Nephrocalcinosis: another cause of renal erythrocytosis

Although erythrocytosis is not a recognised complication of nephrocalcinosis, in the course of a study of 250 patients with nephrocalcinosis we found nine patients with raised blood haemoglobin concentration and haematocrit value.

Patients, methods, and results

All patients had radiological medullary nephrocalcinosis, of varying underlying cause (two primary hyperparathyroidism, three renal tubular acidosis, four medullary sponge kidney). Studies of red cell mass and plasma volume were performed on six patients using ^{51}Cr -labelled autologous red cells.¹ Urine erythropoietin concentration was measured in four of these patients, and in 11 other patients with nephrocalcinosis but no erythrocytosis: the commercially prepared JCL-ECF haemagglutination-inhibition assay for erythroid stimulating factors (JCL Clinical Research Co, Knoxville) was used for this assay. Urine was studied fresh or was immediately deep frozen until the assay could be performed. All patients had polyuria and a urine concentration defect, an almost invariable feature of nephrocalcinosis,² so any rise of urine erythropoietin concentration probably represented a true increase in erythropoietin excretion.

The results are shown in the table. Five of the six patients studied had a decreased plasma volume. Four of six patients studied had a definitely raised red cell mass, and one a marginally raised red cell mass. One other patient had significantly increased red cell production despite a blood haemoglobin concentration of 18.2 g/dl and haematocrit value of 57%. Thus, of seven patients studied, five had true erythrocytosis, one marginal erythrocytosis, and one pseudoerythrocytosis. In the three patients studied whole blood viscosity was above the upper limit of normal. Platelet and white cell counts were normal in all patients.

Urine erythropoietin concentration was raised in three of the four patients studied with erythrocytosis, and the normal value in patient 9 may be inappropriately high for someone with a haemoglobin concentration of 18.2 g/dl. Urinary erythropoietin concentration measured in 11 other patients with nephrocalcinosis (four with renal tubular acidosis, seven with medullary sponge kidney) was considerably raised in five, mildly raised in four, and normal in two.

Comment

Erythropoietin is a glycoprotein of molecular weight 36 000,³ and, like small-molecular-weight proteins, is probably filtered by the renal glomerulus and reabsorbed by the proximal tubule. The increased urinary erythropoietin in these patients is unlikely to have been due to tubular damage, as they have no evidence of abnormal tubular handling of amino-acids, glucose, or β_2 -microglobulin. Thus the increased erythropoietin excretion of these patients is probably secondary to increased erythropoietin production, possibly stimulated by localised tissue hypoxia⁴ related to areas of nephrocalcinosis.

The importance of erythrocytosis in these patients is difficult to assess. Patients with nephrocalcinosis almost invariably have urine concentration defects² and often have salt-losing nephropathy, and are therefore likely to have a low plasma volume and be at particular risk of developing hyperviscosity and thrombotic complications.⁵ The aim of treatment must be to reduce the haematocrit value and whole blood viscosity, and sodium supplements may be useful in an attempt to increase plasma volume. Careful follow-up is indicated and, should thrombotic episodes occur, then venesection using the haematocrit

value and whole blood viscosity as guides to treatment should be started. When red cell production is being driven by an inappropriately high erythropoietin production the use of ^{32}P may be justified. Patient No 7 was treated with ^{32}P and venesection and survived another 20 years before dying of his third myocardial infarct.

Thus medullary nephrocalcinosis, from whatever cause, should be added to the list of causes of renal erythrocytosis, the increase in blood haemoglobin concentration being due to a combination of diminished plasma volume and the increased red cell mass due to raised production of erythropoietin.

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¹ Belcher, E H, and Vetter, H, *Radio-isotopes in Medical Diagnosis*, p 319. London, Butterworth, 1971.

² Wrong, O M, and Feest, T G, *Advanced Medicine*, ed D K Peters, p 394. London, Pitman Medical, 1976.

³ O'Sullivan, M B, et al, *Journal of Laboratory and Clinical Medicine*, 1970, **75**, 771.

⁴ Adamson, J W, Eschbach, J, and Finch, C A, *American Journal of Medicine*, 1968, **44**, 725.

⁵ Erslev, A J, in *Haematology*, ed W J Williams, p 204. Maidenhead, McGraw Hill, 1970.

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Intrathoracic perforation of hiatus hernia

Perforation of a hiatus hernia is rare. Usually no definite acute event precedes it, although a sudden rise in chronically raised intra-abdominal pressure must be important. I describe a patient in whom perforation occurred during a period of raised intra-abdominal pressure due to acute intestinal obstruction.

Case report

A 70-year-old woman was admitted to hospital with a 48-hour history of central colicky abdominal pain and distension. A small painless lump had appeared in the groin three days previously. Apart from occasional heartburn,

Patients with medullary nephrocalcinosis and raised haemoglobin concentration. Figures in parentheses are normal ranges in the laboratories concerned

Patient	Sex	Diagnosis	Age	Plasma creatinine ($\mu\text{mol/l}$)	Haemoglobin (g/dl)	Haematocrit value (%)	Red cell mass (ml/kg)	Plasma volume (ml/kg)	Whole blood viscosity (centipoise) (3.5-4)	Erythropoietin (in urine mIU/l) (15-40)
1	M	Renal tubular acidosis	26	123	19.0	55	27.2 (26-33)	29.2 (36-50)		
2	M	Renal tubular acidosis	26	85	18.0	53.4	39.8 (26-33)	37.0 (40-50)		
3	M	Renal tubular acidosis	52	190	18.2	57	RBC production 15% above normal			
4	M	Hyperparathyroidism	47	130	19.0	55	39.2 (24.7-35.9)	46.7 (35.5-46.7)		
5	M	Hyperparathyroidism	22	292	18.3		29.2 (20-27)	23.5 (36-50)	6.23	75
6	F	Sponge kidney	50	170	17.7	52	39.9 (20-27)	30.9 (36-50)	6.0	112, 50
7	F	Sponge kidney	59	109	18.0	50.9	27.8 (20-27)	35.2 (36-50)	4.15	75, 50
8	F	Sponge kidney	43	235	17.4	50.6				
9	F	Sponge kidney	67	94	18.2	53				25

she had been well. Her general condition was good and her temperature was normal. She was not obese. The abdomen was uniformly distended. A non-tender irreducible right femoral hernia was present. Obstructive bowel sounds were heard. Plain abdominal x-ray films confirmed a small bowel obstruction but also showed a mediastinal fluid level. This fluid level remained even though nasogastric aspiration produced 500 ml of normal gastric fluid.

The femoral hernia was explored through a combination of a low and high approach. The sac contained frank pus and necrotic small bowel. About 15 cm of ileum was resected with end to end anastomosis. The hiatus hernia was palpated through the laparotomy wound; it admitted three fingers and the intrathoracic stomach was easily reducible. Initially she made a good recovery but about 36 hours postoperatively developed signs of septicaemic shock and died a few hours later despite intensive treatment. At necropsy half the stomach was intrathoracic through a sliding type of hiatus hernia. The intrathoracic portion was necrotic; it was extremely thin and had three large perforations in it. The pleural cavities contained two litres of gastric fluid. The small bowel was moderately distended and peritonitis was present in the right iliac fossa. The anastomosis was intact.

Comment

Hiatus hernia is liable to the same complications as hernias elsewhere.¹ Obstruction or torsion of the stomach in the hernial sac is rare but may cause gangrene and perforation with a high mortality rate.² Paraoesophageal hernias are more dangerous than oesophageal ones.³ Obesity is an important cause of chronically raised intra-abdominal pressure.

Perforation usually does not follow any definite event, although Watts⁴ has described ruptures resulting from the sudden increase in intra-abdominal pressure which accompanies retching and vomiting. In this patient probably postoperative distension of the bowel caused a sustained period of increased intra-abdominal pressure with compression of blood vessels at the hernial ring and ischaemic necrosis of the intrathoracic stomach. This sequence of events has not been reported.

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¹ Gerson, D E, and Lewicki, A M, *Radiology*, 1976, **119**, 257.

² Christianses, L A, Blichert-Toft, M, and Bertelsen, S, *American Journal of Surgery*, 1975, **129**, 574.

³ Skinner, D B, and Belsey, R H R, *Journal of Thoracic and Cardiovascular Surgery*, 1967, **53**, 33.

⁴ Watts, H D, *Gastroenterology*, 1976, **71**, 683.

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Phaeochromocytoma with lactic acidosis

Although adrenaline administration in man has been shown to increase lactic acid concentrations,¹ the clinical coincidence of a catecholamine-secreting tumour with lactic acidosis has not yet been reported. We describe here a patient with phaeochromocytoma whose main feature on admission was severe lactic acidosis.

Case report

A 33-year-old Italian woman had been treated by her family doctor over 12 months for epigastric pain. She complained of cramps in her stomach associated with spells of paleness and sweating. Evaluation by a gastroenterologist, including gastroduodenoscopy, showed no abnormality, and symptomatic treatment was started. Repeated blood pressure recordings were normal.

On the morning of the day of admission she suffered from acute pain in the back, nausea, and palpitations. Her doctor referred her to a local hospital because of ventricular ectopic beats and epigastric pain. On admission she was pale and had dyspnoea and cold extremities. The patient was transferred to our hospital later that day because of rapidly increasing dyspnoea. She

was in acute respiratory distress; she was fully conscious but her pupils were dilated and unresponsive to light. The blood pressure was 180/130 mm Hg, and an electrocardiogram (ECG) showed sinus tachycardia and suggested a subendocardial lateral wall infarction. Chest radiography showed diffuse pulmonary oedema and a normal sized heart. A naso-tracheal tube was inserted, and artificial ventilation with positive end-expiratory pressure was started. Blood gas analysis on admission showed severe metabolic acidosis. The table shows the laboratory values on admission and four hours later.

Laboratory values

	Normal range	On admission	Four hours after admission
Plasma lactate (mmol/l)	0.2-1.2	22.0	17.9
Blood glucose (mmol/l)	4.4-6.7	51.0	34.2
Plasma β -hydroxybutyrate (mmol/l)	0.02-0.10	0.67	
Plasma creatinine (μ mol/l)	53-123	185	247
Plasma phosphorus (mmol/l)	0.32-0.81	6.26	
Haemoglobin (g/dl)		15.1	14.2
Arterial pH	7.35-7.45	6.67	6.9
Arterial P_{CO_2} (kPa)	4.67-6.0	6.13	4.93
Arterial P_{O_2} (kPa)	9.33-13.33	6.26	11.20
Base deficit (mmol/l)	3.3-(-1.2)	34	27
Plasma insulin (6-14 mU/l)	6-14	47	
Plasma glucagon* (pmol/l)	17.1-42.9	24.3	23.4
Plasma noradrenaline (nmol/l)	0.95-2.19	4581	3635
Plasma adrenaline (nmol/l)	0.05-0.66	3357	742
Plasma dopamine (nmol/l)	0.39-0.98	320	197

*30 K-antibody (Dr R Unger).

Conversion: SI to traditional units—Lactate: 1 mmol/l $\approx$ 9.0 mg/100 ml. Glucose: 1 mmol/l $\approx$ 18 mg/100 ml. β -Hydroxybutyrate: 1 mmol/l $\approx$ 10.4 mg/100 ml. Creatinine: 1 μ mol/l $\approx$ 0.0113 mg/100 ml. Phosphorus: 1 mmol/l $\approx$ 3.1 mg/100 ml. Blood gas: 1 kPa $\approx$ 7.5 mm Hg. Glucagon: 1 pmol/l $\approx$ 3.48 ng/l. Noradrenaline: 1 nmol/l $\approx$ 16.9 ng/100 ml. Adrenaline: 1 nmol/l $\approx$ 18.3 ng/100 ml. Dopamine: 1 nmol/l $\approx$ 15.3 ng/100 ml.

A raised blood lactate concentration and severe hyperglycaemia were present. Plasma catecholamine concentrations were measured using radio-enzymatic techniques. Plasma adrenaline and noradrenaline were over 5000 times the normal range determined in normal volunteers. Drug intoxication was excluded by examining a blood specimen and by the history. Four hours after admission and after treatment with 200 mmol (mEq) bicarbonate and with 20 U of regular insulin her blood pH was still 6.9, her base deficit 27 mmol(mEq)/l, and her blood lactate 17.9 mmol(161 mg/100 ml)/l. Haemodialysis was started to try to correct the severe metabolic acidosis. Shortly afterwards the patient's condition rapidly deteriorated. Her blood fibrinogen concentrations fell to undetectable levels, which suggested the presence of disseminated intravascular coagulation. Her diastolic blood pressure dropped from 110 to 75 mm Hg; she developed pump failure and died of a cardiac arrest one hour later.

Necropsy showed a left adrenal phaeochromocytoma (52 g) with a typical histological pattern. Other pathological findings included pulmonary oedema and focal necrotic areas of the heart.

Comment

This was an unusual case of phaeochromocytoma in which the clinical course was characterised by the development of severe lactic acidosis and pulmonary oedema. The fact that the blood pressure was maintained and lactic acidosis persisted despite adequate ventilation indicates that lactic acidosis was a direct consequence of the excessive concentration of circulating catecholamines. According to Cohen's classification,³ this was a case of type B lactic acidosis. The increase in lactate concentrations might have been caused by increased production by peripheral tissues or by a reduced rate of removal by the liver. The stimulatory effect of adrenaline on glycogenolysis and insulin resistance was probably responsible for the persistent severe hyperglycaemia. Despite the raised blood glucose value, endogenous insulin concentrations were relatively low, probably because of the inhibitory effect of the catecholamines on insulin secretion. Excessive circulating dopamine concentrations have not yet been reported in phaeochromocytoma, though raised urinary dopamine excretion has been found in rare cases of malignant phaeochromocytoma.⁴

This patient died because her condition was not diagnosed and treated before heart failure occurred. Myocardial infarction and focal myocarditis are sometimes associated with phaeochromocytoma.⁵ The absence of a history of hypertension suggests that the β -adrenergic effects of the raised adrenaline concentrations dominated the early clinical course, whereas on admission vasoconstriction, decreased gut motility, and dilatation of the pupils were signs of α -adrenergic stimulation. Pupillary dilatation represented a further unique feature of the case.

The differential diagnosis of idiopathic lactic acidosis should