Hypoglycaemia in Chronic Alcoholism

The following case is unusual and presented certain difficulties in diagnosis.

CASE REPORT

The patient, a man aged 54, was known to be a chronic alcoholic. The doctor was sent for one morning because of difficulty in rousing him. Initially it appeared that he had been mentally very confused; about an hour later he was found by his daughter to be completely unconscious. He had spent the previous day normally and retired to bed about 9.30 p.m., apparently sober. There was no admission of any immediate alcoholic excess.

When he was examined there was a strong smell of ketones in the small airless room. He was deeply comatose, lying flat on his back, with open eyes and giving an occasional twist of his head. The skin was distinctly moist, but unfortunately the significance of this was not realized until later. The pupils reacted to light; all tendon reflexes were present and equal; abdominal reflexes were present, and no plantar responses were obtained. A catheter specimen of urine showed Rothera's test quickly and strongly positive, and Gerhardt's and Benedict's tests negative. Other systems were all normal. By this time he had been in coma for about three hours.

Treatment was based on a provisional diagnosis of diabetic—that is, hyperglycaemic—coma without glycosuria. In view of some uncertainty, however, it was decided to administer dextrose intravenously before giving the insulin. At the conclusion of an injection of 25 ml. of 25% dextrose the patient at once regained immediate consciousness, in the dramatic manner associated only with recovery from hypoglycaemia.

The differential diagnoses considered at this stage were (1) ketosis and hypoglycaemia due to liver insufficiency, and possibly aggravated by inadequate food intake; (2) spontaneous hypoglycaemia; (3) diabetes mellitus.

He was admitted for investigation. One hour later his blood urea was 31 mg. per 100 ml., and blood sugar 253 mg. per 100 ml. (in view of recent glucose administration, this was not of much value). Twenty-four hours later his fasting blood sugar was 94 mg. per 100 ml. The latter was taken to exclude diabetes mellitus, of which there really was no positive evidence. The urine was tested on frequent occasions during the next few days, and no glycosuria was found. The ketosis resolved after about 36 hours without specific treatment, although he was encouraged to eat.

Liver-function tests at this stage showed: Serum alkaline phosphatase, 3 units; serum thymol turbidity, 4 units; icterus index, 3 units; serum proteins, 9.8 g.% (albumin 5.8 g., globulin 4 g.); A/G ratio, 1.45:1.

The glucose-tolerance test gave the following results:

		Urine Sugar	Urine Acetone
Fasting blood sugar	91 mg./100 ml.	—	—
½ hour after 50 g. glucose	101 "	—	—
1 " " " "	121 "	Ft. trace	—
1½ hours " " "	171 "	++	—
2 " " " "	100 "	+	—
2½ " " " "	88 "	—	—

The change in the serum proteins suggests some degree of liver damage. The delay in storage of glucose supports this. The glucose-tolerance test also suggests a lowered renal threshold.

Three days after admission he had a classical episode of delirium tremens, which was treated in the usual way, and from which he recovered quite normally.

Five months later a similar incident of hypoglycaemia occurred in which he became mentally confused and disorientated. He did not go into coma and the blood sugar was 62 mg. per 100 ml. Frank ketosis was again present. Treatment and subsequent progress were as recorded in the first instance.

DISCUSSION

The recognition of hypoglycaemia dates from 1849, when Claude Bernard found that the mobilization of liver glycogen was the source of blood sugar. Between this discovery and the isolation of insulin, which does not concern us here, attention was mainly directed to the liver. Hepatic poisons were used experimentally—for example, phosphorus (Frank and Isaac, 1911)—to induce the condition.

Le Count and Singer (1926) have pointed out that alcoholics with huge fatty livers may die suddenly and unexpectedly. The large globules of fat take up most of the room in the liver cell, leaving no space for glycogen. The probable cause of death is hypoglycaemia. In this patient a similar condition probably was present, although there was no clinical evidence of hepatic enlargement.

Failure of endogenous sugar may also occur from wasting muscles and failure to replenish the stores, as in starvation. There was no evidence of either of these conditions in this case.

Ketosis has been established as due to carbohydrate lack, but many conflicting views have been put forward regarding how exactly this is brought about. One of the most recent theories is that propounded by Macallum (1930) by which ketone bodies are regarded as normal products of metabolism having an energy value of which most tissues, except the liver, could make use. In 1926 Raper and Smith suggested that the factor responsible for mobilizing fat in excessive amounts was a reduction of the liver glycogen below a certain level. MacKay (1943) has summarized the position as follows. The body is supplied with two types of fuel: "slow fuel" which represents the fat used directly by the tissues without any liver intervention, and "quick fuel"—namely, glucose and ketone bodies. He suggested that the production of ketone bodies, in times of need, was a device to conserve glucose for the central nervous system, which is unable to metabolize them. Mirsky (1942) asked, If ketone bodies are normal oxidation products why does excess ever occur? He answered this by saying that there was a maximal rate at which muscles could use ketone bodies, just as there was a maximal rate at which they could use glucose.

It is therefore postulated that hypoglycaemia and ketosis could both be explained by diffuse hepatic lesions. What evidence is there for this in the present case? The patient is a known addict to an established hepatic poison. The liver-function tests and the glucose-tolerance test show changes consistent with this argument.

This hypothesis seems to account for most of the features. However, it does not explain why such an episode should suddenly occur in a long-standing condition which showed no other immediate change for the worse. Further, if the liver involvement was severe enough to produce this picture, it might reasonably be anticipated that the liver-function tests would be more upset; but these are well known to be not unduly reliable. Also, it might be thought that the combination of hypoglycaemia and ketosis would be more common in other more obviously gross diseases of the liver than it is.

It is concluded that this is a case of fatty change in the liver due to alcohol poisoning, producing the clinical picture of hypoglycaemia and ketosis—a series of events which may be summarized thus: "Alcoholic hepatitis"→Depletion of hepatic glycogen→hypoglycaemia→production of ketone bodies by the liver.

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