PRIMARY HYPERALDOSTERONISM: ANESTHETIC EXPERIENCE WITH TWO CASES

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The realization of the importance of the adrenal glands began when Addison, in 1849 (1), described the syndrome which now bears his name. This description prompted the laboratory experiments of Brown-Séquard in 1856 (2) which demonstrated that the adrenals are necessary for life. Around the turn of the century the medullary hormone was discovered and attention diverted from the cortex. Indeed, it was not until about 1920 that it was generally recognized that the cortex rather than the medulla was the vital element. Eventually serious work was begun on the role of the cortex. This proved very difficult because although the adrenal glands produce large quantities of hormone they store very little; hence the glands themselves are a relatively poor source. An intensive effort was then made to synthesize the steroids. As it turned out, the 11-desoxycorticosterone (DOCA) was the easiest to synthesize and its synthesis was accomplished in 1937 (3). It was found to have a considerable influence on electrolyte metabolism, but had almost no effect on carbohydrate metabolism, inflammatory reactions, etc. Also, when DOCA was isolated from adrenal extracts in 1938 it was found in such minute quantities that it was thought to be not a "normal" cortical hormone (4).

Later the more difficult cortisone and hydrocortisone were synthesized and found to be effective in meeting the demands of acute stress. They had little effect on electrolyte composition, however.

It was observed that when all the known steroids were crystallized from adrenal cortical extract, an amorphous fraction remained which had more effect on sodium retention than any known steroid. This principle was isolated by Simpson *et al.* (5) and was determined to be an aldosterone which they named electrocortin. It is roughly thirty times more potent on sodium retention and five times more potent on potassium excretion than DOCA.

At the same time Luetscher and his associates (6) were working on a sodium retaining factor isolated from urine of nephrotics which later turned out to be identical with the electrocortin of Simpson *et al.* (7). This compound is now called aldosterone. In solution the major portion exists as the hemiacetal.

Subsequently it has been shown that the secretion of aldosterone is associated with changes in hydration and electrolyte composition, so

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that it serves as a homeostatic mechanism. Aldosterone secretion is but little affected by ACTH. Hypophysectomy does not abolish the ability of the adrenals to increase aldosterone secretion in response to sodium deprivation (8).

In 1955 Conn (9) presented a new syndrome, primary hyperaldosteronism, which in its pure form is simply overproduction of aldosterone by the adrenals or by an adrenal adenoma, resulting in periodic muscular weakness, intermittent tetany and paresthesias, polydipsia, polyuria, and hypertension. The laboratory shows normal to high serum sodium, very low serum potassium, high sweat and salivary potassium, low sweat and salivary sodium. The mechanism of the hypertension has not been elucidated.

Case Reports

Case 1.—The patient was a 44 year old white female who was 64 inches tall and weighed 166 pounds. She had had hypertension for ten to twelve years, but had shown no symptoms except for a tendency to gain weight excessively during her pregnancies—as much as 100 pounds. In July 1957, she had been hospitalized elsewhere for evaluation of her hypertension, which had become symptomatic. At that time, persistent hypokaliemia and a thyroid nodule were discovered. The nodule was removed in August.

The patient was hospitalized again in September, 1957 for evaluation of hypertension. Her blood pressure was 210–230/115–140; an electrocardiogram showed low or inverted T waves; examination of her urine revealed high potassium loss despite low serum levels and the assays for aldosterone showed excessive production. On the basis of these findings the diagnosis of hyperaldosteronism was made.

A diagnosis of adrenal adenoma was proposed and the patient was prepared for surgery with high potassium, low sodium intake. Electrocardiograms and electrolyte patterns were normal prior to surgery. Premedication consisted of cortisone acetate 100 mg. given intramuscularly the evening before and again the morning of surgery (the cortisone to be gradually withdrawn postoperatively), promethazine 50 mg. given intramuscularly three hours before and meperidine 75 mg. and scopolamine 0.4 mg. given intramuscularly one hour before operation.

The patient, however, was apprehensive on arrival in the operating room. Anesthesia was induced with thiopental 400 mg.; 60 mg. succinylcholine and 2 cc. cocaine spray in a concentration of 10.0 per cent were administered; and the trachea was intubated. Respiration was controlled and the anesthesia was maintained with nitrous oxide-oxygen 4:2 supplemented by intermittent doses of meperidine (100 mg. total). Relaxation was obtained with *d*-tubocurarine chloride (33 mg. total). Total anesthetic time was 2 hours, 15 minutes. Her anesthesia remained light during the procedure and she awoke promptly at the end of the procedure. A small adenoma was found and removed from the left adrenal gland.

The most interesting variable to observe was her blood pressure. On arrival in the operating room her blood pressure was 190/100. Following induction it dropped to 140/90 and then gradually returned to its initial value in about an hour, where it stayed for the remainder of the procedure. During the first two

hours following operation, the blood pressure gradually fell to 130/90 and remained there for about 20 hours. The patient was alert and in no distress. There were no signs of hemorrhage. Thereafter the blood pressure became quite labile, swinging from 120/80 to 190/110. After about one week of fluctuations her pressure became stable at 136/90. She was discharged on the 14th postoperative day. At that time her blood pressure and electrolyte pattern were normal and she was eating a regular diet.

Case 2.—The patient was a 34 year old white female who was 69 inches tall and weighed 149 pounds. She had had hypertension for six years, and had been treated with reserpine and ganglionic agents without much effect. She led an active life, but felt that she had to force herself. On admission she had a blood pressure of 230–190/140–120, a negative phentolamine (Regitine) test, abnormal T waves in the electrocardiogram, low serum potassium, low sweat sodium and high sweat potassium, and high urinary potassium loss. Both 17 keto steroids and 17 hydroxy corticoids were slightly above normal values, and the aldosterone assay was high. By means of diet and SC 5233 (a synthetic aldosterone antagonist) her electrolytes and electrocardiogram were brought to normal prior to surgery.

For premedication she was given cortisone acetate 100 mg. four hours prior to surgery (the cortisone being gradually withdrawn during the next two days), seconal 100 mg. two hours prior, meperidine 100 mg. and scopolamine 0.4 mg. one hour prior to surgery. The patient was alert on arrival in the operating room. Her blood pressue was 190/100. Anesthesia was induced with thiopental 325 mg. and her trachea was intubated with the aid of 60 mg. succinylcholine. Then nitrous oxide-oxygen 4:2 was administered, supplemented with 50 mg. of meperidine and respiration was controlled throughout the operation. None the less, when the skin incision was made her blood pressure rose to 240/120. At this time an Arfonad drip (1 mg./cc.) was begun and her pressure was lowered to 160/110. Relaxation was obtained with *d*-tubocurarine chloride 38 mg. (total for operation). During the exploration of the left adrenal gland, which contained the adenoma, her pressure rose sharply. The Arfonad drip was increased to about 200 drops per minute and meperidine 40 mg. was given. Even so, her pressure rose to 270/150 within three to four minutes, pulse rate reaching 150 at that time. The tumor was quickly removed and the manipulation stopped. The pressure then dropped rapidly to 130/80, the pulse dropping more slowly; the Arfonad drip was discontinued. The right adrenal was explored and found to be normal. This exploration caused a brief rise of pressure to 180/100, but this returned rapidly to 130/80.

It was noted at the time of the right adrenal exploration that the patient's anesthesia was very light. In the following 30 minutes, 120 mg. of meperidine and 50 mg. of thiopental were given and the nitrous oxide increased to 6:2, but her anesthesia became progressively lighter and she would respond to simple commands, i.e., open eyes, nod yes or no in response to questions. As instructed, the patient remained quiet during the closure, despite fair muscle power (tested by hand squeeze on command). Her respirations were controlled until the last skin suture was placed, then she was instructed to breathe spontaneously. At that time her trachea was extubated and she was alert enough to ask about the operation. She denied pain, but remarked on a heavy buzzing in her head. There was no memory of the operation. In fact, it was more than an hour

before her memory span was greater than a few minutes. In the recovery room and for the next two days her pressure was labile, but usually high (180/110). However, in the succeeding days it dropped and stabilized around 130/80.

The patient had a satisfactory postoperative course, and her electrolyte pattern was normal when she was discharged from the hospital.

Discussion

The two aspects that were of greatest interest were the behavior of the blood pressure and the tendency to remain conscious. The nature of the hypertension associated with primary hyperaldosteronism has not been elucidated. The hypertension does not respond to Regitine tests and it tends to disappear when the tumor is removed. In case 2 a large dose of Arfonad did not prevent a marked hypertensive episode on manipulation of the gland containing the tumor.

During both operations, anesthesia remained light despite adequate to large doses of anesthetic agents. In Case 2 this effect progressed to the point where verbal communication was possible. Something was exerting a strong analeptic effect at a time when her pressure was 100 mm. below her usual pressure.

Summary

Adrenal adenomas were removed from two patients with hyperaldosteronism. Anesthetic management was complicated by unusual fluctuations of blood pressure and resistance to depressing drugs.

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