

Case Report

Perioperative management of a fluctuating glycaemic state – a rare case of malignant insulinoma

Kalpani Ruwanari Kannangara¹, Anuja Abayadeera²

¹National Hospital, Colombo, Sri Lanka, ²University of Colombo, Sri Lanka.

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Corresponding Author: Kalpani Ruwanari Kannangara, E-mail:<ruwanari88@gmail.com >

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Introduction

Insulinomas are a rare form of pancreatic endocrine tumour with an incidence of 1-4 people per one-million-person years [1]. Metastatic insulinomas are extremely rare and account for about 10% of total insulinoma cases [2]. Malignant insulinoma describes a tumour with local invasion or distant metastasis. Patients present with neuroglycopenia and sympathoadrenal symptoms due to severe hypoglycaemia. They can also have seizures, coma and permanent neurological deficits due to severe hypoglycaemia. Due to hypersecretion of insulin, patients often have weight gain contributed to by overfeeding. Clinical diagnosis is by a classic triad of symptoms known as Whipple's triad; symptoms of hypoglycaemia induced by fasting or exercise, documented hypoglycaemia of <50 mg/dl and relief of symptoms with glucose administration.

Perioperative management is focused on avoiding major swings in the blood glucose level. Medical management is commonly used in the perioperative period including inhibition of insulin hypersecretion by beta cells using pharmacological agents. Curative management in non-metastatic disease is by resection of the tumour along with subtotal or total pancreatectomy. In metastatic disease it is mainly palliative.

Here we describe a rare case of a 20-year-old woman with a malignant insulinoma with liver metastasis who had a long period of diagnostic delay due to nonspecific presentation and underwent distal pancreatectomy, radiofrequency ablation plus

resection of liver metastasis successfully without any surgical or anaesthetic complications.

Case report

A 20-year-old woman presented with a history of frequent fainting attacks and inability to wake up from sleep in the morning for a period of 4 years. Her symptoms were relieved with ingestion of sugar-containing drinks. She had been treated for generalized seizures and was on psychiatric follow up as well. The most recent medical encounter was due to prolonged sleep in the daytime which revealed severe hypoglycaemia with a blood glucose of 19mg/dl on admission with full recovery following correction of hypoglycaemia.

A prolonged, supervised fast revealed a serum insulin level of 23.64mu/l (<3 mu/l) and C-peptide level of 1.86ng/ml (<0.6ng/ml) in the presence of hypoglycaemia of 50mg/dl which was suggestive of an insulinoma. Contrast enhanced computerized tomography of the abdomen and pelvis revealed an enhancing mass lesion measuring 9cm×8cm×6.6cm in the pancreatic tail, suggestive of a neuroendocrine tumour or pancreatic malignancy with liver metastasis. She was scheduled for surgical resection.

During the ward stay, she was advised to take frequent small meals and capillary blood sugar was monitored every 2 hours. Overnight hypoglycaemia was treated with a 10% dextrose infusion. She was started on oral diazoxide but changed over to subcutaneous octreotide due to unresponsiveness to treatment.

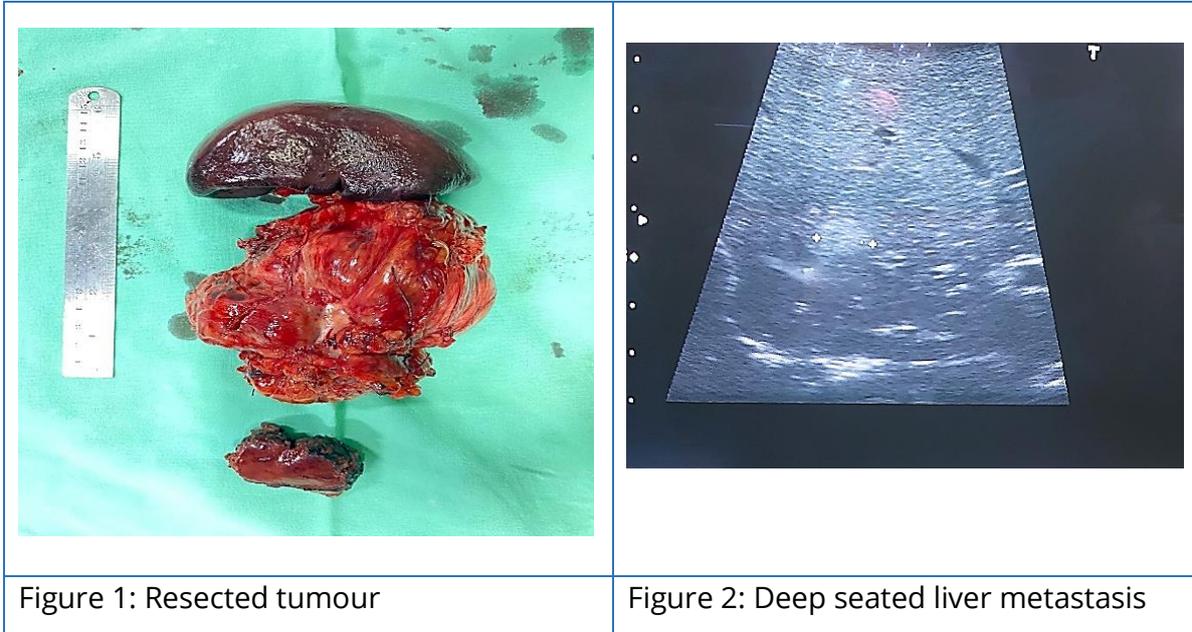
Preoperatively, she was started on an overnight 10% dextrose 60ml/hr infusion. Before induction of anaesthesia, an 18G cannula was inserted and Ringer's lactate solution was started. A thoracic epidural was inserted at the T10/11 intervertebral space for perioperative pain management. Standard monitoring was done with addition of central venous pressure, invasive blood pressure, hourly urine output and capillary blood glucose. Capillary blood sugar (CBS) was monitored half hourly from induction and at 15-minute intervals during tumour handling. It was targeted to maintain the blood glucose level between 60mg/dl and 200mg/dl intra-operatively. General anaesthesia was induced with IV fentanyl and IV propofol and muscle relaxation provided with iv atracurium. Intubation was done with direct laryngoscopy and IPPV was started. Maintenance of anaesthesia was done with oxygen, air and sevoflurane.

Epidural infusion was started with 0.1% plain bupivacaine with fentanyl and was titrated accordingly. A total of 7.5mg IV morphine was given. IV octreotide 100mcg was given at tumour resection. IV cefuroxime was given at induction and repeated in 4 hours. One unit of packed red cells was transfused due to a blood loss of 700ml associated with marginal haemodynamics.

Capillary blood sugar was maintained within the target levels until the tumour was resected, after which an insulin infusion was started to control hyperglycaemia. CBS was

234mg/dl soon after the tumour was resected. The lowest CBS recorded intra-operatively was 98mg/dl and the highest recorded value was 362 mg/dl.

En-bloc distal pancreatectomy and splenectomy (Figure 1) with non-anatomical resection and radiofrequency ablation of liver metastasis (Figure 2) was done. Total surgical duration was 8 hours.



It was planned to extubate the patient in ICU. Post-operative analgesia was provided with epidural infusion and IV paracetamol 6 hourly. Maintenance fluid was given with Ringer's lactate solution. Postoperative blood sugar was monitored 2 hourly for the first 24 hours and 3 hourly for the next 48 hours. Insulin infusion was titrated during the initial 24 hours and converted to subcutaneous insulin at a regular dose. Insulin was omitted on the 3rd postoperative day. Postoperative course was uneventful and the patient was discharged on the 13th postoperative day.

Discussion

Malignant insulinoma is a rare type of neuroendocrine tumour. More than 99% of them occur in the pancreas, commonly in the tail and body. Intra-abdominal and loco regional dissemination is seen with the liver being a frequent site and a major indicator of prognosis [3]. The prognosis of malignant insulinoma is poor despite many treatment modalities.

The usual presentation is in the 5th or 6th decade of life, without any gender predominance. Diagnostic delay may vary from 1 month to 17 years from first onset of symptoms [3]. Clinical manifestations of both malignant and benign tumours are features of hypoglycaemia due to excessive production of insulin by the tumour cells. Malignant tumours may have exaggerated symptoms due to extra production from metastatic sites. Symptoms usually interfere greatly with the lifestyle of patients leading to a significant psychological impact.

Localisation of the tumour is difficult due to its small size. Multiple imaging modalities, including transabdominal USS, CT or MRI improves the success rate. Intraoperative ultrasound (IOUS) has an 86-90% success rate in identifying the tumour [4]. During this case, the surgeon had to use IOUS to identify the liver metastases.

Sevoflurane was used for maintenance due to its ability to inhibit insulin secretion [5]. Perioperative anaesthetic management was mainly focused on prevention of major fluctuations in blood sugar levels. Anti-insulin drugs were continued and a dextrose infusion was given preoperatively. Meticulous monitoring of blood sugar levels were done at resection of tumour and after removal of tumour to detect hypoglycaemia and rebound hyperglycaemia, respectively.

Conclusion

Insulinoma and malignant insulinoma are rare encounters which need meticulous perioperative management to prevent severe hypoglycaemic attacks. Due to its rarity, there is a lack of evidence in the perioperative management of patients and this may impose a challenge to anaesthetists.

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