

Delayed Diagnosis in a case of insulinoma due to hypoglycaemia unawareness

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Introduction

- Insulinomas are most common form of Islet cell tumours(60%), 90% are benign. Common in females, measure less than 2cms in most patients. Make it difficult to localise them.
- Insulinoma are most common cause of hyperinsulinaemic hypoglycaemia in adults. Delayed diagnosis is quite common due to varied presentation, late and reluctance to seek medical help by patients or failure of practitioners to suspect hypoglycaemia.
- We would like to present this case of insulinoma which took nearly 30 months to diagnose and multiple visit by the patient to 4 different medical specialties
- Hypoglycaemic unawareness is serious complication of hyperinsulinaemic hypoglycaemia which makes it difficult to diagnose these cases

Case Summary

Mrs. X, 50 years initially presented with episodes of atypical "funny dos".

- First episode was in the gym. While she was exercising, she became wheezy. While trying to take salbutamol inhaler, she was found her eyes rolled up and she appeared dazed for about 20 minutes by bystander.
- Second episode a year later, which happened as an unwitnessed fall in her work place. She had multiple bruises on her head and body due to the fall and was incontinent of urine but no tongue bite.
- Third episode a year later. She felt like her legs were giving way and felt like jelly while she was walking. However she did not fall or loose consciousness.
- She had no other episodes of any sort which she could remember.
- She was seen in different clinics including neurology clinic, cardiology clinic and Falls clinic. Various investigations were performed in these clinics failed to identify cause for all the above symptoms which varied from episode to episode. Some of relevant investigations are mentioned below.
- She was seen in the falls clinic and had a tilt table test which was normal. Even her driving licence was returned at this stage.
- GP thought of referring her to endocrinology as one of blood glucose was low.
- She was investigated for possible hypoglycaemia causing these falls.
- Hence, she was given blood glucose meter. To our surprise she had very frequent hypos as seen below in patients own blood sugar diary.



- She was educated about hypoglycaemia and its treatment. She was advised against driving, sports, heights and swimming in particular.
- Hence mixed meal test was done which confirmed the diagnosis.

Investigations

Relevant tests	
Mixed meal test resulted in hypoglycaemia. Serum Insulin level along with C Peptide were measured	Glucose - 2.1, Insulin-63 pmol/L, C-peptide-17pmol/L (hyperinsulinaemic hypoglycaemia confirmed)
24 hour urine catecholamine	Normal
24 hour urine 5HIAA	Normal
Chromogranin A	1.6 nmol/L(0.0-6.0)
Synacthen test-	No adrenal insufficiency
Urine Sulphonylurea	Negative
Anti-insulin antibodies	negative
ECG, 24 hr tape ,Postural blood pressure, EEG, MRI head, tilt test	All these tests were normal

Fig 2. CT scan showed 13mm hyper vascular lesion in the pancreatic neck

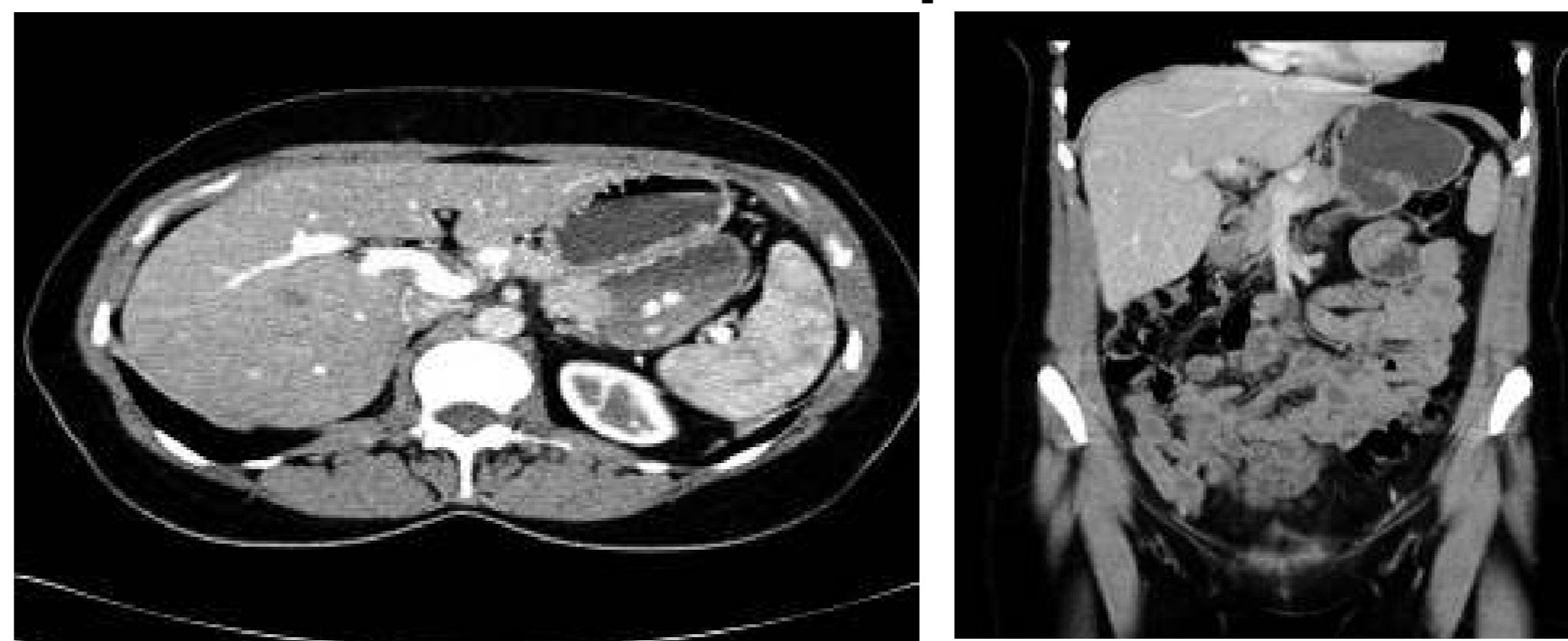
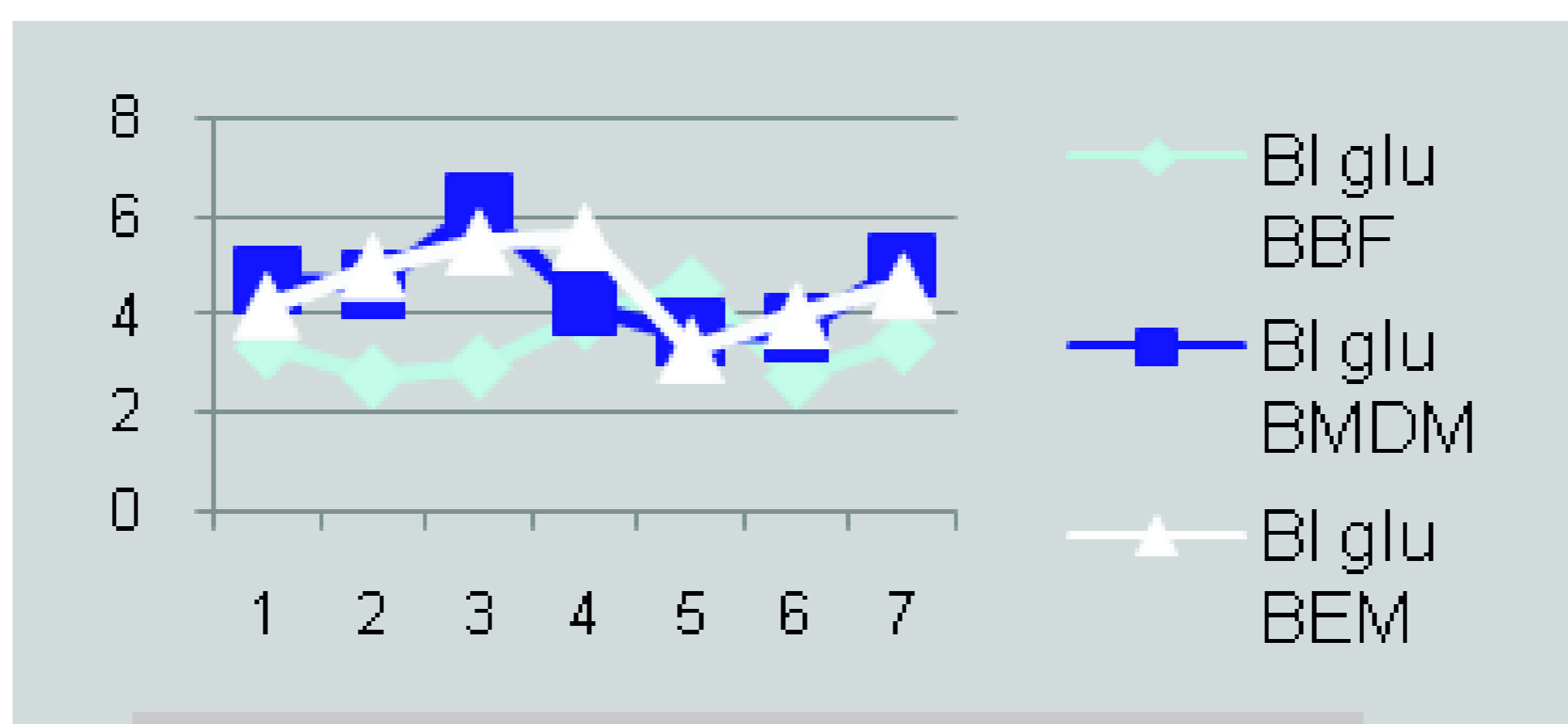


Fig 3. Blood glucose pattern before surgery



Treatment

- She was referred to upper GI MDT.
- Started on diazoxide, which she did not tolerate.
- Octreotide injections tried as next option which was maintained till surgery. This alleviated her symptoms.
- She had partial pancreatectomy and histology confirmed benign insulinoma.
- In this case, the main investigative tool was the blood glucose monitoring diary and confirmation by mixed meal test.

Fig 4. Blood glucose monitoring (after surgery)

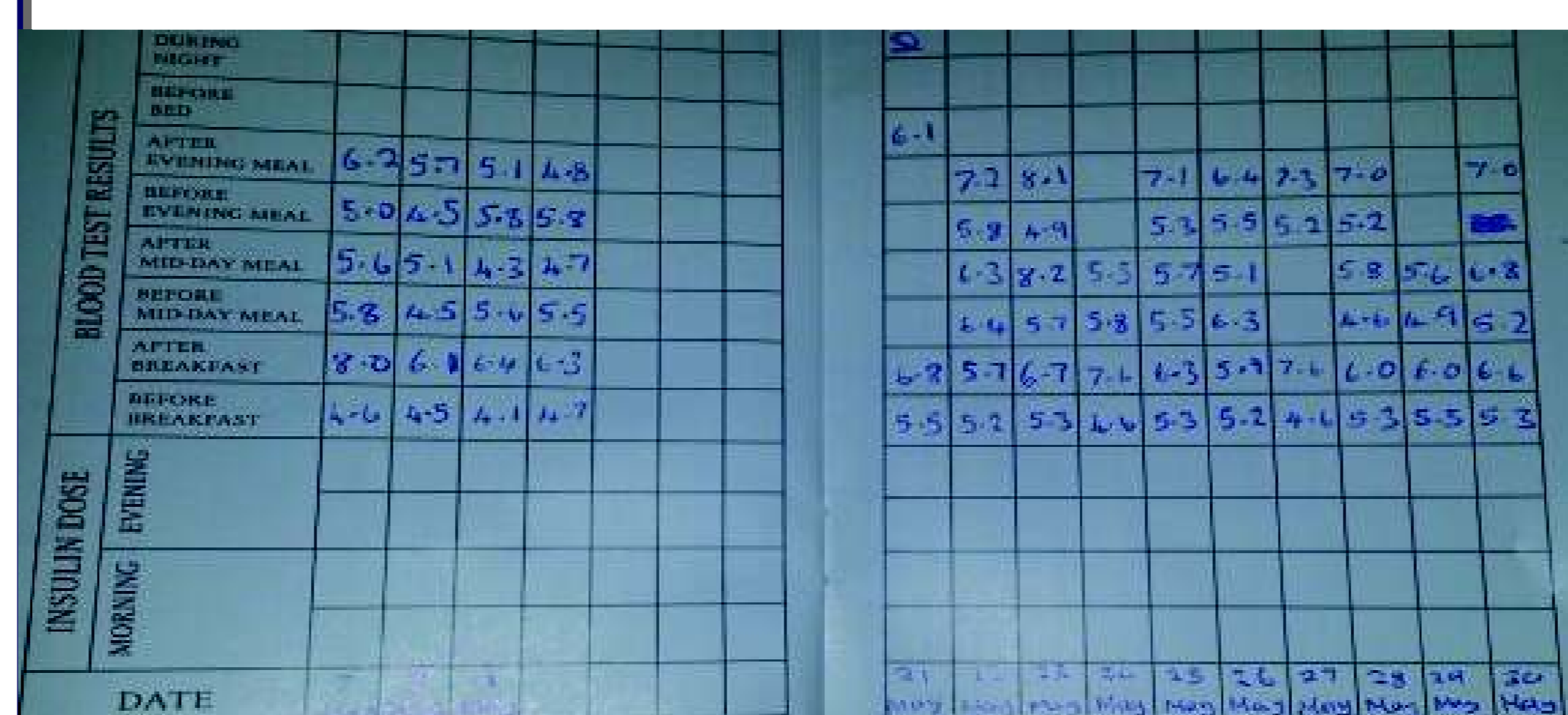
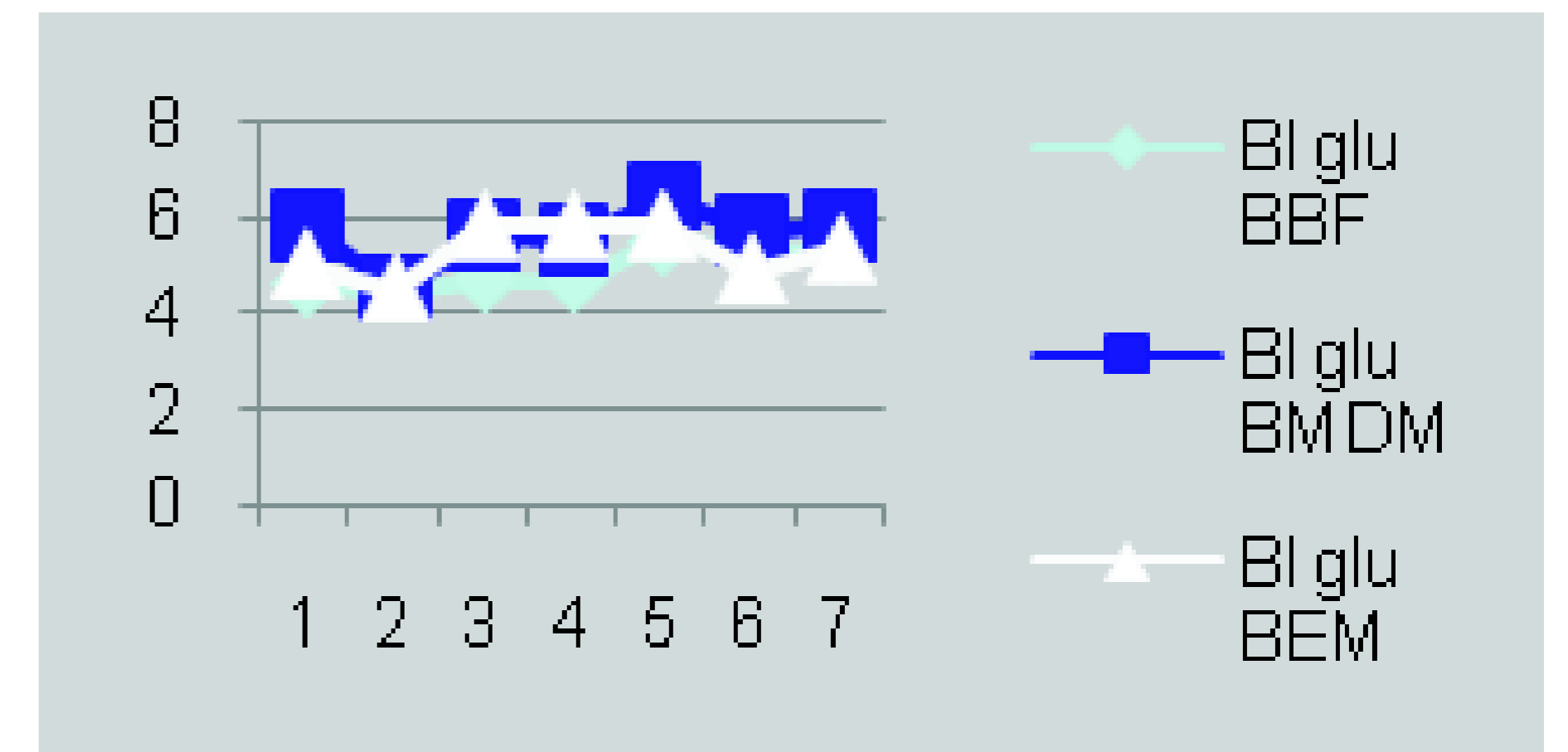


Fig 5. Blood glucose monitoring (after surgery)



Conclusion

- Diagnosis of insulinoma may delay because symptoms are nonspecific. Delay in diagnosis is almost always the consequence of reluctance by the patient to seek help, or failure of the practitioner to suspect hypoglycaemia. In majority of cases duration of symptoms were more than one year before diagnosis. In this case, it was due to hypoglycaemia unawareness.
- Sometimes neuroglycopenic symptoms are chiefly seen in patients and these groups of patient are misdiagnosed as epilepsy or neuropsychiatric disease

Discussion

- Tumours producing hypoglycaemia include:
 - 1) insulin-secreting tumours;
 - 2) non-islet cell(insulin-like growth factor-II (IGF-II)-secreting) tumours;
 - (3) myeloma, lymphoma and leukaemia;
 - (4) metastatic neoplasia.
- Hypoglycaemia produced by tumours other than insulinomas are usually referred to as 'non-islet cell tumour hypoglycaemia' (NICTH) and has more than one cause.
- The commonest ectopic sites are the duodenum and the immediate vicinity of the pancreas, but less than 1% of the 677 insulinomas collected from the literature by Laurent and co-workers prior to 1971 were located outside the pancreas.
- Insulinomas can occur sporadically or in conjunction with MEN-1 syndrome.
- The mixed-meal test should be the evaluation of choice in a patient suspected of postprandial hypoglycaemia. This should ideally be performed over five hours as hypoglycaemia can occur in the late postprandial phase and early termination could lead to a false negative result.
- Hypoglycaemia was mostly seen after exercise and prolonged fasting. In insulinoma cases no other signs or symptoms can be found except hypoglycaemic symptoms and obesity. Approximately 25% of cases are overweight because of the hyperalimentation due to hypoglycaemic symptoms.

References

Marks, V., & Teale, J. D. (1998). Tumours producing hypoglycaemia. Endocrine Related Cancer, 5, 111-130.