CASE REPORT

Adrenalectomy for Cushing's Syndrome—Paroxysmal Tachycardia and a Unique Tumor

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Harrison *et al.*[1] have noted that there are rare exceptions to the usual finding of normal catecholamine metabolism in Cushing's syndrome. These authors concluded that the significance of several unusual adrenal tumors cannot be determined at the present time. Recently, an additional case in which Cushing's syndrome was associated with paroxysmal tachycardia during adrenalectomy has been observed, with increased urinary catecholamine levels discovered retrospectively, and with an apparently unique mixed adrenal cortical adenoma–pheochromocytoma.[2] The anesthetic course of this patient will be presented and analyzed here.

CASE REPORT

A 39-year-old woman weighing 65 kg was admitted with a diagnosis of Cushing's syndrome. The patient had been in good health until her final pregnancy seven years prior to admission, during which numerous violet striae had appeared over the abdomen and upper thighs, and following which hirsutism and low back pain had developed. These symptoms gradually progressed to include facial roundness and puffiness, fragility of the skin of the legs, intermittent ankle edema, and amenorrhea. On physical examination arterial pressure was 135/90 mm Hg; pulse rate 80 beats/min. The face was round and ruddy with fine hair growth and hyperemic thin skin. The patient was slightly obese, with a protuberant abdomen covered with numerous bluish-violet striae, a slight dorsal hump, and 2+ pitting pretibial edema. Baseline urinary 17-hydroxycorticosteroid level was 14.8 mg/24 hours; after dexamethasone (8 mg/24 hours for two days) it was 13.7 mg/24 hours. The plasma cortisol level was 23.4 μg/100 ml. A diagnosis of Cushing's syndrome probably due to an adrenal cortical adenoma was made.

On readmission five weeks later, the patient's arterial pressure was 150/90 mm Hg; pulse rate 88 beats/min, with rare premature contractions; hematocrit 46 per cent; the electrocardiograph revealed normal sinus rhythm with rare premature ventricular contractions, a Q wave in leads III and A.V.F., and S-T depression in leads II, A.V.F. and V4 through V6. Preoperative preparation consisted of cortisone acetate (100 mg) intramuscularly, every 12 hours for two days, and pentobarbital sodium (125 mg) and atropine sulfate (0.4 mg) intramuscularly, one hour prior to surgery on the eighth hospital day. An intravenous infusion of 1,000 ml of 5 per cent dextrose in water, containing hydrocortisone sodium succinate, 100 mg, was started, an electrocardioscope attached, and anesthesia induced at 8:05 AM with thiopental sodium, 250 mg intravenously, followed by cyclopropane, 1,000 ml/min, and oxygen, 1,000 ml/min. Succinylcholine chloride, 80 mg, was given intravenously at 8:10 AM and the trachea was intubated. Anesthesia was maintained with cyclopropane using a closed carbon dioxide absorption circle system, and controlled ventilation (Air-Shields Ventimeter).

(Laparotomy was started at 8:25 AM.) At 8:40 AM arterial pressure, pulse rate and ECG were stable. During palpation of a left adrenal tumor at 8:45 AM the pulse became impalpable and arterial pressure unobtainable. The ECG revealed rapid paroxysmal tachycardia. Abdominal exploration and cyclopropane were discontinued, and the patient was hyperventilated with oxygen by hand. At 8:50 AM the pulse was palpable at a rate of 120 beats/min, and the arterial pressure was obtained at 250/170 mm Hg. The paroxysmal tachycardia gradually slowed and evolved into a sinus tachycardia, at a rate of 120 beats/min, over a period of approximately ten minutes. Anesthesia was re-established with diethyl ether, using a closed carbon dioxide absorption circle system and controlled ventilation, and abdominal exploration continued. At 9:00 AM the arterial pressure was 160/100 mm Hg; pulse rate 120 beats/min. At 9:07 AM phentolamine methanesulfonate (Regitine®, 0.5 mg) was given intravenously because of the appearance of scattered extrasystoles. There was a transient fall in the arterial pressure to 90/70 mm Hg, but no alteration in the frequency of the extrasystoles. When the left adrenal gland was removed at 9:25 AM the arterial pressure fell from 155/110 to 60/? mm Hg; pulse rate from 120

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to 80 beats/min. Mephentermine (Wyamine, 10 mg), given intravenously at 9:30 AM, raised systolic arterial pressure to 110 mm Hg. During the remaining 95 minutes of surgery the arterial pressure varied between 120/95 and 90/60 mm Hg; pulse rate between 85 and 100 beats/min. The postoperative course was entirely uneventful and the patient was discharged from the hospital on the tenth postoperative day, on cortisone acetate, 37.5 mg daily.

Review of the history prior to surgery revealed no evidence to suggest catecholamine excess; however, two frozen aliquots of urine obtained preoperatively were available. Elevated individual catecholamine levels were found in both, but a normal total level was present in a sample obtained five weeks postoperatively (table 1). Eleven months postoperatively the patient had none of the features of Cushing's syndrome, was taking cortisone acetate, 25 mg, and fluorocortisone acetate, 0.1 mg, daily, and had only mild musculoskeletal symptoms.

Macroscopically, the left adrenal gland weighed 22 g and contained a large tumor (4 × 3 × 3 cm). On cross section the tumor was mottled golden-yellow–brown with paler grey–yellow central areas. It appeared well encapsulated by a thin golden-yellow capsule, and was semisoft. A few small fragments of compressed but otherwise normal-appearing adrenal tissue were seen on its external surface.

Microscopically,* the tumor contained both cortical-type and medullary-type cells, apparently mixed. The cortical-type cells had either pale vacuolated or eosinophilic granular cytoplasm, and had round, regular, and rather small nuclei. Some contained fat. The medullary-type cells tended to have basophilic cytoplasm and nuclei which were more varied in appearance. Sections from portions of the tumor fixed in potassium dichromate solution demonstrated chromaffinity of both medullary-type cells and some cortical-type cells.

Discussion

In 1952 Papper and Cahill [3] noted that there had been too little experience in the administration of anesthesia for adrenalectomy for Cushing's syndrome validly to recommend the use of specific anesthetic agents and techniques. These authors found nitrous oxide and diethyl ether to be a satisfactory combination. Subsequent reports have favored: the above [4]; cyclopropane [4]; nitrous oxide, meperidine, thiopental, and a muscle relaxant [5]; diethyl ether and *d*-tubocurarine [6]; spinal anesthesia.[7] In 1958 Bellville *et al.*[8] found no significant difference between the severity of anesthetic complications following palliative adrenalectomy in patients who had received diethyl ether and those who had received cyclopropane.

Table 1. Urinary Catecholamine Levels

	Epinephrine (μg/24 hours)	Norepinephrine (μg/24 hours)	Total Catecholamines (μg/24 hours)
Preoperative	99	181	—
Preoperative	145	170	—
Postoperative	—	—	34

However, Papper and Cahill [3] noted that cyclopropane was an unwise choice of agent for pheochromocytoma because of the production of serious ventricular arrhythmias in the presence of epinephrine. In 1953, Riddell *et al.*[9] reported four patients who died of unsuspected pheochromocytomas during gynecological procedures. Three of these patients were receiving cyclopropane. These authors noted that, while the operative mortality for the removal of pheochromocytoma had fallen, that for the undiagnosed pheochromocytoma had remained constant, and they pointed out that the danger in the use of cyclopropane in the presence of a pheochromocytoma is fatal ventricular arrhythmia.

There is little reason to doubt that the paroxysmal tachycardia exhibited by the patient described here was due to release of catecholamines from the unsuspected mixed adrenal cortical adenoma–pheochromocytoma, in the presence of moderately deep cyclopropane anesthesia. It is unfortunate that a permanent record of the tachycardia, which was thought to be ventricular in origin, could not be obtained before it was corrected, as ventricular tachycardia is difficult to differentiate from supraventricular tachycardia with aberrant conduction.[10–12] Favoring ventricular tachycardia in this patient are the presence of premature ventricular contractions on the preoperative electrocardiograph [10–12] and the classic concept that catecholamines,in the presence of cyclopropane, tend to cause ventricular arrhythmias.[13, 14] Clinically, under these circumstances, however, any tachycardia of this type must be considered to be ventricular in origin, and treated as such, because of the danger of

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ventricular fibrillation. Fortunately, in this patient the condition was quickly and spontaneously followed by effective cardiac output and marked arterial hypertension. A somewhat similar picture of a cardiac arrest in which marked hypertension followed resuscitation during surgical manipulation of a known pheochromocytoma has been described by Priestley *et al.*[15]

Although arterial blood analysis was not performed in the case presented, data obtained from other patients under similar conditions[16] indicate that the arterial carbon dioxide tension was probably below 40 mm Hg, somewhat less than the mean threshold value for ventricular arrhythmias, 72 mm Hg, noted by Lurie *et al.*[13] in patients with an average arterial cyclopropane concentration of 18 mg/100 ml, although the threshold value in individual patients ranged from 44 to 107 mm Hg. Diethyl ether was chosen as an alternative anesthetic agent because it has been shown to have a beneficial effect on cyclopropane epinephrine arrhythmias[17] and is accepted as not having a "sensitizing" effect on the heart.[18]

The incidence of these unusual adrenal tumors must be extremely low; nevertheless, they obviously constitute a significant hazard, as they amount to unsuspected pheochromocytomas, and in this regard Mathison *et al.*[2] have stressed the need for careful assessment of both adrenal cortical and medullary function in patients with clinical evidence of a disturbance in either. The possible presence of these tumors, however rare, should be considered when the choice of an anesthetic agent for adrenalectomy for Cushing's syndrome is made, particularly if adrenal medullary activity has not been evaluated. Suitable monitoring during anesthesia, and awareness on the part of the anesthetist, remain additional significant safeguards.

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