Primary Aldosteronism and Its Relationship to Diabetes Mellitus

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Primary aldosteronism now is a recognized entity, and aldosterone-producing tumors can be clinically diagnosed. Aldosterone is 20 to 30 times as effective as desoxycorticosterone in maintaining electrolyte balance and well-being in patients with Addison's disease, and approximately one-third as effective as cortisone in causing deposition of hepatic glycogen in adrenalectomized animals.

Twelve cases of primary aldosteronism have been reported in the literature,[1-5] excluding the three cases summarized here. Of the total of 15 patients, 11 have been cured — 10 by removal of adrenocortical adenoma and one by bilateral adrenalectomy. Three of the remaining four cases were diagnosed only at autopsy when adrenal adenoma was found.[3] Finally, one patient had adrenocortical carcinoma that produced solely mineralocorticoid effects, presumably due to excessive aldosterone secretion.[6] A diagnosis of primary aldosteronism has been proved by demonstration of a tumor in some cases previously diagnosed as "potassium-losing nephritis."[1, 5]

Since aldosterone has a cortisone-like effect, it is probable that some patients having severe or long-standing aldosteronism will have diabetes. Diabetes has not been a prominent feature among the few known cases; however, our own limited experience with three cases suggests that diabetic tendency in aldosteronism may be shown only by a glucose tolerance test. In the cases reported heretofore, the absence of diabetes has been definitely established by a normal glucose tolerance test in only one case, that reported by Conn.[1] In the case reported by Mader and Iseri[2] the fasting blood sugar level was 76 mg. per 100 ml.

We have observed three patients having primary aldosteronism; full reports of these cases will be published soon.[7] All three patients had proved adrenocortical tumors associated with an excess of aldosterone in the urine which was identified as the diacetate by fractionation of chloroform extracts of urine, using chromatography and ultraviolet spectrometric analysis. One of four fractions showed a sodium-retaining power eleven times that of desoxycorticosterone, and a homogeneous material prepared from this fraction had an absorption spectrum and a bioassay identical to those of aldosterone. Details of this fractionation method are to be published elsewhere. Each of the three patients had some evidence of abnormal carbohydrate metabolism.

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SUMMARIES OF CASES

The first patient, a 44-year-old man, for several years had had attacks of generalized weakness lasting one to two days. He had had arterial hypertension since the age of nineteen years. The blood pressure was 200/128 mm. Hg. There was questionable early papilledema, but there was no peripheral edema.

Outstanding laboratory features were high serum sodium levels of 140 to 148 mEq., depressed serum potassium levels of 2.6 to 3.0 mEq., alkalosis with CO_2-combining powers of 32 to 36 mEq. per liter, and normal levels of serum chloride. An oral glucose tolerance test yielded the following results: fasting, 107 mg.; one-half hour, 145 mg.; one hour, 261 mg.; two hours, 222 mg.; three hours, 171 mg.; and four hours, 80 mg. per 100 ml. There was no glycosuria. Repeated urinalyses never showed an acid urine. An Addis test showed that there was inability to concentrate urine and there was some excess of cells. Urinary 11-oxysteroid and 17-ketosteroid titers were normal. The electrocardiogram was compatible with hypokalemia. Retroperitoneal oxygen insufflation demonstrated an adrenal tumor; on removal, it weighed 25 gm.

On the fourteenth postoperative day the serum sodium level was 133 mEq., CO_2-combining power 26 mEq., serum chloride level 96 mEq. per liter; and the serum potassium level was abnormally high, 5.5 mEq. per liter, and remained so for some months. The blood pressure was 140/84 mm. Hg. The glucose tolerance test after three days of a high-carbohydrate diet yielded the following results: fasting, 81 mg.; one-half hour, 111 mg.; one hour, 104 mg.; two hours, 148 mg.; three hours, 119 mg.; four hours, 78 mg. per 100 ml.

Six and one-half months after surgery the glucose tolerance was as follows: fasting, 86 mg.; one hour,

152 mg.; four hours, 45 mg. per 100 ml. The serum potassium level was 5.3 mEq. and the CO_2-combining power was 22.3 mEq. per liter.

The second patient, a 63-year-old woman, was admitted to the hospital with generalized paresis. During the preceding year she had lost 25 lb., and now weighed 97 lb. The blood pressure was 170/100 mm. Hg.

Outstanding laboratory findings included: serum sodium level, 139 mEq.; serum potassium level, 1.7 mEq.; CO_2-combining power, 31.2 mEq.; serum chloride level, 90.3 mEq. per liter; fasting blood sugar values, 309 and 406 mg. per 100 ml.; and urinary corticoid and 17-ketosteroid titers, normal. There was inability to concentrate urine and the patient had polyuria. The urine never was found to be acid. An Addis test showed a specific gravity of 1.010 and a urinary volume of 1,100 ml.

The diabetes was controlled with a 1,638-calorie diet containing 177 gm. carbohydrate, 74 gm. protein, and 20 units of NPH insulin per day. The insulin requirement gradually decreased to 7 units per day.

An encapsulated adrenocortical adenoma, 1 cm. in diameter, was removed. Immediately preoperatively on a carbohydrate intake of 213 gm. and without insulin, blood sugar levels before each of three meals had been 132 mg., 182 mg., and 285 mg. per 100 ml. Thirteen days postoperatively on a carbohydrate intake of 210 gm., blood sugar levels were 103 mg. fasting and 106 mg. per 100 ml. one and one-half hours after the noon meal. Glycosuria was noted only on the first day of her admission and after intravenous administration of glucose.

Three months after operation she had gained sixteen pounds and had no further weakness; the blood pressure was 150/100 mm. Hg, and the electrolyte pattern was normal. After an unrestricted diet for three months, blood sugar levels were 158 mg. per 100 ml. three hours after eating and 132 mg. per 100 ml. four hours after eating. Oral glucose tolerance remained abnormal: fasting, 112 mg.; one-half hour, 207 mg.; one hour, 275 mg.; two hours, 428 mg.; three hours, 437 mg.; and four hours, 300 mg. per 100 ml.

The third patient, a 42-year-old woman, had had increasing spells of weakness, sometimes with unconsciousness, for two years. Blood pressure was 220/120 mm. Hg and there was no peripheral edema. The electrolyte pattern was similar to that found in the other two patients; and, as in the other patients, there were inability to concentrate urine and a tendency toward alkaline urine.

In December 1952, the oral glucose tolerance was as follows: fasting, 70 mg.; one-half hour, 127 mg.; one hour, 173 mg.; two hours, 163 mg.; three hours, 135 mg.; and four hours, 62 mg. per 100 ml. In May 1955, before the adrenal adenoma was removed, the glucose tolerance was as follows: fasting, 100 mg.; one-half hour, 160 mg.; one hour, 153 mg.; two hours, 133 mg.; three hours, 86 mg.; and four hours, 66 mg. per 100 ml.

Four and one-half months postoperatively the patient was asymptomatic, but still had some arterial hypertension.

CONCLUSIONS

On the basis of the limited experience to date, the incidence of diabetes in primary aldosteronism cannot be determined. It appears that the diabetes that does arise as a result of excess of aldosterone is of a very mild variety. In one of our three patients having primary aldosteronism, the diabetes has not disappeared completely following the removal of the tumor, yet there appears to be no family history of diabetes.

SUMMARIO IN INTERLINGUA

Aldosteronismo Primari e Su Relation a Diabete Mellite

Super le base del limitate experientias nunc disponibile, le incidentia de diabete in aldosteronismo primari non pote esser determinate. Il pare que le diabete que occurre como effecto de un excesso de aldosterona representa un levissime varietate. In un de nostre tres patientes con aldosteronismo primari, le diabete non ha disparite completemente post ablation del tumor, sed apparentemente le caso es sin historia familial de diabete.

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