# Clinical Reports

# Anaesthetic management of a patient with glycogen storage disease type 1b

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***Purpose:*** *A rare case of a ten-year old patient with type 1b glycogen storage disease (GSD), scheduled for extracorporeal shockwave lithotripsy (ESWL), is described.*

***Clinical features:*** *Patients with type 1b GSD manifest a range of clinical symptoms, including mental retardation, hepatosplenomegaly, renal enlargement, stomatitis, hypoglycaemic convulsions, bleeding diathesis, lactic acidosis and leukopaenia, thus creating a challenge for the anaesthetist. Following preanaesthetic administration of glucose-containing fluids, general anaesthesia was induced and the patient was mechanically ventilated. Except for mild hypoglycaemia after induction of anaesthesia, and moderate intraoperative metabolic acidosis which was attributed to the underlying disorder, anaesthesia was uneventful. No postoperative complications occurred and the patient was discharged home three days after lithotripsy. Clinical features of this rare inborn error of metabolism are reviewed and the approach for the anaesthetic management is discussed.*

***Conclusions:*** *A skillful perioperative management of patients with type 1b GSD can be achieved by cautious attention to the metabolic and homeostatic derangements that occur with the disease.*

***Objectif:*** *Présenter en cas rare de glycogénose de type 1b chez un patient de dix ans programmé pour lithotripsie extracorporelle par ondes de choc.*

***Caractéristiques cliniques:*** *Les patients souffrant de glycogénose de type 1b présentent une grande variété de symptôme, dont un retard mental, une hépatosplénomégalie, une hypertrophie rénale, une stomatite, des convulsions par hypoglycémie, une diathèse hémorragique, une acidose lactique et une leucopénie, ce qui représente tout un défi pour l'anesthésiste. Après l'administration de solutions glucosées, l'anesthésie générale a été induite et le patient ventilé mécaniquement. L'anesthésie s'est déroulée sans incident, à l'exception d'une hypoglycémie légère après l'induction, et d'une acidose peropératire modérée attribuée à la maladie sous-jacente. Il n'y a pas eu de complications postopératoires et le malade est retourné chez lui après trois jours. Les caractéristiques cliniques de cette rare maladie congénitale et la gestion de l'anesthésie sont discutées.*

***Conclusions:*** *Il est possible de gérer la période périopératoire des patients souffrant de glycogénose de type b1 avec succès si on tient compte des dérangements métaboliques et homéostatiques qui surviennent avec cette maladie.*

**Key words**
ACID-BASE EQUILIBRIUM: acidosis, lactic;
ANAESTHESIA: paediatric;
METABOLISM: glycogen storage disease.

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Glycogen storage disease type 1b is a rare autosomal recessive disease, in which glucose 6-phosphate, a product of metabolic cleavage of glycogen, cannot be transported to the inner surface of the microsome due to a deficiency of its transport system – glucose 6-phosphate microsomal translocase.[1] It is a variant of type 1a glycogenosis (Von Gierke's disease), in which the enzyme glucose 6-phosphatase is deficient. Therefore, glycogen cannot be hydrolyzed in hepatocytes, neutrophils and possibly other cell types.[1,2] The presenting clinical manifestations of these patients include a large variety of clinical and laboratory pathological findings

including mental retardation, hypoglycaemia, bleeding diathesis and organomegaly.[3] Thus, the perioperative management of these patients presents a challenge for the anaesthetist.

A few case reports have been published describing some anaesthetic considerations in patients with type 1 GSD,[4–6] with no attention to the various sub-types of the disease. In this case report, we describe, for the first time, anaesthesia for ESWL in a patient with GSD type 1b, and review the anaesthetic considerations relevant for these patients.

## Case report

A ten-year-old, 26 kg mentally retarded Beduin child was admitted to the urology department at the Hadassah University Hospital for lithotripsy of a left renal stone which had manifested by several episodes of renal colic. The patient was previously diagnosed as suffering from type 1b GSD. Unfortunately, the child's parents did not understand the importance of dietary control and he suffered from recurrent episodes of hypoglycaemia, resulting in convulsions, and ultimately in brain damage and mental retardation. Other manifestations included massive hepatosplenomegaly, renal enlargement, hyperuricaemia, chronic lactic acidosis, leukopaenia (2900 per $mm^3$ and granulocytopaenia (12%), and recurrent infections such as pneumonia, otitis media, cellulitis, gastroenteritis and stomatitis. His medical history was negative for epistaxis or any other bleeding episodes.

On examination, the child was lying in a semirecumbent position. Vital signs were normal except for mild tachypnoea. No oral lesions were seen. The abdomen was distended and periumbilical caput medusae was noted. The liver was palpated 14 cm under the right costal margin (span 20 cm), and the spleen was palpated 4 cm below the left costal margin. The rest of physical examination was normal. Blood count revealed leukopaenia (3300 leukocytes per $mm^3$, 27% of which were granulocytes) and anaemia (haemoglobin concentration of 10.7 $g \cdot 100\ ml^{-1}$). Platelet count was normal, but bleeding time was 12 min (normal 2.3–9.5). Plasma glucose concentration was 4.4 $meq \cdot L^{-1}$ (normal 4.0–6.0), and serum electrolytes were normal. Uric acid concentration was 584 $mmol \cdot L^{-1}$ (normal 150–380). Serum creatinine concentration was 24 $mmol \cdot L^{-1}$ (normal 60–106) and urea nitrogen concentration was 2.7 $meq \cdot L^{-1}$ (normal 3.3–6.5). Higher than normal plasma liver enzyme activity and normal bilirubin concentrations were noted as well. Urine culture was sterile and urine test for cystine was negative. Intravenous pyelogram revealed a 20 × 12 mm semiopaque stone in the left renal pelvis causing moderate to severe hydronephrosis. The left ureter and the rest of the urinary system were normal. Massive enlargement of the liver shadow was noted. Extracorporeal shockwave lithotripsy of the left renal stone was planned. Intravenous infusion of 0.18% normal saline with 10% glucose, at a rate of 78 $ml \cdot hr^{-1}$, was started the night before surgery, and continued during operation and after it, until resumption of oral feeding. No drugs were given before the anaesthetic induction. Intraoperative monitoring consisted of ECG, non-invasive automatic arterial pressure, pulse oximeter and a capnograph.

General anaesthesia was induced with propofol 120 mg in three devided equal doses, and lidocaine 40 mg, and muscle relaxation was achieved with succinylcholine 25 mg. Orotracheal intubation was easily accomplished using a 5.5 mm ID Portex tube, and the lungs were mechanically ventilated. Anaesthesia was maintained with nitrous oxide 70% in oxygen, isoflurane 2% and muscle relaxation was maintained with atracurium 45 mg. Ampicillin 750 mg and gentamicin 45 mg were administered and an external stent was retrogradely introduced into the left ureter with its proximal end positioned in the renal pelvis. The patient was transferred from the cystoscopy table to the hydraulic chair of the Lithotriptor (HM3 Dornier, Munchen, Germany). He received 1800 shocks with 24 volt intensity. Dye contrast was injected through the ureteral stent in order to visualize the anatomy of the left kidney better, and to direct part of the shockwaves to the lower calyces, where stone fragments were located. The treatment was completed within 30 min. The stent was then internalized under fluoroscopy. Oxygenation, ventilation, and the hemodynamic status were normal and stable. Venous blood was sent for gas analysis and for plasma glucose concentration measurments. Except for mild hypoglycaemia (plasma glucose concentration of 3.1 $meq \cdot L^{-1}$) at the beginning of the procedure, which was corrected by intravenous administration of glucose, there were no episodes of hypoglycaemia. Venous blood gas analysis showed moderate metabolic acidosis (pH-7.21, and base deficit of 10).

Recovery from anaesthesia was uneventful. The patient was positioned in a semirecumbent position and transferred to the postanaesthesia care unit. The patient was discharged home after three days of hospitalization. Ultrasonography performed ten days following discharge, demonstrated few stone fragments in the left lower calyces, and residual hydronephrosis. The stent was in place. No renal, hepatic, splenic or retroperitoneal haematomata were visualized.

## Discussion

Glycogen storage diseases occur as a result of enzymatic abnormalities that lead to abnormal concentrations or

structures of glycogen.[2,7] In type 1b glycogen storage disease, glycogen accumulates in the liver, kidneys and intestinal mucosa, and glucose availability to various tissues is impaired.[3] Hypoglycaemia and chronic lactic acidosis ensue.[3] These patients may present a wide variety of clinical symptoms and signs, most of them common to both types 1a and 1b: mental[3] and growth retardation;[1,3,8] facial and truncal adiposity;[9] delayed adolescence;[1] convulsions as a result of hypoglycaemia;[3,6,10] chronic metabolic acidosis which can lead to negative calcium balance and osteoporosis;[6] hepatomegaly;[1,8] hepatic adenomas[1,8] and hepatomas;[6,9] renal enlargement;[1,8,11] hyperuricaemia,[3,6] gout[9] and chronic pyelonephritis;[9] bleeding diathesis[3,6] due to impaired platelet aggregation and adhesion,[6,11] which might lead to recurrent epistaxis and bleeding after minor trauma or surgery;[6,10] various oral mucosal[8,13,14] and dental[6,8,10,11,13] lesions. In addition, type 1b patients may suffer from recurrent pyogenic infections due to neutropenia[11-14] and disturbed neutrophil motility,[11,12] migration,[11-13] adherence[11] and bactericidal capacity.[15]

In preparing these patients for anaesthesia and surgery, meticulous attention should be paid to aseptic techniques. The mental retardation[3] might create difficulties for the anaesthetist, both during anaesthetic induction and recovery. Preoperative fasting should be as brief as possible and glucose-containing fluids should be intravenously administered perioperatively[4,5] at a rate of 4–8 $mg \cdot kg^{-1} \cdot min^{-1}$.[16] Blood glucose concentrations must be carefully monitored since hypoglycaemia can be severe.[3] Moreover, intraoperative hypoglycaemia may be difficult to recognize,[3] since anaesthesia can mask its clinical signs and symptoms. During surgery, convulsions should be anticipated[3] and treated by the immediate intravenous infusion of glucose solution.

Inasmuch as lactate may not be completely converted to glycogen in patients with type 1b GSD,[3] lactic acidosis can develop. Therefore, blood pH should be monitored[4] and lactate-containing fluids (e.g., lactated Ringer) would be avoided.[3,4] It is advisable to mechanically ventilate these patients during anaesthesia, in order to prevent respiratory acidosis.[6] If metabolic acidosis does occur, sodium bicarbonate should be intravenously administered according to the base deficit. However, hyperventilation should also be avoided, since respiratory alkalosis can lead to the release of lactate from muscle tissue, the excess amount of which cannot be efficiently metabolized, aggravating the metabolic acidosis.[4,6,17] It is advised that a peripheral artery be cannulated for major surgeries, in order to monitor arterial blood glucose concentrations and arterial blood acid-base status.[4,6]

The anaesthetist has to consider the possibility of bleeding diathesis in patients with type 1b GSD (see above), although no post ESWL renal, hepatic or splenic bleeding was reported in these patients. The only parenchymatous bleeding during lithotripsy, in a patient with Von Gierke's (type 1a) GSD, was attributed to a mistaken transmission of the shock waves through the lung parenchyma.[18] Moreover, ESWL was uneventfully performed in patients with haemophilia.[19] Platelet dysfunction in Type 1 GSD has been associated with the biochemical derangements of the disease, and reversed by correction of these.[5] Although it is not clear which of the biochemical derangements is responsible for the platelet dysfunction[5] some investigators have claimed that adequate control of blood glucose concentrations can correct the platelet dysfunction.[6] Therefore, preoperative control of blood glucose concentrations by a regulated diet and total parenteral nutrition have been suggested in order to avoid excessive bleeding during surgery in such patients.[5,6]

In this case, ESWL was performed under general, rather than regional anaesthesia, due to lack of cooperation, the apprehensive behavior of the patient and the bleeding tendency. Before induction of anaesthesia and after recovery, the patient was positioned in a semirecumbent positioning in order to lessen the effects of the enlarged liver on the respiratory system. Stent placement allowed exact location of the stone during the treatment, minimizing any possible trauma to the kidney. It also allowed smooth passage of stone fragments.

Mechanical ventilation was necessary in our patient not only because of anaesthetic depression of ventilation, but also due to elevation of the diaphragm by the enlarged liver, which could have impaired pulmonary function. A peripheral artery was not cannulated since the procedure was not a major operation, and without fluid shifts. Plasma glucose concentrations and acid-base status were monitored by drawing blood from an intravenously-placed cannula; normocapnoea was also affirmed by capnography. The mild hypoglycaemia detected in the beginning of the procedure was treated by an intravenous infusion of a glucose-containing solution. The mild metabolic acidosis was attributed to the underlying disease.

In summary, a safe perioperative management of a patient with type 1b glycogen storage disease can be achieved by careful attention to the metabolic and homeostatic derangements that occur with the disease. Meticulous attention to the prevention of hypoglycaemia, acidosis and infections, as well as appropriate management of bleeding, are important issues in the perianaesthetic management of these patients.

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