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Urgent anaesthetic management of glycogenosis type Ia (von Gierke's disease)

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Summary

We describe the anaesthetic management of a massive haemorrhage in a 16-year-old patient with glycogenosis type Ia, also known as GSD-Ia or von Gierke's disease.

GSD-Ia can be manifested at an early age with a broad array of signs and symptoms such as hepatosplenomegaly, kidney failure, mental, height and weight retardation, lactic acidosis and hypoglycaemia. In a programmed anaesthesia, is important to anticipate a certain degree of hepatic and kidney dysfunction, as well as a strict follow-up on glycaemias (a severe tendency to hypoglycaemia) and pH. The emergency nature and instability of the patient due to massive haemorrhage made intra-operative control even more difficult. *Anestezjologia i Ratownictwo 2010; 4: 427-430.*

Keywords: anaesthesia, glycogen storage disease type I, von Gierke's disease, glucosephosphatase deficiencies

Introduction

The definition of glycogenosis includes those genetic disorders (including 18 phenotypes) that affect the pathways for formation and use of glycogen. Glycogenosis can be divided into two categories: those that have a hepatic hypoglycemic physiopathology (type Ia, Ib, III, VI and VIa) and those with a muscular physiopathology (types V and VII and glycolysis defects that do not cause the accumulation of glycogen) [1].

The prevalence of glycogenosis is 1/20.000-1/25.000 (types I, II, III and IV are the most frequent). All of them are transmitted by autosomal recessive inheritance, with the exception of phosphorylase-b-kinase deficiency (linked to the X chromosome) [2,3].

Clinically, glycogenoses differ as far as age at their onset, their affect on other organs and their clinical gravity. The most serious form appears in the first year of life where patients present symptomatic hypoglycaemia; generalised hypotonia and muscular weakness due to deficiencies in their feeding; macroglossia; hepatomegaly; cardiac failure, and usually die before 24 months. In their juvenile form, beginning in childhood, the most prevalent are muscular manifestations, the absence of cardiac involvement and a slow, progressive evolution that begins with the loss of motor skills and walking difficulties, with subsequent difficulties in swallowing, proximal weakness and involvement of respiratory muscles [1].

The specific characteristics of type Ia glycogenosis can be seen in table 1. The keypoints in anaesthesia are: tendency to hypoglycaemia, reiterative lactic acidosis and hypocalcaemia, impairment of the platelet function due to hyperuricaemia and possibility of liver and kidney failure.

Case report

We present a 16-year-old female patient, 45 Kg, 140 cm, with glycogenosis type Ia and clinical antecedents of hypertriglyceridemia and 3 episodes of pancreatitis. She came to the hospital due to abdominal pain

Table 1. Specific characteristics of type Ia glycogenosis

Type Ia glycogenosis (GSD-Ia) (Code CIE-9-MC: 271.0)	
Other names	Hepatorenal glycogenosis, glucose-6-phosphatase deficiency, glycogen deposit disease Ia, von Gierke's disease [4]
Inheritance	Autosomal recessive
Prevalence	1/100.000 or 400.000 inhabitants [1].
Etiology	Deficiencies in the glucose-6-phosphatase system producing an abnormal accumulation of glycogen in different organs [2,3].
Clinical findings	Large hepatomegaly, moderate nephromegaly, discreet splenomegaly, a rounder 'doll's face', stunted growth but normal mental development, and occasionally light muscular hypotonia, hepatic adenomas (sometimes become malignant), diarrhoea (due to inadequate intestinal absorption of glucose) and osteoporosis (due to the chronic effects of acidemia and kidney failure) [5].
Analytics	Moderate anaemia, tendency to hypoglycaemia, neutropenia, hyperlipemia (with production of xanthomas and atherosclerosis), hyperuricaemia (more relevant from adolescence due to the increase in purine metabolism and kidney failure, with dripping and frequent haemorrhaging from secondary impairment of the platelet function). Increased seric levels of creatin kinase (not always so high in adults), glutamic-aspartic transaminase and lactate dehydrogenase, especially in nursing babies. Reiterative lactic acidosis and hypocalcaemia are relatively usual [6].
Definitive diagnosis	Determining the levels of glucose-6-phosphate-phosphatase and the aggregate presence of glycogen in the hepatic tissue.
Differential diagnosis	Type Ib glycogenosis (microsomal translocase deficiency), with severe neutropenia and recurrent infection.
Prognosis	Medium or good because when the patient grows the metabolic problems become less serious and more easily controllable.
Basic treatment	Is addressed to control hypoglycaemia and lactic acidosis with frequent feeding during the day and continuous nocturnal feeding by catheter and infusion pump. The diet must contain 60% carbon hydrates free of galactose or fructose. Appropriate dietary restrictions and treatments are added when necessary, to control other metabolic disorders such as hyperuricaemia and hyperlipidemia.
Palliative surgery	Consisting of a portacaval shunt to prevent lactic acidosis, does not usually give good results. Sometimes, in serious cases where all other therapeutic possibilities have failed and to prevent the complications of malignancy, hepatic transplant may be considered [4,5].

lasting several hours, with systolic arterial pressure (SAP) of 90 mm Hg and cardiac rate of 130 beats min^{-1}. Abdominal echography revealed the existence of a large amount of free liquid of hematic aspect in all abdominal compartments without locating the origin of the bleeding. A computed tomography detected voluminous hepatomegaly and bilateral renal involvement. The remaining supplementary explorations were normal, excepting an initial hematocrit of 13.8%, haemoglobin of 5 $g.dL^{-1}$, glycaemia of 170 $mg.dL^{-1}$ and creatinine of 2.9 $mg.dL^{-1}$. The patient's physical aspect showed evident retardation in growth, with a protuberant belly, thin extremities and thorax, a 'doll's face' with swollen cheeks, and a short neck. She had been deteriorating progressively despite emergency transfusions, so a surgical emergency exploratory laparotomy due to massive hemoperitoneum (the hepatomegaly contraindicated a surgical approach by laparoscopy) was decided.

The patient was not considered to have difficulties for intubation (Mallampati II). General anaesthesia was induced with fentanyl, propofol and rocuronium ($2ED_{95}$), and she was intubated without problems. Anaesthetic maintenance was done with supplemental doses of fentanyl, rocuronium, an oxygen–air mixture (FiO_2 at 45%) and sevoflurane at 1.3 MAC.

She was monitored with ECG, pulse oxymetry, capnography, radial artery and central venous pressures, esophagic temperature, entropy, diuresis and neuromuscular block with accelerometry (TOF-Watch SX) in the *adductor pollicis* muscle (with delayed latency of rocuronium and prolonged recovery - table 2).

An abundant hemoperitoneum (1300 mL aspirated) was found due to a haemorrhagic ovarian follicle. The progressive instability during surgery (SAP of 75-80 mm Hg) and the patient's loss of heat despite the convective hot air blanket used, advised her progressive extubation. Upon conclusion of the surgery (2 hours)

the patient was transferred, intubated, to the Critical Care Unit, where she recovered without incident.

Table 2. Neuromuscular blocking effect of rocuronium ($2ED_{95}$)

Neuromuscular monitoring parameter	Time
Beginning of action of 95%	3 min 15 s
Beginning of action of 100%	3 min 30 s
Recovery of 1st response to the train-of-four stimuli	25 min 45 s
Recovery of 2nd response to the train-of-four stimuli	33 min 30 s
Recovery of 3rd response to the train-of-four stimuli	36 min 15 s
Recovery of 4th response to the train-of-four stimuli	39 min 15 s
5% duration of action	27 min 45 s
10% duration of action	32 min
25% duration of action	36 min 45 s
Time from 25% duration of action to recover again 25% duration of action of 25 mg of rocuronium	53 min

Discussion

Regarding the anaesthetic technique, it should be emphasised that the emergency nature of the operation did not allow us to prepare a more exhaustive bibliographical review. The patient was hemodynamically stabilized with emergency transfusions previously to the surgery. Arterial pH was normal at the beginning of the surgery and tendency to hypoglycaemia and lactic acidosis was treated with glucose continuous infusion.

The selection of the anaesthetic technique was not easy, because we have to choose between two not completely satisfactory alternatives: a total intravenous anaesthesia or an inhalational one. We decided to use a balanced general anaesthesia with sevoflurane due to the patient's hemodynamic state (to avoid hypotension after a propofol-based anaesthesia) and to prevent a lipid overload (due to the continuous infusion of propofol in a patient with previous antecedents of pancreatitis). Against this decision was the risk of malignant hyperthermia but, on the other hand, we had no certainty of a direct association of GSD-Ia with this syndrome. It is also remarkable that GSD-Ia is a glycogenosis with predominant metabolic (not neuromuscular) affectation, and there were no familiar history of malignant hyperthermia.

We selected propofol and rocuronium for intubation instead of etomidate and succinylcholine for several reasons: in the first place, intubation conditions after propofol are better than those after etomidate (and the hemodynamic situation allowed us its use), secondly, we avoided administering succinylcholine (even though GSD-Ia is not a glycogenosis with predominant myopathy) because the patient had enough fasting period to be not considered as a "full stomach" one. We selected rocuronium as neuromuscular blocking agent due to the rapid initiation of action, although the profile for metabolic elimination of rocuronium is not the most suitable in patients with a presumed certain degree of hepatorenal dysfunction (it could be preferable atracurium or cisatracurium), but we had initially the intention of extubating the patient in the operating room, so we used rocuronium on the possibility of fast and complete reversing the residual neuromuscular block with sugammadex.

The selection of an adequate intra-operative fluidotherapy was also very important. An infusion with glucose solution at 10% was maintained at a rate of 4-8 $mg.kg^{-1}.min^{-1}$ in order to prevent the development of hypoglycaemia, which usually occurs unnoticed. For this reason, in emergency surgery, serial capillary glycaemia checks must be made every 30 minutes [7,8] (in this case, the results were within normal values). The tendency to develop lactic acidosis requires continuous assessment of pH and avoidance of fluidotherapy that contains lactate (Ringer's lactate was not used) as well as hyperventilation [6]. In this case, due to the previous intense haemorrhage, volume replacement was done with colloids (hydroxyethyl almidon 6%) and packed red blood cells [7,8].

Finally, we must indicate the patient's haemorrhagic diathesis, with continuous bleeding to minimal surgical stimuli, from points of venipuncture, etc, an aspect that is also typical of patients with GSD-Ia.

Conclusion

Glycogenosis type Ia is a rare disease, complicated in this case by the emergency situation, that requires detailed knowledge of its physiopathology in order to be able to prevent its characteristic metabolic (mostly hypoglycaemia and acidosis) and hemodynamic complications.

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