Lesson of the Week

Hypoglycaemia in acute myelomonoblastic leukaemia: report of two cases and review of published work

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True hypoglycaemia complicating leukaemia is a rare event. Most reported cases have been ascribed to in vitro glycolysis by abnormal leucocytes and been labelled "artefactual" hypoglycaemia.[1 2]

Symptomatic hypoglycaemia has been reported in three patients with chronic granulocytic leukaemia.[3-5] So far as we know in acute leukaemia there has been only a single report of true hypoglycaemia, associated with acute monocytic leukaemia.[6] We have recently observed the occurrence of hypoglycaemia in two cases of acute myelomonoblastic leukaemia.

Emergency blood glucose analysis should be performed on any patient with malignant disease who presents with confusion, drowsiness, or loss of consciousness

Case 1

A 62 year old man presented with tiredness and bleeding gums. Physical examination showed an anaemic man with severe gum hypertrophy and an enlarged liver and spleen. Peripheral blood values were haemoglobin concentration 6·4 g/dl, white cell count $6·7\times10^9$/l (polymorphs 30%, lymphocytes 27%, monocytes 14%, metamyelocytes 10%, myelocytes 3%, promyelocytes 3%, blast cells 13%), and platelet count 65×10^9/l. Bone marrow examination showed a hypercellular marrow with depressed normal haematopoiesis and pronounced infiltration by leukaemic blast cells. Cytochemical reactions of the marrow confirmed the diagnosis of acute myelomonoblastic leukaemia.

The patient was transfused with packed red cells and started on chemotherapy with TAD protocol (thioguanine, cytarabine, and daunorubicin). On the fourth day of chemotherapy he was found to be semiconscious with minimal response to verbal stimulation and was complaining of severe dizziness, headache, and blurred vision. Liver and renal function values were normal. Coagulation screen was abnormal, with prolongation of prothrombin and partial thromboplastin times. Blood glucose concentration was 1·65 mmol/l (30 mg/100 ml). The patient was given an intravenous infusion of 5% dextrose solution. He regained consciousness and showed dramatic improvement with the disappearance of symptoms and signs of hypoglycaemia.

Despite six courses of chemotherapy complete clinical and haematological remission of leukaemia was not achieved. Four months later the patient died at home; necropsy was not performed.

Case 2

A 47 year old man presented with tonsillitis and gum hypertrophy. His blood count was abnormal, with haemoglobin concentration 10·2 g/dl, white cell count 93×10^9/l (polymorphs 18%, lymphocytes 11%, blast cells 70%, nucleated red cells 1%), and platelet count 30×10^9/l. Bone marrow showed acute myelomonoblastic leukaemia, 90% of the cells resembling monoblasts and a small population of myeloblasts exhibiting Auer rods. Serum lysozyme concentration was 456 mg/l (normal range 3-7 mg/l). At the time of presentation he had renal impairment, with a blood urea concentration of 9·2 mmol/l (55·4 mg/100 ml) and a plasma creatinine concentration of 154 μmol/l (1·74 mg/100 ml).

The patient was treated with cytotoxic chemotherapy using thioguanine, cytarabine, and daunorubicin (daunorubicin injection on day 1 and five days' treatment with cytarabine and thioguanine). During the third course of chemotherapy he became acutely unwell with severe hyperventilation. He rapidly went on to become sweaty, exhausted, and mildly feverish. Blood gas measurements showed appreciable acidosis, which became more pronounced as his condition deteriorated. Shortly before his death from cardiac arrest biochemical values were: hydrogen ion concentration 211·8 nmol (ng)/l, pressure of carbon dioxide 5·05 kPa (38·0 mm Hg), pressure of oxygen 14·1 kPa (106 mm Hg), standard bicarbonate 1·9 mmol(mEq)/l, base excess −32·1 mmol(mEq)/l, blood urea concentration 22 mmol/l (133 mg/100 ml), plasma creatinine concentration 340 μmol/l (3·8 mg/100 ml), and blood glucose concentration unrecordable. Necropsy showed neither any other cause for his death nor gross leukaemic infiltration.

Discussion

In man reports of hypoglycaemia in leukaemia are rare.[3-5] In all the reported cases the leukaemia was of chronic myeloid type and the patients presented with very high white cell counts (>200× 10^9/l). Hypoglycaemia in leukaemia may be artefactual, caused by increased in vitro glycolysis by abnormal leucocytes.[1 2] In our first patient hypoglycaemia was not artefactual, as peripheral blood leucocytosis was absent. The patient had characteristic symptoms and signs of hypoglycaemia. He improved dramatically with an intravenous infusion of 5% dextrose solution. In the second case hypoglycaemia was more prolonged and resistant to treatment. Both patients had acute myelomonoblastic leukaemia with prominent monoblastic component.

Various theories have been suggested to explain the occurrence of hypoglycaemia in patients with non-pancreatic tumours. They include increased glucose consumption by large tumour masses,[7] secretion of insulin like substance or substances that promote the production of insulin by the pancreatic endocrine glands,[8 9] and the direct hepatotoxic effects of chemotherapy leading to impaired hepatic glycogenolysis.[10 11] In our first case the normal liver and renal function values and the occurrence of hypoglycaemia shortly after the start of cytotoxic chemotherapy may be explained by the

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release of insulin like substance or substances that promote insulin production as a result of lysis of leukaemic blast cells. In the second case the renal failure may well have been due to lysozymuria and proximal tubular damage,[12 13] and this would certainly account for the patient's profound acidosis.

Lactic acidosis has been associated with hypoglycaemia in several clinical settings, and both lactic acidosis[14 15] and concurrent lactic acidosis and hypoglycaemia[6] have been reported in association with acute leukaemia. Probably the rapid demise of our second patient was due to rapid release of lysozyme from leukaemic blast cells damaged as a result of chemotherapy and the resultant lysozymuria led on to proximal tubular damage, lactic acidosis, and hypoglycaemia.

We conclude that hypoglycaemia complicating the management of acute leukaemia may lead to considerable morbidity and mortality. Regular monitoring for this compliction should be part of management. Emergency blood glucose analysis should be performed on any patient with malignant disease who presents with confusion, drowsiness, or loss of consciousness.

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What is the life expectancy of the roundworm (Ascaris lumbricoides) and of the hookworm (Ancylostoma duodenale)? Information would be helpful for advising patients who have lived in areas where these infestations are common.

Adult *Ascaris lumbricoides* have a relatively short life span, mostly less than one year, although a few may live as long as 18 months. By contrast, the hookworms *Ancylostoma duodenale* and *Necator americanus* are long lived. Palmer described an experimental infection of *N americanus* in a human volunteer that continued after treatment and in the absence of reinfection for 15 years.[1] According to Miller, however, most reports show considerable reductions (70-80%) in hookworm burdens in the absence of reinfection within one to three years.[2] Although absolute longevity of worms is of interest, it may be more helpful to give the probable duration of significant pathogenicity in the absence of reinfection or other contributing health factors. With *A duodenale* pathogenic effects may occur for up to four years, as Boycott and Haldane described patients in whose faeces moderate to abundant ova were found and in whom severe anaemia persisted for this period after the last known date of exposure to infection.[3]—JAMES C CHUBB, reader in zoology, Liverpool.

1 Palmer ED. Course of egg output over a 15 year period in a case of experimentally induced necatoriasis americanus, in the absence of hyperinfection. *Am J Trop Med Hyg* 1955;**4**:756-7.
2 Miller TA. Hookworm infection in man. *Adv Parasitol* 1979;**17**:315-84.
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Is there any contraindication to the long term administration of hexanone in an elderly patient who suffers from recurrent cystitis?

The important question here is diagnosis. The nature and reason for the recurrent cystitis might make other treatment more appropriate and long term treatment either unnecessary or possible with a simpler, less expensive, and better tried agent. The most important distinction will be between a recurrent bacterial cystitis and one which is abacterial, though a trial of treatment on the basis that there may be a bacterial component, even when repetitive cultures are negative, is worth a try. A more common omission is not to consider in women such things as recurrent symptoms of cystitis due to postmenopausal changes. In all patients of all groups it is also important to consider such diagnoses as stone or obstruction and also to test the response of the patient's complaints to common sense advice on, for example, the amount of fluid drunk (and therefore the amount of urine passed) and the use of inappropriate chemicals in the perineal area (which might even be the use of an inappropriate cleansing method to which there is some local allergy such as a clothes washing fluid or compound). There are other local conditions in both the bladder and urethra, and adjacent to them, that may cause symptoms attributed to "recurrent cystitis." One unusual, but underdiagnosed, condition is that of interstitial cystitis.[1] It is now important to identify this condition, and variants of it, because several successful treatments are available. I have had successes with glucocorticosteroids, given in the large doses used in patients with glomerulonephritis of the kidney who are resistant to steroids. Local chemical agents inserted into the bladder are also sometimes effective. Several patients with major problems, even to the extent of cystectomy being suggested, have been cured or have shown dramatic and useful responses with these treatments.

A patient who has not been carefully considered by an appropriate consultant or by a practitioner with considerable experience in this group of disorders should therefore be referred for further consideration as they may have one of these alternative conditions. If all curable possibilities are considered, and excluded, and when a range of simpler "hygiene" manoeuvres and a long term trial of simple antibacterial treatment—for instance, sulphadimidine 1 g at night after emptying the bladder or 50 mg nitrofurantoin—have failed a trial of hexamine may be merited. It is unlikely to cause important side effects but will only be effective in some cases and then probably only if sufficient care is given to keep pH below 6·4 most of the time. This may cause some morbidity from minor side effects and gastric disturbances but is safer than most medications taken on a regular basis.—MARTIN S KNAPP, nephrologist senior research fellow, Nottingham.

1 Messing EM, Stamey TA. Interstitial cystitis. *Urology* 1978;**12**:381-92.

What is meant by venous insufficiency and how does it account for muscular cramp?

Insufficiency in the valves of the veins gives rise to primary or secondary varicose disease. The term "venous insufficiency" is, however, usually reserved for severe forms of the disease in which the skin and subcutaneous tissue of the ankle show evidence of chronic venous hypertension. Incompetent calf perforating veins may generally be identified in addition to incompetence of the saphenous vein. In the erect posture these veins convey high pressures to the unsupported superficial venous system both on standing and during exercise. Haemodynamic tests such as direct manometry, Doppler ultrasound, and volumetry will show a disorder of the deep veins in nearly all cases. This takes the form of obstruction by previous deep vein thrombosis (the post-thrombotic syndrome) or reflux down a patent deep system owing to valvular incompetence. In such a limb not only the superficial but also the deep tissues are subjected to sustained and chronic venous hypertension. This gives rise to ache, swelling, and, if the deep veins are obstructed, venous claudication. Restless legs and cramps are well recognised to occur when the patient rests. The horizontal posture results in a fall in pressure at the venous end of a capillary bed and fluid and electrolyte shifts undoubtedly occur. The precise mechanism at neuromuscular or cell membrane level that cause this muscle spasm is, however, not known.—C V RUCKLEY, consultant vascular surgeon, Edinburgh.