Case Report

Anaesthetic Management In A Pediatric Patient With Malignant Transformation Of Hepatic Adenoma In Glycogen Storage Disease Type 1 (Von-Gierke) For Liver Transplantation: A Case Report

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ABSTRACT

Anaesthetic Management in a Pediatric Patient with Malignant Transformation of Hepatic Adenoma in Glycogen Storage Disease Type 1 (Von-Gierke) for Liver Transplantation: A Case Report.

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Glycogen storage disease type Ia (GSD-Ia; Von Gierke disease) is an inherited disease caused by glucose-6-phosphatase deficiency. Perioperative management of patients with GSD has important implications for anaesthesiologists due to different system involvements. In the case reported here, an 8-year-old patient with GSD type-Ia underwent liver transplantation (LT) for hepatic adenoma that had malignant transformation, severe hypoglycemia and metabolic acidosis, occurred in this patient intraoperatively. The metabolic complications were managed successfully by administering balanced volume of glucose and sodium bicarbonate intravenously (iv). Although liver transplantation is an important treatment option in these patients, anesthesia management requires a multidisciplinary approach, comprehensive perioperative assessment and close intraoperative follow-up for successful outcomes.

Keywords: Glycogen storage disease, anaesthetic management, hypoglycemia, lactic acidosis, liver transplantation.

INTRODUCTION

Glycogen storage disease (GSD) is a group of inherited metabolic disorders caused by defect in some enzymes which are essential in glucose homeostasis. GSD-Ia, also known as von Gierke disease, is a rare autosomal recessive metabolic disease with an annual incidence of approximately 1/100.000[1]. In Von Gierke disease, due to the deficiency of glucose-6-phosphatase glycogen stored in the liver cannot be metabolized. This condition is associated with poor tolerance to fasting and increased risk of severe hypoglycemia and lactic acidosis[2].

The other clinical manifestations of the disease include hyperuricemia, hyperlipidemia, hyperproteinemia, hepatomegaly, truncal obesi-ty, a rounded doll- like face, growth retardation, wasted muscles, osteoporosis and bleeding tendency. Also, glycogen accumulation due to enzyme deficiency may cause hepatocellular adenomas, which may undergo malignant transformation as the long term complications[3,4].

Prevention of hypoglycemia with dietary treatment has a key role in the treatment of pa-tients with GSD. The usual dietary management may consist of frequent meals, continuous gastric tube feeds or the admini-stration of uncooked cornstarch. Despite dietary interventions and medical manage-ments, when there is severely poor metabolic control, progressive liver failure, worsening hepatic adenomatosis, development of hepatocellular carcinoma, LT is considered as the curtive treatment[5].

At perioperative period in LT, maintaining metabolic homeostasis, avoiding hypoglycemia and lactic acidosis should be the primary target. Altered pharmacology of anaesthetic drugs due to hepatic dysfunction, bleeding disorders from impaired platelet function, difficulties in ventilation, intubation and aspiration risks can be challenge for anaesthesiologist. Herein, we present our anaesthetic management in a pediatric patient with malignant transformation of hepatic adenoma in GSD Type Ia (Von-Gierke) for LT.

CASE PRESENTATION

An 8-year-old, (Weight 30 kg, height 122 cm, BMI 20.2) pediatric patient diagnosed with GSD type-Ia was referred to our hospital for surgical treatment. Owing to the death of her sister eight months of age and her parents' consanguinity, she was tested by the pediatric metabolism department, 3 months after birth. The patient experienced just one episode of hypoglycemic seizure 7 months of age, but now her neurological examination was normal. She was under oral sodium bicarbonate, allopurinol, fish oil treatment. Also, she had a special diet therapy that contained cornstarch and avoided lactose, sucrose. On physical examination, short stature, a rounded doll's face, fatty cheeks, massive hepatomegaly, abdominal ascites were noted, laboratory tests on admission revealed elevated values of liver enzymes (aspartate ami-

notransferase: 114 IU/mL; alanine aminotransferase,:84 IU/mL), hyperlipidemia (triglyceride: 509mg/dL; cholesterol: 252 mg/dL). Serum total bilirubin, alkaline phosphatase, albumin, and prothrombin time (PT), blood urea nitrogen (BUN), and creatinine levels were all within normal limits. Fasting blood glucose level was 49 mg/dL and she had lactic acidosis (6.4 mmol/L). Serum alpha-fetoprotein was 1.73 ng/ml. Preoperative her electrocardiography (ECG), echocardiograhpy, thorax computed tomography (CT) were unremarkable. Child class B, PELD score is 0. We have obtained written informed consent from the parents of the patient for publication of this report.

Abdomen ultrasonography (USG) showed a hypoechoic solid lesion in segment 3 with a size of 20x15 mm and increased in size compared to the previous examination (Figure1).

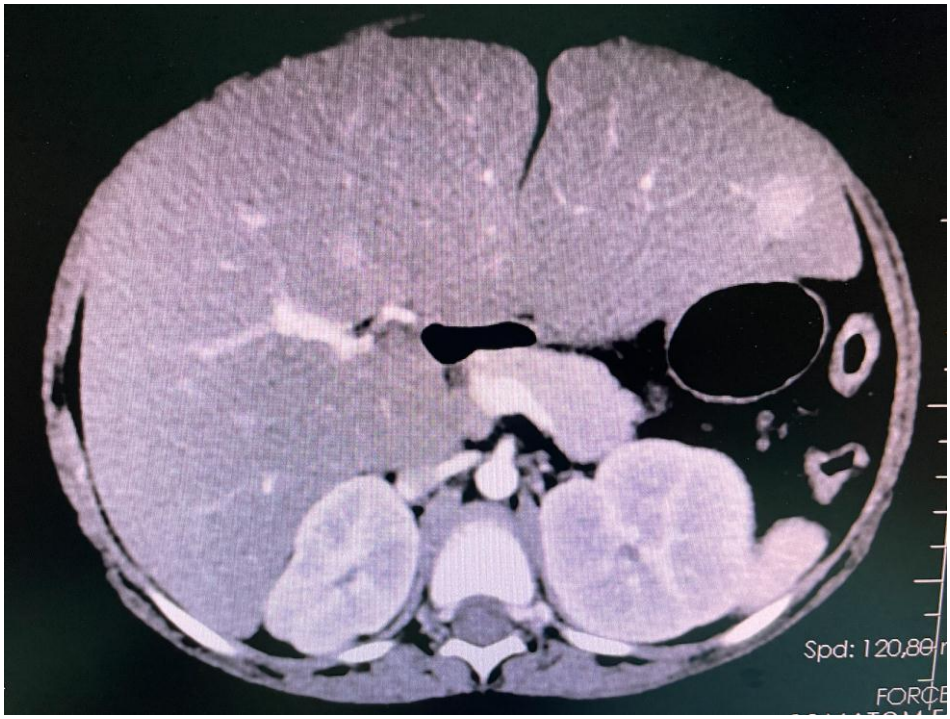

Figure 1. Abdominal computed tomography image of lesion in left hepatic segment.

The surrounding liver parenchyma showed mild diffuse steatosis. Diagnosis was confirmed as malignant transformation of liver adenoma by abdominal CT and liver biopsy after USG. Despite a complex dietary regime and extensive adjuvant medical treatment, her metabolic derangements remained resistant to treatment. Since, the patient's metabolic disease could not be controlled, and the lesion was compatible with well differentiated hepatocellular carcinoma (HCC), LT was decided to perform.

The American Society of Anesthesiologists (ASA) physical classification of the patient was class III and her Mallampati score was II. 45-year-old ASA I father prepared as a donor of the left lateral lobe. The patient was fasted for 6

hours before surgery. To prevent hypoglycemia, 10% dextrose solution infusion was started and close blood glucose monitoring was performed. On the operating room, the patient received standard monitors, including pulse oximetry (SpO_2), ECG, noninvasive blood pressure, capnography and temperature. After preoxygenation by 80% O_2 for 3 min, general anaesthesia was induced with propofol 2-3 mg/kg, fentanyl 1 μg/kg, and rocuronium 0.6 mg/kg and she was intubated with a size 5.0 cuffed endotracheal tube without difficulty. A right subclavian central venous catheter, a left radial artery catheter for hemodynamic monitoring, and a left femoral artery catheter for PiCCO monitoring were performed postinduction. Maintenance of anesthesia was provided by infusion of remifentanyl 0.02-0.05 mcg/kg/min with a mixture of 2% sevoflurane and 50% oxygen in the air and 0.3 mg/kg/h rocuronium infusion. At the beginning of the operation severe hypoglycemia (glucose:28 mg/dL) and lactic acidosis (lactate:12 mmol/L), metabolic acidosis (pH:7.18, base excess:-13.9 mmol/L) were observed. Aggressive supplementation in-cluding 10% dextrose and sodium bicarbonate infusion iv were performed for hypoglycemia and metabolic acidosis which persisted throughout the surgery. Glucose, lactate levels and blood gases measurement were frequently checked because of this condition. Intraoperatively, the lactate level peaked at 25 mmol/L. The patient had persistent hypotension secondary to the metabolic acidosis, requiring significant circulatory support with noradrenaline infusion (0.01-0.15 mg/kg/min). We targeted mean arterial pressure >60 mm Hg with inotropic support.

The operation was technically difficult due to massive hepatomegaly (Figure 2) and bleeding tendency. Since the nature of the disease may be platelet dysfunction and it is major surgery, blood products were prepared before surgery for the possibility of intraoperative transfusion. Although intraoperative blood salvage method was prepared for autologous blood transfusion it was not used because of HCC.

On neohepatic phase, the patient's blood glucose level and hemodynamic parameters markedly improved the patient was weaned from inotropes. Estimated blood loss was less than 1250 mL. Fluid therapy was administered, guided by an algorithm depending on the PiCCO parameters. In total, 1500 mL of crystalloid, 2200 mL of 5% albumin containing colloid, 2 units of erythrocyte suspension were replaced, and 500 mL of urine output was observed. The operation continues for 8 hours without complications. The explanted native liver weighted 2755 gr.

After the operation, sugammadex (4 mg/kg) was administered iv. She was extubated in the operating room when they fulfilled standard clinical criteria. Patient's neurological examination was normal after extubation, therefore no complication due to intraoperative hypoglycemia. The patient was transferred to intensive

care unit (ICU) postoperative. In ICU her lactate level was 19 mmol/L and pH was 7.34, within 39 hours the patient's lactate level and pH had normalized and, and hepatic transaminases were only mildly elevated (alanine aminotransferase and aspartate aminotransferase of 389 U/L and 126 U/L, respectively). After day 3 of ICU follows up, she was discharged at 6 th postoperative day on the ward, with close follow-up as an outpatient.

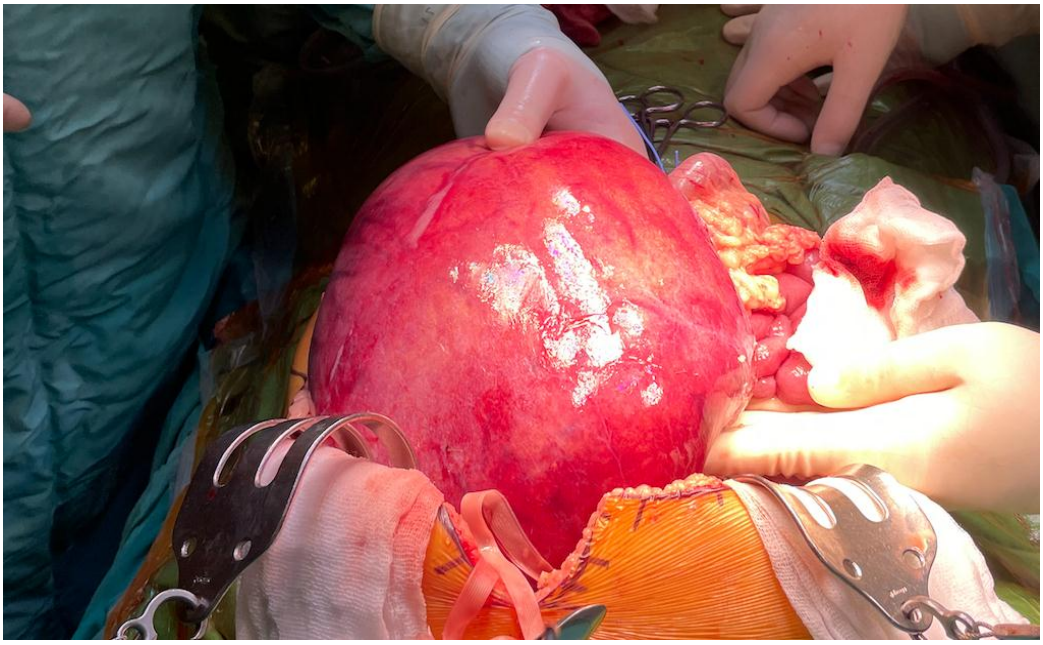

Figure 2. After laparotomy, gross hepatomegaly was detected.

DISCUSSION

Patients with GSD-Ia are at risk for developing liver failure, hepatic adenomas, HCC and poor metabolic control which is the severe and fatal. HCC in children has a mortality rate of over 70%[6]. Therefore, LT is recommended as a definitive therapy for improving metabolic control, quality of life, removing premalignant lesions as noted by Boers et al[7]. Perioperative management of LT in patients with GSD-Ia is challenging as there is a risk for particularly hypoglycemia and lactic acidosis. In these patients, it is important to supply adequate dextrose, monitor blood glucose and lactate levels closely as mentioned bey Gurrieri et al[8].

We checked glucose and lactate levels frequently with arterial blood gases (ABG) tests. Also, with ABG monitoring we administered sodium bicarbonate and glucose supply intraoperatively which were adjusted according to the degree of blood sugar and metabolic acidosis.

Surgical stress can precipitate lactic acidosis. Besides, neither glycogenolysis nor gluconeogenesis can be catalyzed, as these patients lack the enzyme complex glucose-6-phosphatase, which is responsible for delivering glucose to the blood. This condition results in fasting hypoglycemia. As fasting hypoglycemia is the most important problem of the disease, a short

duration of preoperative fasting is recommended for such patients. Özer et al. recommended 4 hr fasting preoperatively to a patient with GSD-Ia in an elective day case surgery[9]. In our case, since LT is a major surgery, the patient was fasted for 6 hr preoperatively, but she was hospitalized and preoperative dextrose infusion started for the adequate control of blood glucose concentrations.

In some GSD cases, difficult intubation or mask ventilation may be presented due to short, thick neck. Moreover, as the intraabdominal pressure is increased due to hepatomegaly and ascites, these patients are at risk of gastroesophageal reflux and aspiration[10]. All airway equipment (intubating stylet, bougies, video laryngoscope, laryngeal mask airway, fiberoptic bronchoscope) were prepared to prevent difficult airway. We haven't experienced any airway or aspiration problems in our case.

Hepatic dysfunction due to GSD can potentially change pharmacology of anaesthe-tic drugs. We preferred sevoflurane as a volati-le anaesthetic whose potential of hepatic injury was negligible in the pediatric group. Bustamente et al. reported a case with GSD-Ia who required tonsillectomy and adenoidectomy under general anesthesia[11]. They had used continuous iv infusion of propofol with remifentanil as maintenance of anaesthesia. Postoperatively, was detected pancreatitis, which was associated with propofol use. Besides other metabolic abnormalities of GSD the lipid abnormality is the consequence of an elevation of the triglyceride levels and cholesterol. Secondary to the lipid abnormalities there is an increased risk of propofol induced hypertriglyceridemia or acute pancreatitis although it is rare. We used propofol just a single bolus in the induction of anaestheasia. After induction, maintenance of anaesthesia was provided by infusion of remifentanil which is safe because it is short acting, its metabolism is independent of liver function and has a lower hemodynamic effect. We didn't observe any metabolic decompensation about pancreatitis. Since propofol was only used as an induction agent, we may not have encountered a problem.

Bleeding tendency in GSD is associated with platelet dysfunction. Moreover, the decreased concentrations of vonWillebrand Factor (vWF) may cause prolonged bleeding after surgery in these patients[12]. LT is a major surgery that may require large volume blood transfusion because of surgical technique, coagulopathy of patients. Intraoperative blood salvage method is a simple technique to cope with blood loss and to reduce the amount of the allogeneic blood transfusion. However, active malignancy is relative contraindications to autologous transfusion due to the presence of malignant cells in salvaged blood which may contain tumor cells and metastasize after reinfusion[13]. Current studies have shown that intraoperative autologous transfusion is not associated with in-

creased risk of cancer recurrence[14]. To our knowledge, there is not literature on the effect of autologous transfusion on oncologic outcomes in pediatric LT. Therefore, we didn't use intraoperative autologous blood transfusion.

CONCLUSION

GSD type-Ia is a rare metabolic disorder and LT is important therapeutic option. Anaesthetic management of these patients undergoing LT requires special planning, because they are prone to the development of hypoglycemia, organic acidemia. Close perioperative monitoring of blood glucose and lactate concentrations, preparing for the risk of bleeding and airway difficulties are essential. Therefore, we think that multidisciplinary approach, comprensive perioperative assessment and intraoperative close follow-up is critical for these patients.

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No

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Authors' contributions:

SD: conceptualisation, study design, data collection, paper draft, literature review, manuscript preparation and is the lead author. TO: data collection, literature review, EZ: study design, paper draft, literature review, and manuscript preparation, ÇN: conceptualisation, study design, paper draft, TA: conceptualisation, paper draft, literature review. All authors approved the manuscript.

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