukaemia treatment proved ineffective, however, and during another hypercalcaemic episode she died. Necropsy showed extensive leukaemic blast-cell infiltration of the bone marrow and reticuloendothelial system. Severe calcification was found in blood vessels, heart, pulmonary alveoli and bronchi, and kidney. Extensive bone lysis was present and osteoclastic activity increased. Pathognomonic lesions were normal.

Case 2—A 34-year-old man presented in October 1974 with malaise, left hypochondrial pain, weight loss, and hepatosplenomegaly. Results of investigations were: haemoglobin 7 g/dl; white cell count 6.2 \(\times\) 10\(^9\) (6200/mm\(^3\)) (polymorphs 2.5 \(\times\) 10\(^9\), lymphocytes 3.2 \(\times\) 10\(^9\), and monocytes 0.5 \(\times\) 10\(^9\)); and platelets 97 \(\times\) 10\(^9\). Bone marrow contained 60\(^\circ\), lymphoblasts. Cyto genetic analysis showed three cell lines, one normal and two with the Philadelphia chromosome.\(^7\) The diagnosis was acute lymphoblastic trans formation of clinically occult CGL. Serum calcium was 3.25 mmol/l (13 mg/100 ml). Treatment with vincristine, prednisone, and colaspase resulted in a partial haematological remission with return of the serum calcium concentration to normal. In June 1975 an asymptomatic recurrence of hypercalcaemia was treated with prednisone but he subsequently presented with bone pain, confusion, and a fluctuating level of consciousness. Serum calcium was 4 mmol/l (16 mg/100 ml) and radiography showed lytic lesions in several ribs. Intravenous mithramycin 2 mg temporarily restored the calcium concentration and mental state to normal but he was subsequently readmitted in hypercalcaemic coma and died.

Case 3—A 23-year-old man was diagnosed in November 1972 as a case of Philadelphia-chromosome-positive CGL. The disease was controlled with hydroxyurea until November 1976, when severe splenomegaly recurred. Results of extensive investigation, however, were consistent only with the chronic phase of CGL. In January 1977 he was readmitted with malaise, vomiting, and generalised bone pain. Investigations showed: haemoglobin 10.7 g/dl; white cell count 42 \(\times\) 10\(^9\) (blast cells 1.6 \(\times\) 10\(^9\)); platelets 25 \(\times\) 10\(^9\); serum calcium 3.9 mmol/l (15.6 mg/100 ml); and normal serum urea and electrolyte concentrations. The serum calcium concentration rose rapidly and he became comatose. Despite intensive resuscitative measures including calcitonin and mithramycin he died.

Comment

As has been noted previously, the occurrence of hypercalcaemia in leukaemia is a grave prognostic sign and in CGL may perhaps partially reflect the more rapidly associated change in the course of the disease. Though in two of our cases hypercalcaemia was not a major factor influencing disease outcome, in one it was the cause of relatively sudden death. The presence of increased osteoclastic activity in case 1 is of aetiological importance as both parathormone and osteoclast stimulating factor production have been described in haemopoietic neoplasms.\(^5\)

The imprecise and variable symptomatology of hypercalcaemia in CGL may result in failure to recognise the presence of a potentially reversible complication.


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Prediction of postdialysis hypophosphataemia

Phosphate retention is a normal accompaniment of chronic renal failure, and phosphate-binding agents (such as aluminium hydroxide) are commonly used to prevent hyperphosphataemia. Patients receiving these binding agents may develop phosphate depletion,\(^1\) which may produce osteomalacia in patients with impaired renal function\(^2\) and those undergoing maintenance haemodialysis.\(^3\) It has also been suggested that phosphate depletion prevents severely osteomalacic renal patients from responding to 1,25-dihydroxycholecalciferol, a synthetic analogue of 1,25-dihydroxycholecalciferol,\(^4\) and that phosphate depletion may be a factor in the syndrome of dialysis dementia. It is