FUNCTIONAL REACTIVE HYPOGLYCAEMIA — A CASE REPORT

T. F. NGEOW

SYPNOSIS

A case of functional reactive hypoglycaemia is described. The diagnostic difficulty of this condition is discussed, with particular reference to the differential diagnosis of anxiety neurosis. The clinical features, pathophysiology and a possible relationship to diabetes mellitus are outlined.

INTRODUCTION

Hypoglycaemia is a clinical problem which can be most perplexing to diagnose but therapeutically very satisfying. It may be defined as a clinical state with blood sugar below 50 mg% usually with symptoms (Finestone & Wohl, 1970).

Functional reactive hypoglycaemia is not uncommon. However, in the great majority it is asymptomatic. A case is described here where the diagnosis was completely missed for three years because the attending doctors failed to recognise the characteristic symptoms and therefore to carry out the appropriate investigations.

CASE REPORT

A 40 year old Sikh court interpreter complained of feeling giddy in the morning for the last three years. His giddiness occured about 3 to 4 hours after his breakfast and was associated with cold sweat, general weakness, blurring of vision, tremor of hands and a marked sensation of hunger. These symptoms would disappear completely and almost immediately after food, but not on lying down. He never lost consciousness. There was no significant change in weight. He was disturbed by these symptoms not so much because of physical incapacity as embarrassment from having to rush out of the court for a quick cup of tea and snacks.

He had been seen at the outpatient department on many occasions for these complaints, and finally was admitted to Segamat Hospital in 1973 for investigation. A modified glucose-

District Hospital, Segamat, Johore, Malaysia.

T. F. Ngeow, MBBS (S'pore), M.Med. (Int. Med.), MRACP, MRCP (UK).
Physician

tolerance test (GTT) was done with these results: Fasting blood sugar 91 mg per cent. One hour after 50 G glucose: 182 mg per cent. Two hours after glucose: 91 mg per cent. Urine was free from glucose throughout.

Subsequently he was given chlordiazeposide 10 mg b.d. He continued to have these symptoms, however, and over the last two years, they became more frequent, occuring almost every morning, and sometimes in the evening when he missed his afternoon tea. As a result, he found it necessary to carry food for his car journeys for outstation cases.

He had operation for deviated nasal septum in 1968, and had been treated for epigastric pain with antacids off and on since 1971. There was no history of gastric surgery. In 1972 he had severe left sided throbbing headache of sudden onset, associated with numbness and paralysis of left upper limb which lasted half an hour followed by full recovery. He was diagnosed as migraine. Since then he had two more episodes of severe headache unaccompanied by other neurological manifestations.

He described himself as rigid and disciplined, and highly strung with fits of temper occasionally. He consumed small amount of alcohol occasionally for social purposes.

There was no family history of diabetes mellitus and none of the members of his family had ever experienced any of the symptoms described.

On examination, he was well built and of good nutrititional status. There was no abnormal finding in either the cardiovascular or neurological system. ECG was normal. An extended 6 hour GTT was done (Fig. 1). About 3 hours after the ingestion of glucose, the patient complained of feeling weak and cold sweat which disappeared after 20 minutes, and was followed by mild bitemporal headache.

The diagnosis of functional reactive hypoglycaemia was made. Patient was then advised to follow a low carbohydrate high protein diet, especially for his breakfast. In essence, he was asked to omit bread and chapati which he normally had for his breakfast, and to reduce his sugar and rice intake.

He became completely free of symptoms from the first day of withdrawal of carbohydrates from his diet, and had remained well on follow up six months later.

DISCUSSION

The clinical picture of hypoglycaemia may be one of two patterns. Symptoms related to overactive sympathoadrenal system are faintness, anxiety, hunger, nausea, headache and profuse sweating.

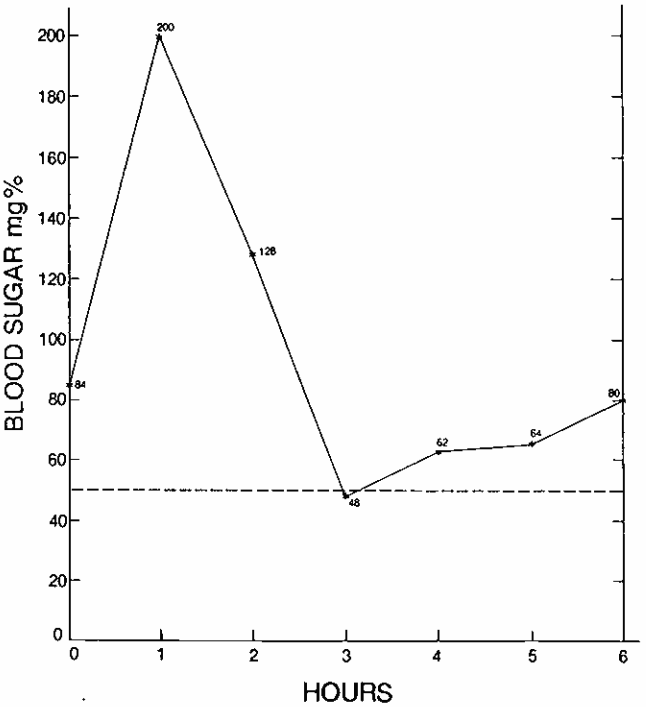

FIG. 1 6 Hour Glucose Tolerance Test.

Symptoms due to decreased brain oxygenation are stupor, loss of memory, change of behaviour, rest-

TABLE 1 CLASSIFICATION OF HYPOGLYCAEMIAS

FASTED HYPOGLYCAEMIA

UNDERPRODUCTION OF GLUCOSE
1. Heptatic disease
2. Adrenal or pituitary insufficiency
3. Alcohol induced hypoglycaemia

OVERUTILISATION OF GLUCOSE
1. Insulinoma
2. Extrapancreatic neoplasms
3. Exogenous insulin or oral hypoglycaemic drugs

FED HYPOGLYCAEMIA
1. Alimentary hypoglycaemia (Post gastrectomy)
2. Pre-diabetes
3. Functional reactive hypoglycaemia

lessness, speech disturbances, diplopia and convulsions. In any patient, the signs and symptoms of hypoglycaemia usually conform to a given pattern easily recognised and most commonly unique to him. The patient in this case exhibited hypoglycaemic symptoms of overactive sympathoadrenal pattern.

Once the patient's symptoms have been recognised to be due to hypoglycaemia, a specific cause must be determined. Table 1 lists the more common causes of hypoglycaemia in clinical practice from pathophysiological point of view.

The history of the patient clearly indicated hypoglycaemia occuring in the fed state. Since this patient was not known to have diabetes mellitus and gastric surgery, the most likely cause of hypoglycaemia would be functional. This was confirmed by a 6 hour GTT which showed a normal fasting blood sugar, an exaggerated rise at 1 hour, a sharp fall to 48 mg per cent at 3 hour, when the accompanying symptoms of hypoglycaemia experienced by the patient before were reproduced, and a slow climb back to normal blood sugar level at 6 hour.

The syndrome of functional reactive hypoglycaemia has been well established, particularly in the Unites States. However, some workers are sceptical of this condition. It is said that 23 per cent of the normal population during a GTT exhibit blood sugar levels below 50 mg per cent if sampling is done at hourly intervals between 2 and 5 hours, usually without symptoms (New Eng. J. of Med. 1974). Moreover, the symptoms of hypoglycaemia are also commonly found in anxiety neurosis. In the United States, a lot of neurotic patients are labelled as "hypoglycaemic" either by patients themselves or by their attending physicians, because the term appears to be more socially acceptable. The extent of misattribution is so great that Yager & Young (1974) called it an epidemic condition of Non-Hypoglycaemia.

To overcome this diagnostic confusion, a two step diagnostic procedure has been suggested (New Eng. J. of Med. 1974). Firstly, select patients who have transient postprandial symptoms falling into the constellation of hunger, emptiness, sweating, palpitation, piloerection, irritability and headache, and avoid those with chronic fatigue, anxiety, lethargy, mental dullness, loss of vitality. Secondly, assess blood glucose tolerance response to an oral GTT to see which are biochemically hypoglycaemic at the same time that they are clinically hypoglycaemic. When symptomatic evidence of chemical hypoglycaemia exists with clinically characterised synchronous symptoms and signs, diet changes, including low carbohydrate and high protein multiple meals may be tried.

The patient reported in this paper satisfied all these criteria for the diagnosis of functional reactive hypoglycaemia:

1. Characteristic post-prandial symptoms of hypoglycaemia as stated above.
2. Synchronous appearance of chemical hypoglycaemia and clinical hypoglycaemia during GTT.
3. Excellent response to dietary treatment.

Typically, functional reactive hypoglycaemia is commoner in women, the age of incidence being 30 — 50 years. Hypoglycaemic episodes may occur 2 to 5 hours after eating in patients with characteristic personality patterns. These patients are emotionally labile, with symptoms of weakness, faithness, nervousness, palpitation, anxiety, hunger, headache and vertigo. Loss of consciousness is rare. Symptoms are rather unusual in the evening after dinner, being more common in mid-morning or mid-afternoon.

In some patients with advanced cerebrovascular disease, functional reactive hypoglycaemia may be the trigger which initiates a cerebral ischaemic episode. Similarly, episodes of functional reactive hypoglycaemia may precipitate attacks of angina, acute pulmonary oedema and ectopic tachycardias of various types, in predisposed cardiac patients. For this small but important group of patients serious cerebral and cardiovascular complications may be minimised by recognising the possible role that functional reactive hypoglycaemia may play as an initiating factor (Harrison et al 1966).

The exact pathophysiological explanation for functional reactive hypoglycaemia is lacking, but is believed to be due to disturbance of the body's normal response to carbohydrate ingestion, which includes an elaboration of an as yet unidentified hormonal (gut) factor from the upper intestine. This factor sensitises the beta cells to release more insulin per unit increase in glucose concentration. This amplification mechanism may become abnormal in one of these situations: too rapid gastric emptying, too much gut factor per unit glucose mass released from the upper intestine or a too sensitive beta cell population. Any one of these factors may operate in patients with functional reactive hypoglycaemia.

The 6 hour GTT used in investigating patients with suspected reactive hypoglycaemia produces a wide range of patterns. Some show hyperglycaemia during the first 2 to 3 hours of the test and hypoglycaemia later. It has been claimed that when this initial hyperglycaemia is diagnostic of diabetes

mellitus, the patients go on to develop clinical diabetes mellitus, the patients go on to develop clinical diabetes mellitus, whereas when the initial phase is normal, diabetes does not ensure. This has since ben disproved; there is no clear distinction between the two types of response (Jarrett R.J. 1971). Nevertheless, it would be interesting to watch for diabetes developing in this patient.

ACKNOWLEDGEMENT

The author thanks the Director-General of Medical & Health Services, Malaysia, for permission to publish this case.

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