Diabetic Coma and Pituitary Necrosis in an Acromegalic Patient

A Case Report

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Pituitary destruction or hypofunction occurring in the course of diabetes mellitus is usually followed by insulin sensitivity, hypoglycemia, and amelioration of the diabetes. The patient whose case is recorded herein suffered from acromegaly, presented with diabetic coma, and died in pituitary apoplexy following necrosis of an eosinophilic tumor without apparent reduction in severity of the diabetic state.

CASE HISTORY

A forty-nine-year-old man was admitted in diabetic coma, glycosuria having been discovered first a few hours previously. He had suffered from thirst, polyuria, loss of weight, and cramps in the legs for nearly two months but had been able to work and had not sought medical advice. These symptoms establish an antecedent diabetes beyond reasonable doubt.

The year before, the patient's physician had diagnosed myxedema because of coarsening of the facial features, and he had taken 3 gr. of thyroid a day ever since. There was no known history of headaches, visual disturbances, or enlargement of the hands or feet. Thirty-six hours before admission the patient felt unwell, and after returning from work he became mentally confused. That night his breathing was noticed to be heavy, but next morning he felt better and ate breakfast. Later in the day he vomited, and after becoming drowsy and more irrational he passed into coma four hours before reaching the hospital.

PHYSICAL EXAMINATION

The patient was a heavily built man with a prominent lower jaw, heavy orbital ridges, and large hands characteristic of moderately advanced acromegaly. He was dehydrated, had air hunger and smelt of acetone, and resisted examination in spite of being comatose. His condition was not typical of diabetic coma, restlessness and episodes of violence suggesting a complicating cerebral factor. The pulse was 128 and the blood pressure 120/70. There were no signs of disease in the heart, lungs, or abdomen. Examination of the central nervous system was difficult and failed to reveal any localizing signs, yet the pupils were unequal in size and moderately dilated and failed to react to light. Signs of papilledema and retinopathy were absent.

LABORATORY DATA

At admission, the urine contained sugar graded four plus. The Rothera test was three plus, the ferric chloride one plus. The test for albumin was two plus and chlorides zero. The blood sugar was 740 mg. (Folin and Wu). After six hours of treatment the serum sodium was 320 mg. per 100 ml. (139 mEq.), the serum potassium 13.7 mg. per 100 ml. (3.5 mEq.), the plasma chlorides 369 mg. per 100 ml. (104 mEq.), the alkali reserve 34 vols. carbon dioxide, and the blood urea 56 mg. per 100 ml.

TREATMENT AND PROGRESS

In the first eight hours the patient was given 140 units of soluble insulin subcutaneously and a total of 4.5 liters of normal and later 0.18 per cent saline intravenously. There was definite clinical improvement by this time, and he would respond slowly to loud speech. The blood sugar had fallen to 280 mg. per 100 ml.

Four hours later in spite of a blood pressure of 140/90 and a blood sugar of 210 mg. he became more deeply comatose. He had pinpoint pupils, Cheyne-Stokes respiration, and equivocal extensor plantar reflexes. He was occasionally violent and had to be given paraldehyde intramuscularly and barbiturates parenterally. In case that acute liver failure should be an added cause of coma he was also given 20 gm. of glutamic acid intravenously and large doses of vitamin B complex; this treatment was without benefit.

Twenty hours after admission the temperature was 103.4° F. Aureomycin was given in addition to the usual prophylactic penicillin and streptomycin. The patient's diabetic condition gave rise to no anxiety, since the blood sugar averaged 230 mg. with 10 to 20 units of insulin every four hours, while an infusion of 4 per cent glucose

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in 0.18 per cent saline was continued; the serum potassium remained in the region of 14 mg. per 100 ml.

During the last twenty-four hours the patient remained deeply comatose and cyanosed, with shallow and irregular respiration. The temperature rose to 104.6° F. and he died suddenly without signs of peripheral circulatory failure.

POST-MORTEM EXAMINATION

Thirty-six hours after death the body was 188 cm. in height with definite signs of acromegaly. The heart weighed 375 gm. (normal 355 ± 40 gm.) and was normal save for a small auricular septal defect, with healthy coronary arteries. Examination of the skull and brain revealed no sign of subarachnoid or intracerebral hemorrhage, and the vessels were normal. The pituitary gland was almost entirely necrotic and consisted of brown semi-liquid material with a slight rim of glandular tissue. Slight enlargement of the sella turcica with bulging of the diaphragma sellae suggested a tumor, although the growth had not extended beyond the fossa.

The anterior pituitary tissue which remained was composed of eosinophilic tumor cells arising from an adenoma which had undergone widespread necrosis and liquefaction. There was no microscopic evidence of significant recent hemorrhage.

DISCUSSION

The importance of the anterior pituitary in carbohydrate metabolism has been shown by the work of Houssay[1] and Young,[2] and the association of acromegaly and diabetes is well recognized.

In reviewing 650 cases of acromegaly in which the results of urine analysis were available, Atkinson[3] found glycosuria in 32 per cent, and 18 patients were considered to have died in diabetic coma, mostly before insulin was available. Coggeshall and Root[4] also found glycosuria in 36 per cent of the 153 cases which they reviewed, but only 9 patients with acromegaly were seen in a series of 30,000 diabetics, indicating that this disease is an infrequent factor in the etiology of diabetes. On the other hand, hypopituitarism leads to spontaneous hypoglycemia, as emphasized by Sheehan and Summers,[5] and increased insulin sensitivity has been noted should this develop in diabetic patients (Lyall and Innes,[6] Kotte and Vonderahe,[7] Feldman and his associates,[8] Clark, Franklin and Sahs,[9] Williams,[10] Poulsen,[11] Root,[12] and Martin and Pond[13]).

Complete pituitary necrosis usually takes two or three days to develop, and there may be insufficient time for endocrine dysfunction to become apparent before death.

A characteristic clinical syndrome resulting from acute pituitary necrosis has been described by Brougham, Heusner and Adams[14] as pituitary apoplexy. They observed five patients in whom evidence of pituitary adenomas had been present for some years before sudden necrosis of the tumor led to pituitary apoplexy, which was fatal in all but one case. Common signs and symptoms included sudden headache, diplopia, amblyopia, drowsiness, confusion, and eventually coma. Fever, unequal or fixed contracted pupils, and neck rigidity were also encountered, and death usually occurred after a few days. One of their patients was a woman with diabetes who did not apparently show signs of hypoglycemia before death. Factors responsible for the necrosis included the tumors outgrowing its blood supply, compression of blood vessels by growth extending beyond the pituitary fossa, and primary thrombotic occlusion. Changes were seen in the cerebrospinal fluid such as the presence of red and white cells, xanthochromia, increase in protein, and elevation of the pressure.

The frequency of fever may be explained by irritation of the anterior hypothalamus due to pressure from the tumor or a bulging pituitary diaphragm, or because of a local meningitis. The differential diagnosis may be difficult. In my case, the typical diabetic history, followed by loss of consciousness, hyperglycemia, and ketosis, suggested diabetic coma as the prime cause, and the initial response to insulin and fluids given intravenously supported such a diagnosis. Later, the increasing depth of coma, restlessness, pinpoint pupils, irregularity of respiration, and pyrexia suggested either a cerebral cause such as a tumor, meningitis or subarachnoid hemorrhage, or acute liver failure. The paradox of pituitary destruction in the presence of severe diabetic ketosis was never considered, and the correct diagnosis was revealed only at autopsy.

The diagnosis of pituitary apoplexy should be considered in a comatose patient with a history of a pituitary tumor, even in the presence of severe diabetes. When destruction of the anterior pituitary is rapid and death takes place in a few days, no amelioration of the diabetes can be expected.

SUMMARY

A forty-nine-year-old man became comatose after a brief period of drowsiness and confusion and was found to have acromegaly and diabetic ketosis. In spite of a satisfactory initial response to insulin he died with signs of pituitary apoplexy. At autopsy a necrotic eosinophilic pituitary tumor was discovered.

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SUMMARIO IN INTERLINGUA

Coma Diabetic e Necrosis Pituitari in un Patiente Acromegalic. Reporto de un Caso

Es reportate le caso de un homine de 49 annos de etate qui deveniva comatose post un breve periodo de somnolentia e confusion e in qui esseva constatate acromegalia e ketosis diabetic. In despecto de un satisfacente responsa initial a insulina, ille moriva con signos de apoplexia pituitari. Al autopsia esseva discoperite un tumor pituitari eosinophilic necrotic.