Anaesthetic Challenges in Management of Patient of Insulinoma

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Abstract

Introduction: Insulinoma is a rare neuroendocrine tumor of the pancreas that produces symptoms due to hypersecretion of insulin from β-cells. They are often misdiagnosed or have delayed diagnosis due to their bizarre clinical presentation. Diagnosis is made based on history (Whipple's triad), biochemical tests and imaging modalities. Surgical resection is the curative treatment. General anaesthesia is an ideal technique as it reduces the cerebral metabolism and oxygen consumption. We present a case of an 45 year old female patient diagnosed with insulinoma who had history of recurrent hypoglycemic attacks. Surgical enucleation of the tumor was undertaken. Perioperative management of blood sugar in these patients is of utmost importance. As anaesthesiologist our target is to prevent severe hypoglycemic episodes which may lead to permanent neurological damage and severe hyperglycemia post procedure which has to be managed by titrating the dose of insulin and dextrose.

Keywords: Insulinoma, Anaesthetic management, Hypoglycemia, Surgical excision, Neuroendocrine tumors

Introduction

Insulinomas are rare neuroendocrine tumors with a yearly incidence of 1 in 250,000.[1] However, insulinomas are the most common pancreatic endocrine tumors. The most common clinical manifestation is recurrent attacks of hypoglycemia with or without neuroglycopenic symptoms. Surgical resection has always been the treatment of choice since its first detection back in 1924 [21]. Inoperable tumors, or patients who are not surgical candidates, may be managed on diazoxide or somatostatin analogues like octreotide [22,23]. The main challenge in the anaesthetic management of an insulinoma is to maintain optimum glucose levels and prevent wide swings in blood glucose peripherically. Our patient was obese and had history of snoring with obstructive sleep apnea. Thus in our case airway management and maintaining saturation during induction and post extubation was a challenge. The patient was given rapid airway management position and intubated. Intraoperative during tumour handling the challenge was to prevent wide swings in blood glucose concentrations for which we monitored blood sugar levels every 10 minutes when the tumour was reached and accordingly titrated normal saline and 5% dextrose. Post extubation the patient was shifted to intensive care unit for saturation and blood sugar level monitoring to prevent hypoxia and hypoglycemic or hyperglycemic episode.

Case Report

A 45 year old female patient presented with recurrent episodes of hypoglycemia since 2 years. A diagnosis of insulinoma was suspected. A fasting 72 hour test under supervision was done with low fasting sugar and elevated insulin and C-peptide levels. A CT scan of the abdomen revealed a heterogeneously enhancing lesion, measuring 17 × 23 × 20 mm in body of pancreas (Fig 1). EUS (Endoscopic ultrasonography) showed 2.5×1.7cm lesion in upper part of body of pancreas in contact with stomach. She was then posted for enucleation of the tumor. On preoperative examination, she was obese with BMI 31.2kg/m2. The patient also had history of snoring and obstructive sleep apnea. Her vital signs were within normal limits and systemic examination was normal. ECG showed normal sinus rhythm and chest radiograph was normal. A written informed consent was taken after explaining the possible need for postoperative mechanical ventilation. Oral feeds were withheld six hours prior to surgery. Her fasting blood sugar level was 44mg/dl. She was started on 25% dextrose at 100 ml/hour with 2 hourly monitoring of blood sugar level. On shifting her to the operating room, her blood sugar level was 83mg/dl. She was then started on 5%dextrose at 150ml/hour. A right subclavian central venous line and a radial arterial line were secured. Electrocardiogram, pulse oximeter, capnometer and invasive blood pressure monitoring were set up. Epidural catheter 16 G was inserted at T 10-T 11 level. RAMP (Rapid Airway Management Position) position was given. Preoxygenation was done for 3 minutes with 100% oxygen and premedication was done with intravenous midazolam 1 mg and glycopyrolate 5mcg/kg. A rapid sequence induction was done with intravenous propofol 180 mg and succinylcholine 100 mg. Intubation was done with an oral cuffed endotracheal tube sized 7.5 mm. Fentanyl 100mcg was administered intravenously. Neuromuscular blockade was thereafter achieved with atracurium and fresh gas flow of O2:N2O (50:50) initially of 4L/min for 10 minutes and thereafter 2L/min with 1% sevoflurane was used. Blood sugar was recorded once every 30 minute until tumor...
was reached and every 10 minute once tumor manipulation was started. Blood sugar levels ranged between 70 to 180 mg/dl intraoperatively. Intravenous fluids 5% dextrose and normal saline were titrated according to blood sugar level. Epidural analgesic top ups with lignocaine 2% 4ml alternatively with bupivacaine 0.25% 4ml hourly were given. The surgery was completed in 90 min. Intraoperative blood loss was 250ml. She was reversed and extubated after fully awake and shifted to the intensive care unit. Postoperatively, blood sugar was monitored every 30 min for the first 4 hours and every 2 hourly thereafter. Blood sugar ranged between 100-300 mg/dl on the first postoperative day. Insulin therapy was begun if random blood sugar value was above 250 mg/dl. One hypoglycemic episode occurred following insulin therapy. She was administered dextrose/normal saline solution at 100 ml/hour and 5% dextrose was given following the episode of hypoglycemia. Somatostatin analogue – octreotide 100 ug S.C was started immediately after the surgery and then every 8 hourly. Her sensorium improved significantly and after one week she was advised to take feeds orally. Until then her blood sugar level ranged between 120-200mg/dl, while on dextrose/normal saline solution at 100 ml/hour. No further episode of hypoglycemia was noted, and she was discharged after normalization of blood sugar level.

Discussion
Insulinoma is an adenoma of beta cells of islets of Langerhans and the most common cause of endogenous hyperinsulinism. The median age of presentation is approximately 47 years, with a mild female preponderance (female: male 1:4.1) [2-4]. This rare tumor may have variable and nonspecific presentations all referable to the hypoglycemic state. Hypoglycemic symptoms can be divided into neuroglycopenic signs, most common, including confusion, behavioral changes, visual disturbances, weakness, dizziness, seizures and loss of consciousness, and neurogenic signs, such as anxiety, sweating, palpitations, tremors and feeling of warmth [5,6]. These symptoms become typically evident after fasting and are often precipitated by physical exercises. However, the median duration of symptoms before diagnosis remains variable and can reach 12–18 months on an average or even years in rare cases [7]. In our report, insulinoma diagnosis was delayed for several years because symptoms of hypoglycemia had been misinterpreted and misattributed to cardiac and neurological disorders before the insulinoma was recognized. In addition, our patient tried to avoid hypoglycemic signs by eating frequently with resultant weight gain. Diagnosis of insulinoma is by clinical, biochemical tests and localization of the tumour. Clinical diagnosis is based on Whipple’s Triad which includes repeated attacks of hypoglycemia, serum blood glucose levels <50mg/dl during that period and relief of symptoms with glucose administration [8,9]. Biochemical diagnosis includes the supervised 72-hour fasting test which is considered as gold standard with measurement of plasma glucose, insulin, C-peptide, and proinsulin during the onset of hypoglycemic symptoms. We used this test in our case to diagnose hyperinsulinism. Various preoperative procedures can be used to localize the tumor in order to plan therapeutic strategy. The choice of procedure depends upon which tests are available and local radiologic skills. In our context trans-abdominal ultrasonography, CT scan and EUS was used. Some authors consider EUS as the best examination for preoperative localization of insulinoma, with a sensitivity of up to 94 %. It can detect even small tumors of 5 mm, and reveal important relation to the bile duct and adjacent blood vessels. Also, EUS allows performing fine-needle aspiration cytology of suspicious lesions and preoperative marking of tumors to facilitate surgical excision particularly with laparoscopic approach. However, EUS findings depend largely on the examiner’s experience [7,10]. The current treatment of choice is surgical resection of the tumor. Some cases may require distal or partial pancreatectomy. Hypoglycemic symptoms can be medically controlled by diazoxide or somatostatin analogues. Our patient underwent tumor enucleation using open surgical approach.

Anaesthetic implications - The preoperative examination must include a complete neurologcal evaluation and all neurologic damage that has occurred due to the hypoglycemic episodes must be documented. Intravenous infusion of 5% Dextrose or 10% Dextrose should be started during the fasting period prior to surgery. Aim is to maintain blood glucose of more than 50mg/dl [2,8]. Adequate NPO may not be achieved as patients may become symptomatic even after a few hours of fasting and due to poor patient compliance. Hence the risk of aspiration must be considered while inducing these patients and adequate care must be taken. We had started patient on 5% dextrose 12 hours preoperative and nil per oral (NPO) of 6 hr was achieved but there was one episode of low blood sugar level during the fasting state which was managed by giving 100 ml 25% dextrose and the blood sugar level was maintained between 55 to 85mg/dl. The risk of aspiration was minimized by adequate fasting and doing rapid sequence induction. Administration of anaesthesia for removal of these tumors is challenging due to difficulty to maintain a normal blood glucose level. Wide fluctuations in blood glucose levels during tumor handling were observed. Hypoglycemia may be masked under general anaesthesia because signs of hypoglycemia such as sweating, tachycardia, and hypertension and dilated pupils which can also occur due to hypovolemia, surgical stimuli, lighter surgical planes and drugs. Hence, detecting hypoglycemia under anaesthesia is difficult. Intraoperative
hypoglycemia can cause CNS damage and such patients may often require postoperative ventilatory support. In our case to avoid hypoglycemia we monitored blood sugar level initially every 30 minutes and during handling of tumor every 10 minutes and accordingly titrated 5% dextrose and normal saline as intravenous fluid. It is recommended that blood glucose level must be checked before induction and every 15-30 minutes thereafter. It is imperative that glucose levels must be monitored in the recovery period also because of risk of rebound hyperglycemia after resection and multiple adenomas may exist which can cause early postoperative hypoglycemia which is not seen intraoperatively. Due to frequent blood sampling requirement, an arterial line is essential. The effect of various anaesthetic drugs and anaesthetic techniques on blood sugar level vary. During surgery there is surgical stress response which causes hyperglycemia. Midazolam given by intravenous route can decrease sympathetic activation and decrease serum adrenocorticotrophic hormone (ACTH) and cortisol, but can increase growth hormone (GH) secretion. It may possibly suppress the hyperglycemic response to surgery [11]. The effect of hyperglycemia on the function of cerebral cells during ischaemia is due to lactic acidosis and its effect on cellular mitochondria and propofol prevents lactic acidosis and its impact on the cerebral cells [12]. Propofol also decreases cerebral edema and cell injury after period of ischemia. Thus propofol protects endothelial cells against hyperglycemia induced insults [13]. Halogenated inhalational anaesthetic agents like halothane, isoflurane and sevoflurane inhibit the release of insulin [14]. Not much work has been done as far as the effect of muscle relaxants on blood glucose level during anaesthesia is concerned but it is clear that the muscle relaxants have no direct effect on the blood sugar physiology. Any change in the blood sugar level may be due to the other factors like anxiety, hyperventilation or hypoventilation during anaesthesia and lighter plain of anaesthesia [15-18]. Regional anaesthesia has the advantages of decreased stress response, decreased blood loss, minimal risk of thromboembolism, and early resumption of oral intake and preservation of hypoglycemia awareness. The reason of hyperglycemia during surgery may be surgical pain and metabolic response to surgical stress that even deep anaesthesia cannot block these responses, but with enough analgesia with epidural analgesia along with general anaesthesia we can maintain blood glucose in normal limits and prevent hyperglycemia and its complications during perioperative period [19,20]. Anaesthetics which decrease cerebral metabolic rate like propofol or thiopentone should be used. General anaesthesia with propofol combined with epidural is preferred choice of anaesthesia for insulinoma excision [8]. Post resection blood sugars may be high because of anti insulin hormones like GH, glucagon and glucocorticoids, which persist at high levels for a few days after removal of tumor. This hyperglycemia is self-limiting. Post operative hyperglycemia however, should raise the suspicion of either tumor not been found or multiple other insulinomas persisting. Thus the main focus of anaesthetic management is to prevent hypoglycemia during tumor resection and rebound hyperglycemia after resection.

Conclusion
Although surgical resection of insulinomas is the definitive treatment, meticulous management of perioperative sugar plays a key role in preventing permanent neurological damage and overall outcome of the patient. We reinforce the need for frequent glucose monitoring and prompt administration of sufficient glucose or insulin therapy as required perioperatively.

References
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