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Anesthetic Management of Primary Hyperreninism

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The clinical entity of primary hyperreninism was first reported in 1968.[1] The triad of hypertension, hypokalemia, and hyperaldosteronism must be differentiated from primary aldosteronism by the presence of elevated renin levels and must be confirmed by the presence of unilaterally elevated renal-vein renin levels. Since the initial report, seven cases have been reported, all of which were subsequently attributed to neoplasia of the juxtaglomerular apparatus and reverted to normal after operation. Although this syndrome is extremely rare, there is a paucity of data relevant to the anesthetic management of the operative procedure. For this reason we submit the following case report.

REPORT OF A CASE

An 8-year-old black girl was seen at Charity Hospital on February 4, 1976, for evaluation of hypertension of unknown etiology. The hypertension had been unresponsive to conventional medical treatments. Evaluation revealed borderline hypokalemia, a radiolucent, avascular mass disrupting the cortex of the left kidney, and elevated right renal-vein renin levels, pointing to a diagnosis of primary hyperreninism. A left nephrectomy was scheduled for April 20, 1976.

Anesthetic Management. The patient was premedicated with meperidine, 30 mg, hydroxyzine, 40 mg, and atropine, 0.2 mg, im. Upon arrival in the operating rooms she was awake, but well sedated, and an infusion of 5 per cent dextrose 0.45 per cent sodium chloride solution was started. Succinylcholine, 30 mg, facilitated intubation, and anesthesia was maintained with 2.5 per cent enflurane, carried by 60 per cent nitrous oxide and 40 per cent oxygen. Pancuronium was used for muscle relaxation during the procedure.

Vital signs were monitored by an electrocardioscope, an esophageal stethoscope, and right radial arterial catheterization. Induction was uneventful; no arrhythmia or hypertension was detected.

The surgical incision was made at 8:20 A.M., and systolic/diastolic blood pressure gradually increased, reaching 190/140 mm Hg at 8:30 A.M. At this time, sodium nitroprusside was administered as a continuous drip, adjusted to maintain blood pressure at 150/100 mm Hg with an enflurane concentration of 1.5 per cent. The pulse remained 110 beats/min.

At 8:45 A.M. an acute hypertensive episode, with blood pressure reaching 190/140 mm Hg, occurred when the renal artery was clamped. The nitroprusside infusion was increased to return blood pressure to "optimum" levels. No discrete mass could be palpated on gross examination, and a wedge biopsy of the left kidney was taken. While awaiting pathologic interpretation of a frozen section, the blood pressure dropped to 130/100 mm Hg, and nitroprusside administration was discontinued. The biopsy report was equivocal, and the left kidney was removed. During manipulation of the kidney, an acute episode of hypertension, with blood pressure reaching 210/160 mm Hg, was controlled with nitroprusside. Both adrenals and the abdominal viscera were grossly normal.

During the remainder of the three-hour procedure, the blood pressure was maintained at 140/100 mm Hg without nitroprusside. Nine hundred milliliters of 5 per cent dextrose, 0.45 per cent sodium chloride were used, urinary output remained between 70 and 80 ml/hour, and arterial blood gases remained within normal limits throughout the procedure.

Postoperative Course. Postoperatively, blood pressure remained elevated during recovery (156/120 mm Hg), alar flaring was seen, and oxygen therapy initiated. On the first postoperative day blood pressure remained 148/110 mm Hg. It gradually decreased over the next week. On the eleventh postoperative day blood pressure was 160/70 mm Hg, and remained there throughout the hospitalization. Subsequent serum electrolytes and peripheral venous blood renin values were normal.

The pathologic report showed no gross evidence of tumor nodules. Final microscopic examination of the permanent sections showed hyperplasia of the juxtaglomerular apparatus concentrated in the outer cortex and mild arteriolar sclerosis.

DISCUSSION

Renin, a proteolytic enzyme with a molecular weight of 40,000, is produced primarily by the granular cells of the juxtaglomerular apparatus in the kidney in response to a variety of stimuli.

Renin as such has no physiologic effect other than causing the production of angiotensin I from its substrate. Intravenous infusion of renin causes a gradual increase in blood pressure after 15 to 20 seconds. The elevation may last 30 minutes or longer, depending on the amount injected. Intravenous infusion of angiotensin II causes a hypertension that has immediate onset and much shorter duration.[2] The differences in the pressor actions shown are attributed to the enzymatic properties of renin and the kinetics of the liberation and conversion of angiotensin I and II from the plasma substrate.

The renin substrate has been studied by a number of researchers.[3,4] A recent study[5] disclosed that

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the plasma concentration of renin substrate was normally far in excess of that necessary to maintain plasma levels of angiotensin II, and that this large concentration of renin substrate excludes it from exerting a rate-limiting effect in the kinetics of the renin–angiotensin system.

Under normal conditions, the primary modulation of renin levels is by mean renal perfusion pressure, the sensitivity of which is modified by the extent of activation of the renal sympathetics via β receptors, as well as the levels of catecholamines, sodium, potassium, and a number of humoral agents, including antidiuretic hormone and angiotensin II.

In the case of hyperreninism, a complex of sequelae ensues. The persistently elevated plasma renin acts on the substrate and the resultant elevated levels of angiotensin I and II cause hypertension; secondarily, the elevated renin levels cause outpouring of aldosterone, which leads to excessive sodium retention with resultant fluid retention, which augments the hypertension and potassium wasting. The elevated renin levels differentiate hyperreninism from hyperaldosteronism. Hyperreninism can be caused by renal ischemia due to aortic or renal arterial stenosis, or can be primary due to a neoplastic process. Both of these conditions ordinarily result in unilateral elevation of renal-vein renin levels, but renal arterial angiography would differentiate the two.

All of the previous cases of primary hyperreninism have been treated with unilateral nephrectomy with good results, but the anesthetic management has not been widely reported.

Several anesthetic agents have been reported to elevate renin levels, but in all cases the elevations could be attributed to the concomitant hypotension. When the same agents were used and renal perfusion was held constant, the same anesthetic concentrations produced no increase in plasma renin.[6–11] Accordingly, the choice of agent should be based on the several other factors pertinent to the case.

It would be expected that manipulation of the affected kidney would cause outpouring of renin, resulting in intraoperative hypertension. Epidural anesthesia could be utilized to lower this blood pressure, as in management of pheochromocytoma,[12] but its use would prevent fine control of perfusion pressure levels. The secondary increase in angiotensin II resulting from elevated plasma renin will stimulate the release of epinephrine and norepinephrine from the adrenal medulla; hence, the use of fluothane, with its potential for sensitizing the myocardium to these agents and potentiating ventricular irritability, might produce deleterious arrhythmias intraoperatively.

There are several studies reporting the increased cardiac arrhythmic threshold when enflurane anesthesia is used in the presence of catecholamines.[13,14] Johnstone and Eger have reported that the threshold for epinephrine-induced arrhythmias with enflurane is one-third that with fluothane.‡ Zarbalian, Naraghi and Adriani have used enflurane with epinephrine in more than 800 cases without the appearance of arrhythmia.§

In the present case, an agent was needed to control the acute onset of hypertension anticipated during manipulation of the neoplasm. There are several agents that would have been satisfactory, but nitroprusside was chosen because its rapid onset and short duration of action would allow more sensitive control, and its direct mode of action would not interfere with the later use of other vasoactive substances. Enflurane was selected as the primary anesthetic.

The ease of management of intraoperative hypertension and the benign operative and postoperative course certainly make this regimen worthy of further study for use in patients who have operable primary hyperreninism.

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