Hypoglycemia as a complication of removal of a pheochromocytoma

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In a patient with a solitary pheochromocytoma severe hypoglycemia developed following excision of the tumour. The possible causative mechanism was thought to be a reactive relative increase in insulin production secondary to increased endogenous production of glucose, induced by the large amounts of epinephrine produced by the tumour. Alternatively, epinephrine withdrawal following removal of the tumour under phentolamine infusion may have induced increased insulin production and hence potentiated the development of hypoglycemia. Careful monitoring of the blood glucose concentration during and after the operation is recommended to obviate this potentially fatal complication.

Chez un patient porteur d'un phéochromocytome solitaire une hypoglycémie sévère est apparue après l'excision de la tumeur. On croit que le mécanisme de déclenchement possible puisse-t-être une augmentation réactionnelle relative de la production d'insuline consécutive à l'augmentation de la production endogène de glucose, provoquée par les quantités importantes d'épinéphrine sécrétées par la tumeur. Par ailleurs, la baisse d'épinéphrine qui a suivi l'ablation de la tumeur sous infusion de phentolamine peut avoir provoqué une augmentation de la production d'insuline et potentialisé de la sorte le développement de l'hypoglycémie. Une surveillance prudente de la glycémie durant et après l'opération est recommandée afin de pouvoir obvier à cette complication potentiellement fatale.

The pharmacologic actions and side effects of catecholamines produced by a pheochromocytoma present a considerable challenge to the anesthetist, internist and surgeon. The tumour occurs in only 0.07 to 0.1%[1-3] of all hypertensive patients. Preoperatively patients with these tumours are exposed to all the complications of systemic hypertension, from cerebrovascular accidents, myocardial hypertrophy, cardiomyopathy, myocardial infarction and renal function impairment to generalized peripheral vascular disorders. Hyperglycemia is also a common associated disorder. During the operative period the main complications are uncontrolled hypertension, cardiac arrhythmias and hypotension following removal of the tumour.[4] Such phenomena have been well described.[5]

We report a case in which a pheochromocytoma was successfully excised but postoperatively a potentially fatal complication developed that has not been described in the literature.

Case report

Clinical history and findings

A 60-year-old man weighing 65 kg was admitted to hospital for investigation of "nervous episodes" in which he felt anxious and noted shaking of his body with profuse sweating. The episodes lasted 10 to 15 minutes and had been occurring about three times a week for 12 years. Apart from hypertension (blood pressure, 180/100 mm Hg) he had no important physical abnormalities. His hypertension had been documented for at least 2 years and ischemic changes had been noted on electrocardiograms. Investigation for diabetes mellitus had proved negative.

During this admission, values of urinary vanillylmandelic acid (VMA) and catecholamines were greatly increased on several occasions, VMA values ranging from 18.8 to 32.0 mg/d (normal, up to 9.0 mg/d) and catecholamine values, from 850 to 1634 μg/d (normal, up to 100 μg/d). By selective angiography the tumour was visualized as a solitary lesion in the right adrenal gland.

Preoperative management

Alpha-adrenergic blockade with phenoxybenzamine was begun 28 days preoperatively, the daily dose being gradually increased from 10 to 60 mg over the 4 weeks. The patient was also given propranolol, 20 mg *qid*, because of a tendency to have tachyarrhythmia. Both drugs were stopped 24 hours before the operation. The associated changes in blood pressure and heart rate during pretreatment are shown in Fig. 1. Blood glucose concentration, determined only on admission, was 133 mg/dl.

Operative management

Papaverine hydrochloride, 20 mg, and hyoscine, 0.4 mg, given intramuscularly 1 hour before operation, adequately sedated the patient.

Anesthesia was induced with sodium thiopental, 250 mg, followed by pancuronium bromide, 7 mg, and fentanyl citrate, 100 μg. Systolic blood pressure increased with intubation to 200 mm Hg (Fig. 2). Phentolamine, 5 mg intravenously, reduced the pressure, and anesthesia was maintained with nitrous oxide, oxygen and fentanyl supplements.

The procedure was uneventful except for a further hypertensive episode when the tumour was manipulated. Again phentolamine reduced the blood pressure to within normal values. Multiple ventricular ectopic beats were noted at this time and controlled with a single 1-mg dose of propranolol.

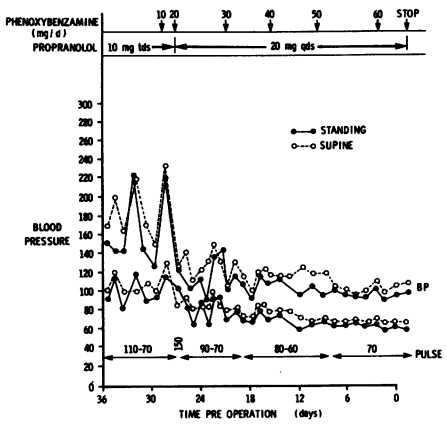

FIG. 1—Preoperative management of patient with pheochromocytoma and data on blood pressure (mm Hg) and pulse rate (beats/min).

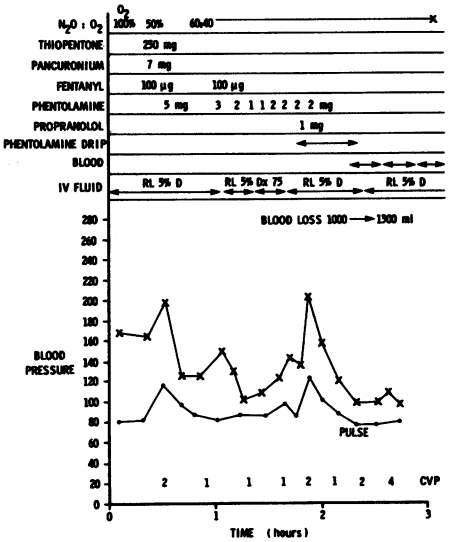

FIG. 2—Operative management and data on blood pressure (mm Hg) and pulse rate. RL 5% D = Ringer's lactate with 5% dextrose. CVP = central venous pressure (cm H_2O).

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During the operation Ringer's lactate with 5% dextrose was transfused together with 3 units of whole blood to maintain a positive fluid balance of 1500 to 2000 ml. The patient became normotensive with no hypotensive episodes after removal of the tumour. Following administration of atropine, 1.2 mg, and neostigmine, 2.5 mg, spontaneous respiration was established, and when the patient arrived on the recovery ward he was awake and answering questions.

Postoperative management

The patient's intravenous infusion was changed to plain Ringer's lactate (Fig. 3). Two hours postoperatively he gradually became comatose over 15 minutes and eventually did not respond to painful stimuli. His blood pressure and central venous pressure remained stable. He was areflexic and had bilateral extensor plantar reflexes, central pinpoint pupils with loss of the doll's eye reflex, and no neck stiffness. Blood glucose concentration was reported by the laboratory to be 35 mg/dl; the initial estimate by Dextrostix was 45 mg/dl.

The patient rapidly regained consciousness after intravenous administration of 100 ml of 50% dextrose. An infusion of 15% dextrose in Ringer's lactate (rate, 150 ml/h) over the next 24 hours maintained his blood glucose value in the range of 90 to 130 mg/dl (Fig. 3). After this his sugar requirement appeared to return to within normal limits, an infusion of 5% dextrose at 100 ml/h keeping the blood glucose value in the normal range.

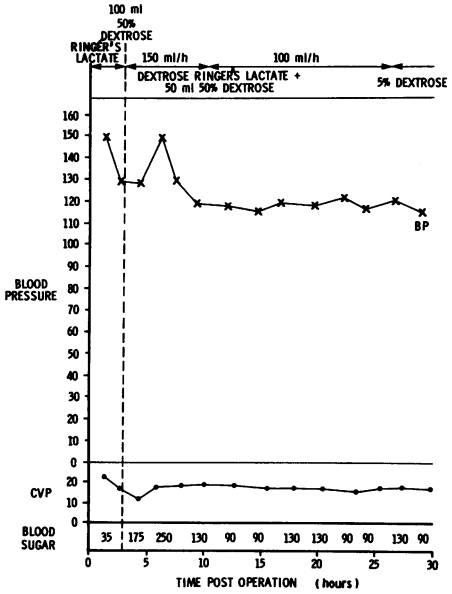

FIG. 3—Postoperative management. Blood sugar values in milligrams per decilitre.

Discussion

The effect of surgical stress on carbohydrate metabolism results in a tendency towards hyperglycemia in the postoperative period.[6-8] The mechanism is a combination of increased production of diabetogenic substances such as cortisol, adrenocorticotropic hormone, growth hormone, thyrotropic hormone and adrenocortical hormones[9,10] and a possible failure of insulin response to a glucose load.[11] Thus, we must explain the episode of hypoglycemia following operation in a patient whose epinephrine load was much greater than normal before the operation. Possible causes are α-cell insulinoma, nonpancreatic tumour (usually of mesothelial origin), hypofunction of the pituitary or the adrenal cortex, or diffuse liver disease. The episode might also have been reactive hypoglycemia secondary to mild diabetes. However, the absence of associated history and clinical or laboratory findings suggests that such causes were unlikely in this patient.

Epinephrine decreases serum insulin concentrations,[12] and following withdrawal of an epinephrine infusion there is a sudden, large increase in the concentration of immunoreactive insulin.[13] This increase is exaggerated if the infusion is accompanied by propranolol treatment.[14] Phentolamine has also been shown to potentiate the insulin response to glucose.[12] Both phenomena may have contributed to the production of our patient's postoperative hypoglycemia. We believe the reactive functional hypoglycemia secondary to hyperglycemia produced by the epinephrine-secreting tumour is the most likely explanation. However, the effects of epinephrine withdrawal following removal of the tumour and phentolamine infusion may have caused the postoperative hypoglycemia.

After tumour removal, insulin secretion may have exceeded that required to maintain a physiologic blood glucose concentration. Within 24 hours the insulin requirement was readjusted to suit the patient's new physiologic state. Although we cannot be certain whether the patient's severe hypoglycemia was associated with tumour removal or concomitant adrenergic blocking medication, it appears that extreme changes in glucose homeostasis may be associated with excision of a pheochromocytoma. It is surprising that problems with glucose homeostasis have not been emphasized, or at least reported, in the literature. As a result of our experience we strongly recommend preoperative assessment of glucose homeostasis before and after adrenergic blockade and careful monitoring of blood glucose concentration in the early postoperative period. We also recommend intraoperative and postoperative administration of dextrose solution of adequate concentration as a precaution.

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