

## Perioperative Management of a Rare Pancreatic Insulinoma Resection: Anaesthetic Challenge!

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### ABSTRACT

Insulinoma is a rare, mostly benign and solitary neuroendocrine tumour of the  $\beta$ -cells of islets of langerhans of pancreas. Clinically it presents with a classical 'Whipple Triad' encompassing symptomatic hypoglycemia, fasting hypoglycemia (<50 mg/dl) and immediate relief of symptoms after glucose administration. Definitive treatment is laparoscopic or open surgical excision of the tumour. We report and discuss the distinctive anaesthetic considerations and implications during perioperative period. A comprehensive approach including preoperative optimization of blood glucose levels with various drugs and dietary modifications, scrupulous hemodynamic and blood sugar monitoring with prompt initiation of dextrose infusion during surgical handling of tumour and meticulous management of rebound hyperglycemia with insulin infusion in postoperative period remains the essence for better outcome in these subset of patients.

Insulinoma is a rare and benign neuroendocrine tumour of the  $\beta$ -cells of islets of langerhans of pancreas [1]. Reported incidence is 1-4 per million populations per year with a slight female preponderance (female: male 1.4:1) and median age of presentation at 47 years [2-3]. It presents with classical pathognomic triad (Whipple Triad) comprising of symptomatic hypoglycemia, fasting hypoglycemia (<50 mg/dl) and immediate relief of symptoms after glucose administration [4]. Associated symptoms are headache, dizziness, amnesia and seizures owing to neuroglycopenia [5]. In addition, in established cases, patients may present with hypoglycemia induced adrenergic response leading to tremors and palpitations [5]. Most of the insulinoma are solitary and benign (90%), where as the malignant form are associated with multiple endocrine neoplasia-1 (MEN-1) syndromes. [4-5]. Definitive treatment is laparoscopic or open surgical excision of the tumour [1-5]. We report an adult female with pathognomic triad of insulinoma, posted for open

surgical resection and discuss the unique challenges faced during its perioperative management.

### Case Report

A thirty-eight-year-old female was referred to our institute from a local hospital with history of multiple episodes of altered sensorium and loss of consciousness with average of one episode every three month, for the last five years. At the time of presentation, she complained of progressive increase in frequency in preceding 3 months with aforementioned episode every week. The episodes were sudden in onset and were associated with frothing of mouth and up rolling of eyes. Previous episodes were initially managed symptomatically at local hospital. She also gained significant weight due to ingestion of frequent meals to curb hypoglycemic episodes. She had no other co-morbid illness. During her in-hospital stay, her blood glucose levels were continuously monitored and were kept on continuous intravenous (IV) infusion of 10% dextrose solution (@1-2 ml/kg body weight) along with

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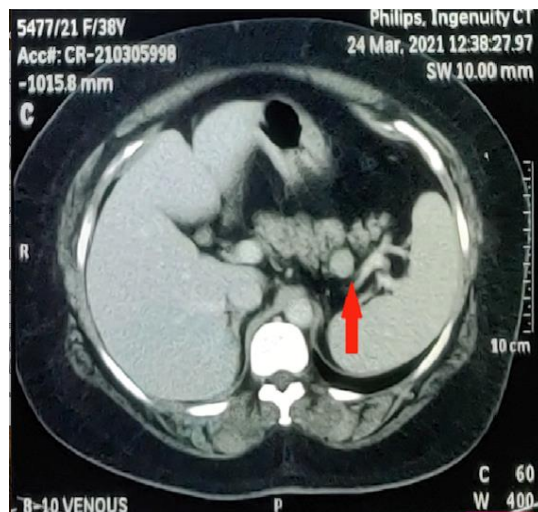
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intermittent bolus (50 to 100 ml) of 25% dextrose during the hypoglycemic episodes. Endocrinologist was consulted to obtain a definitive diagnosis. Contrast enhanced computed tomography (CECT) of abdomen revealed a space-occupying lesion (measuring 1.5 x 1.3 cm) in posterior pancreatic parenchymal region of body of pancreas, suggestive of insulinoma (Figure 1). Laboratory investigations revealed mild anemia (Hb 9.8g/L), elevated fasting plasma insulin (50.8  $\mu$ U/ml), C-peptide levels (7.41 ng/ml) and glycosylated hemoglobin (HbA1c) levels were 3.8 %. Rest all other routine investigations were within normal range. Computed tomography (CT) of brain has normal study. A definitive diagnosis of insulinoma was made based on clinical, biochemical assays and CT image findings. Subsequently, surgeons were consulted and she was planned for exploratory laparotomy with possible distal pancreatectomy, in view of recurrent life threatening hypoglycemia.

**Figure 1- CECT abdomen showing solitary nodule in tail of pancreas near hilum of spleen (Red arrow)**



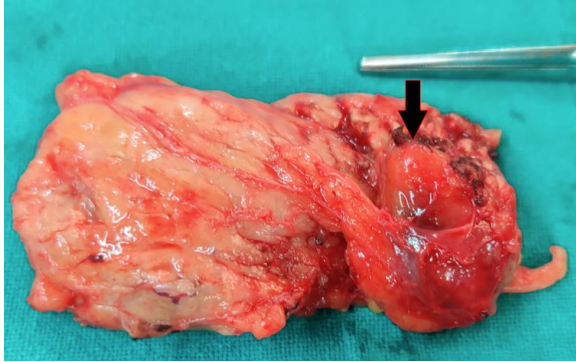
During her pre-anaesthetic checkup, general and systemic examination of patient was grossly normal and she had a good effort tolerance. Patient had a body weight of 85 kg and body mass index (BMI) of 30 kg/m<sup>2</sup>. Pre-operatively, a week prior to the planned surgery, patient was started on oral diazoxide 150 mg twice a day and octreotide 50  $\mu$ g subcutaneously thrice a day for one week to optimize blood glucose level. However, even on the aforesaid medication her blood glucose remains in lower range, hence intravenous 10% dextrose infusion was started. Airway examination revealed normal neck movements, adequate mouth opening with modified Mallampati grade (MMPG) grade of II and thyromental distance (TMD) of more than 6.5 cm.

Patient was kept nil per oral 8 hours for solids and clear glucose containing liquids were allowed till 2 hours prior to the surgery to minimize hypoglycemic episodes. Dextrose 10% solution was continued during fasting period @ 50 ml/hour IV. Premedication with tab

ranitidine 150 mg oral was administered 2 hour prior to surgery. Premedication with sedatives and analgesics were avoided to mask any symptoms of hypoglycemia.

On the day of surgery, patient was transfer to operating room (OR) and standard American Society of Anaesthesiologist (ASA) monitoring device were attached. Under all aseptic conditions, the epidural catheter was inserted at T7-T8 interspace by interlaminar approach. Ropivacaine 0.2% (5 ml) bolus was administered and subsequent continuous infusion @ 3-4 ml/hour was initiated via epidural catheter. General anaesthesia was induced with fentanyl 140  $\mu$ g IV, propofol 130 mg IV and vecuronium 10 mg IV and the trachea was intubated using 7.5 mm cuffed endotracheal tube. A 20 G arterial catheter was inserted aseptically in left radial artery for invasive blood pressure and blood glucose monitoring. Ultrasound guided right internal jugular vein was cannulated and 7Fr central venous catheter was inserted for continuous central venous pressure monitoring (keeping pressures around 8-10 cm of H<sub>2</sub>O), administering hypertonic glucose solutions and if need arises for vasopressors infusion. Anaesthesia was maintained using oxygen-nitrous oxide-sevoflurane (33-66-2%). Neuromuscular monitoring was attached and entropy (Static and Random) was maintained between 40-60. The patient received glucagon 1 mg subcutaneously and octreotide 50  $\mu$ g subcutaneously after induction of anaesthesia. Blood glucose monitoring was done using glucometer every 10 minutes intraoperatively via radial arterial line to target blood sugar between 100 mg/dl and 150 mg/dl. However, during surgical exploration, blood glucose level falls twice below 50 mg/dl for which two boluses of 100 ml dextrose 25% solution were administered. Due to persistent low levels of blood glucose levels, dextrose 25% infusion was subsequently started @ 50 ml/hour to stabilize blood glucose levels till resection of tumour. A firm nodular mass of 2x2 cm was excised from the inferior border of the body of pancreas and distal pancreatectomy was done (Figure 2). Immediately after resection of tumour, dextrose 25% was replaced with dextrose 10% @ 100ml/hour and was continued till completion of surgery. After resection of tumour, blood glucose levels and hemodynamics remain in normal range. After completion of surgery, neuromuscular paralysis was reversed with neostigmine 3.5 mg IV and glycopyrrolate 0.6 mg IV. Trachea was extubated after complete neuromuscular recovery.

**Figure 2- Specimen of distal pancreas resected with insulinoma nodule (Black arrow)**



Patient was then transferred to postanesthesia care unit (PACU), and was kept on continuous infusion of dextrose and 0.9% normal saline (DNS) solution @ 1-2 ml/kg Body weight for next 4 hours. Her blood sugar levels remain within normal range throughout this period. Patient was subsequently shifted to postoperative surgical ward, where DNS infusion was continued for next 24 hours. Patient had an elevated blood glucose levels (>200mg/dl) on post op day one for which dextrose containing infusions were stopped and subcutaneous regular insulin was started according to sliding scale. The blood glucose levels were targeted between 100-150mg/dl and was monitored every 4 hourly. Regular insulin was continued till post-op day 7, after which it was stopped after attaining normal blood glucose. Rest of the course of the patient remains uneventful. The patient was discharged on post-op day nine with normal blood glucose and advised regular blood glucose monitoring at home. During her 3-month follow up after discharge, patient did not have any critical fluctuations in blood glucose levels.

## Discussion

Surgical resection of insulinoma is the treatment of choice and could either be enucleation or distal pancreatectomy, depending upon the extent of tumour [4]. Pre-operatively, a detailed neurological examination must be done to document any pre-existing neurological damage due to recurrent episodes of hypoglycemic seizures [5]. Pre-operative management includes dietary modification of small frequent meals to avoid hypoglycemic episodes [6]. Intravenous infusion of IV dextrose 10% maybe required preventing hypoglycemia during fasting hours [6]. Medical management includes oral diazoxide and subcutaneous doses of somatostatin analogues (octreotide or lanreotide) to decrease the release of insulin [6]. We also started combination of diazoxide and octreotide, however even at maximum permissible dose blood sugar was in lower side of normal range, hence IV infusion of 10% dextrose was started to attain target blood sugar in normal range.

Hitherto, there are no specific guidelines for anaesthetic management of rare insulinoma resection. General

anaesthesia in combination with central neuraxial block is generally preferred and goals should be to reduce cerebral metabolic rate of oxygen consumption and prevent hypoglycemia till tumour resection and prevent hyperglycemia following resection of tumour. [4,7,8] Propofol is the drug of choice, as it does not effect insulin secretion [7-8]. We inserted thoracic epidural catheter before induction of general anaesthesia for perioperative multimodal pain management with considerable success. The signs of hypoglycemia may be masked under general anaesthesia warranting frequent blood glucose monitoring and extreme vigilance [5]. Recommended frequency of blood glucose monitoring is 15-30 minutes [5]. There may be a rebound hyperglycemia following resection of tumour owing to circulating anti-insulin hormones such as growth hormone, glucagon and glucocorticoids and may warrant administration of insulin for strict control of glucose levels [5-6, 9]. Insulin levels usually returns to normal values within an average duration of 20 minutes of tumour resection [9]. However, continuous infusion of dextrose infusion maybe required for next 2-3 days, as observed in our case where in continuous infusion of DNS (5% dextrose, 0.9% normal saline) was administered for 24 hours post-resection. Regular monitoring of blood glucose levels for every 4 hours in postoperative period is advisable to prevent episode of hypoglycemia.

## Conclusion

Perioperative management of insulinoma is foremost challenge for the anaesthesiologist and prevention of hypoglycemia should remain the utmost priority for the anaesthetic team. A closed loop communication between surgeon and anaesthesiologist during tumour handling is imperative for conduction of safe surgery. Conscientious preoperative approach with early initiation of diazoxide and or somatostatin may result in better control of falling blood sugar levels prior to surgical intervention. Perioperative blood glucose monitoring and subsequent expedited correction with dextrose infusion remains the core management strategy and may certainly results in better outcome in these subset of patients.

## References

- [1] Vaidakis D, Karoubalis J, Pappa T, Piaditis G, Zografos GN. Pancreatic insulinoma: current issues and trends. *Hepatobiliary Pancreat Dis Int.* 2010; 9(3):234-41.
- [2] Tucker ON, Crotty PL, Conlon KC. The management of insulinoma. *Br J Surg* 2006; 93(3):264-75.
- [3] Abboud B, Boujaoude J. Occult sporadic insulinoma: Localization and surgical strategy. *World J Gastroenterol.* 2008; 14(5):657-65.
- [4] Goswami J, Somkuwar P, Naik Y. Insulinoma and

- anaesthetic implications. *Indian J Anaesth* 2012; 56(2):117-22.
- [5] Santha N, Madhusudan U, Viswanath P. Anesthetic management of a case of insulinoma. *Anaesth Pain & Intensive Care* 2017; 21:272-74.
- [6] Thomas J, Gupta S, Kilpadi K. Insulinoma-Anaesthetic Implications with Review of Literature. *J Anest Intern Care Med*. 2017; 3: 555605.
- [7] Grant F. Anesthetic considerations in the multiple endocrine neoplasia syndromes. *Curr Opin Anaesthesiol* 2005; 18(3):345-52.
- [8] Maciel RT, Fernandes FC, Pereira Ldos S. Anesthesia in a patient with multiple endocrine abnormalities. Case report. *Rev Bras Anesthesiol* 2008; 58(2):172-8.
- [9] Parate LH, Channappa NM, Anandaswamy TC, Srinivasaih B. Anesthetic management of insulinoma. *J Anaesthesiol Clin Pharmacol*. 2015; 31(3): 420-21.