Oral manifestations and anesthesia considerations in a child with glycogen storage disease type 1b: case report

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Glycogen storage disease (GSD) type 1a, known as von Gierke's disease, is a rare autosomal recessive inborn error of metabolism in which there is an inability to cleave glycogen to glucose due to glucose 6-phosphatase (G6Pase) deficiency.[1,2] The diagnosis currently is established by demonstrating the lack of G6Pase activity in the patient's biopsied liver specimen. Recently, however, a DNA-based diagnostic technique was developed in which mutations in the G6Pase gene can be identified in readily-available tissues such as blood and skin, and in the case of prenatal testing, in chorionic villi or amniocytes.[3] Type 1b is an autosomal recessive variant of von Gierke's 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. Therefore, glucose 6-phosphate cannot be metabolized to glucose even though microsomal glucose 6-phosphatase activity is normal.[1] The diagnosis of type 1b is still based on liver biopsy and enzymatic assays. In both types, glycogen accumulates in several organs, especially the liver[1,2,4] and kidneys.[1,4,5] Glucose availability to various tissues is impaired,[1,2] and hypoglycemia and chronic lactic acidosis ensue.[2] Chronic metabolic acidosis can lead to negative calcium balance and osteoporosis.[6]

Both types have many systemic and oral manifestations. The main systemic manifestations include growth retardation,[1,2,4] hepatomegaly,[1,4] renal enlargement,[1,4,5] bleeding diathesis[2,5-7] manifested by recurrent epistaxis and bleeding after minor trauma or surgeries,[5,6] recurrent episodes of severe hypoglycemia,[2,5,6] and metabolic acidosis.[2,6] Patients with GSD type 1b also suffer from recurrent pyogenic infections due to immunological deficiency.[7-10]

Other clinical manifestations, common to both type 1a and 1b, include possible brain damage[6] and convulsions[2,5,6] as a result of hypoglycemia, growth retardation,[1,2,4] facial and truncal adiposity,[15] and delayed puberty.[1] Hepatic adenomas[1,4] and hepatomas[6,15] may develop. Hyperuricemia, which can be overt,[2,6] can lead to secondary pyelonephritis and gout.[15] Hyperlipidemia also may be found in these patients.[4,6]

The mechanism of the bleeding tendency is related to impaired platelet function with prolonged bleeding time, reduced platelet adhesiveness, abnormal aggregation, and impaired capacity to release adenosine diphosphate in response to collagen or epinephrine.[6,7] These abnormalities can be corrected by improving the metabolic state of the patient.[16]

The immunological deficiency in patients with type 1b GSD is attributed to neutropenia[7-10] and/or disturbed neutrophil function due to impairment in motility,[7,8] migration,[7-9] adherence,[7] bactericidal capacity, superoxide anion production,[17] and intracellular calcium mobilization.[18]

Oral manifestations of the disease include delayed development of dentition,[5,11,12] rapidly progressive periodontal disease,[4,7,9] recurrent stomatitis,[9,10] oral candidiasis,[9,10] oral ulcerations,[4,10] and dental caries[6,9] and abscesses.[9] Treatment of oral lesions may include antiseptic and anti-fungal rinses, as well as oral administration of antibiotic agents.

Perianesthetic management may be complicated by several potential metabolic and homeostatic challenges such as severe hypoglycemia,[2] which can be masked by anesthetic medications,[2] lactic acidosis,[2,6] and bleeding tendency.[5,6]

Only a few case reports describe several anesthetic considerations in patients with type 1 GSD.*[6,13,14] None discriminated between the various subtypes of GSD type 1. We report a case of dental treatment under general anesthesia in a patient with GSD type 1b, describing the clinical presentation of this rare inborn error of metabolism and an approach to the dental and perianesthetic management.

* Since the original submission, a case report distinguishing anesthetic considerations in type 1 GSD has been published. Please see Shenkman Z, Golub Y, Meretyk Y, Shir Y, Landau D, Landau PH: Anaesthetic managment in a patient with glycogen storage disease type 1b. Can J Anaesth 43:467–70, 1996.

Case report

History

A 3-year-old female was admitted to the dental clinic of Sheba Medical Center for treatment of dental caries. The patient was diagnosed previously as suffering from GSD type 1b, manifested by hepatomegaly, hypoglycemia, failure to thrive, recurrent infections (recurrent otitis media, several episodes of pneumonia, furunculosis, and stomatitis), and neutropenia, with absolute neutrophil count frequently below 500/mm^3. The diagnosis had been confirmed by liver biopsy and biochemical assays. Hypoglycemia was prevented by frequent meals and day and night feeding with uncooked cornstarch.

Physical examination

The patient's weight was 10 kg (below the third percentile) and her height was 80 cm (below the third percentile). The abdomen was distended, the lower edge of liver was palpated 10 cm below the costal margin, with enlargement of the left lobe, and the spleen was palpated 6 cm below the costal margin; cervical lymphadenopathy was noted. Extensive dental caries was noted.

Laboratory findings

Abnormal laboratory tests included: hemoglobin 9.8 g/dl (normal 11.5–15.5); absolute neutrophil count 370/mm^3 (5% of 7400 leukocytes, normal 1500–8000/mm^3); uric acid 6.6 mg/dl (normal up to 5.5); triglycerides 595 mg/dl (normal up to 200); lactic acid 24.1 mg/dl (normal up to 16.0); pyruvic acid 1.7 mg/dl (normal up to 0.8). Blood pH at the time was 7.41, with PCO_2 37 mmHg and bicarbonate 24 mEq/L. Neutrophil function tests showed impaired chemotaxis, impaired superoxide formation after stimulation with formyl-methionyl-leucyl-phenylalanine (FMLP), and suboptimal killing of staphylococci.

Management

Restoration and extraction were performed under general anesthesia due to the young age of the patient, her apprehensive behavior, and the length of the procedure. The patient was not premedicated. Preanesthetic fasting lasted 4 hr, during which intravenous infusion of 10% glucose at a rate of 40 ml/hr was started. The same infusion continued during the operation and after it, until resumption of oral feeding. Monitoring consisted of ECG, noninvasive automatic arterial pressure, pulse oximetry, and CO_2 capnography. Blood samples were drawn through an intravenous cannula for monitoring blood glucose concentrations and acid-base status. Anesthesia was induced with nitrous oxide 70% in oxygen and halothane up to 2.5%, administered by a face mask. After an intravenous administration of atropine 0.15 mg, nasotracheal intubation was accomplished using a 4.0-mm-internal-diameter preformed RAE tube, and the patient was ventilated mechanically. Anesthesia was maintained with nitrous oxide 70% in oxygen and halothane. The patient remained hemodynamically stable, oxygenation and acid-base status were normal, and there were no episodes of hypoglycemia or excessive bleeding from the extraction site. Application of local pressure and biological glue were sufficient to control bleeding from the extraction site. Recovery after the 3.5 hr of anesthesia was uneventful.

The following recommendations and maintenance were proposed: a vigorous oral hygiene plan including instructions of the parents in toothbrushing techniques, hygienist inspection, individual fluoride trays, mouth rinses enriched with fluoride and antimicrobial rinses. In addition, the parents were instructed to schedule 3-month follow-up visits in the dental clinic.

Maintenance

Although the importance of follow-up visits in the dental clinic was stressed to the parents, we have not been able to see the patient because of frequent hospitalizations and poor compliance to dental follow-up. Therefore, 3 years lapsed between the dental treatment and her next dental examination, when oral ulcers had appeared. The oral pathological findings noted were: scaling of the lips (Fig 1), recurrent neutropenic ulceration of the lips and oral mucosa, a large neutropenic

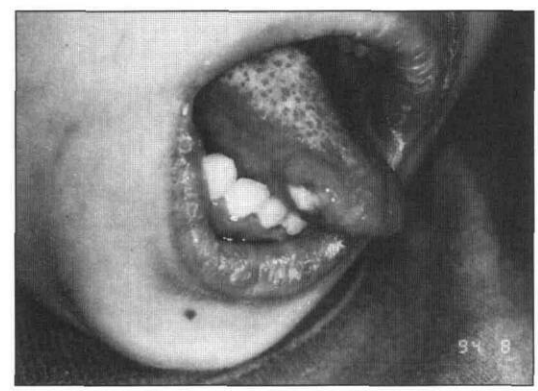

Fig 1: The patient at age 6 years. Note scaling of the lips and the large ulcer on the inferior lateral aspect of the tongue.

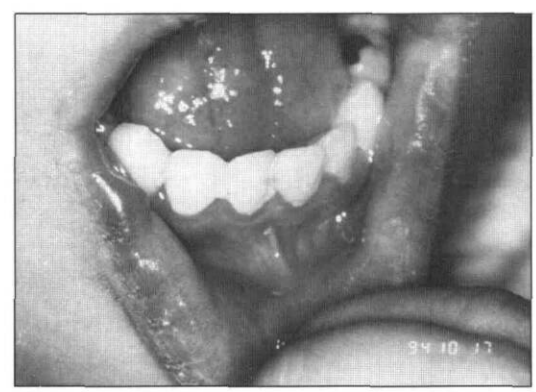

Fig 2: Inflammation of the gingiva at age 6 years.

ulcer (1 cm in diameter) on the right lateral aspect of the tongue, coated on its inferolateral aspect (Fig 1), and gingival inflammation (Fig 2). There was a delay in eruption time, as well as slight hypodontia of the primary teeth. Surprisingly, no caries was observed. The oral ulcers were treated by chlorhexidine 0.2% in aqueous solution mouth rinses, oral nystatin (100,000 units per 5 ml) and oracort E (triamcinolone acetonide 0.1% and esracaine gel), resulting in partial improvement.

Discussion

Specific anesthetic considerations in patients with type 1b GSD include risk of severe perioperative hypoglycemia,[2] lactic acidosis,[2] bleeding tendency[2,6] and immunological deficiency.[7–10] In addition, mental retardation, if present,[2] can disturb anesthetic induction and recovery.

Cannulations should be performed with meticulous attention to aseptic techniques because of the immunological deficiency in these patients.

Blood glucose concentrations must be monitored carefully since hypoglycemia can be severe.[2] Preoperative fasting should be as brief as possible, and glucose-containing fluids, should be administered intravenously perioperatively[13,14] at a rate equal to basal metabolic requirements (4-8 mg/kg body weight/min).[19] Moreover, intraoperative hypoglycemia is potentially unrecognizable,[2] since anesthesia can mask its clinical signs and symptoms. Hypoglycemic convulsions should be anticipated[2] and treated by intravenous infusion of glucose.

Inasmuch as lactate cannot be metabolized completely and converted to glycogen in patients with type 1b GSD,[2] lactic acidosis may develop. Therefore, blood pH should be monitored and lactate-containing fluids (e.g., lactated Ringer) should be avoided in these patients.[2,14] It is preferable to ventilate these patients mechanically during anesthesia rather than permit spontaneous ventilation, since spontaneous ventilation may be inefficient and may lead to respiratory acidosis.[6]

Hyperventilation also should be avoided, as respiratory alkalosis can lead to excessive release of lactate from muscles. Since the lactate cannot be metabolized efficiently in patients with GSD type 1b, it may aggravate the metabolic acidosis.[6] If metabolic acidosis does occur, it should be treated with intravenous administration of sodium bicarbonate according to the base deficit. A peripheral artery should be cannulated for major interventions in these patients to monitor arterial blood acid-base status and glucose concentrations.[14]

The dental surgeon and the anesthesiologist have to consider the possibility of bleeding diathesis in patients with GSD type 1b (see above). Various methods to avoid excessive bleeding during surgery in these patients have been proposed, including meticulous preoperative control of blood glucose concentrations by a regulated diet or total parenteral nutrition.[6] Block anesthesia may be avoided when possible, to prevent bleeding into tissue spaces.[6] Primary closure of extraction sites should be avoided to prevent the formation of hematomata, and bleeding should be controlled by local measures including compression and packing with hemostatic agents such as Gelfoam™ or Surgicel™.[6] The anesthesiologist should be prepared for transfusion of homologous platelets when needed.

Frequent feeding and high carbohydrate diet may lead to development of caries and materia alba accumulation, resulting in enamel decalcification. In addition, chronic metabolic acidosis can contribute to the formation of dental caries. The nature of the caries would be circumferential as seen in rampant caries, especially on the buccal and lingual aspects. Therefore, an intensive oral hygiene plan must be implemented. Fluoride enrichment in the form of trays and mouth rinses also may be added to the maintenance plan. In the case of severe decalcification, crowns are recommended as the treatment of choice. The delayed development of dentition,[5,11,12] rapidly progressive periodontal disease,[4,7,9] and the appearance of oral mucosa ulcerations, which are neutropenic in origin, are characteristic of the disease.[4,10] Oral antimicrobial rinses also may be added. In addition, 3-month follow-up visits in the dental clinic are of paramount importance.

Extraoral manifestations in our patient included hypoglycemia, failure to thrive, hepatomegaly, recurrent infections, neutropenia, impaired neutrophil function, hyperuricemia, and hypertriglyceridemia. Our patient presented with dental caries, which is common in GSD patients mainly because of the excessive amounts of oral glucose used to prevent hypoglycemia. Additional factors such as chronic metabolic acidosis may have contributed to the formation of dental caries.

The perianesthetic course was uneventful. There was no hypoglycemia, acidosis, or major bleeding. It was decided not to cannulate a peripheral artery since the procedure was not a major operation and was without fluid shifts. Blood glucose concentrations and acid-base status were monitored by drawing blood from an intravenously placed cannula; normocapnea was affirmed by capnography. The careful oral feeding by the patient's parents, as well as perioperative glucose supplementation, probably explains the lack of acidosis, since a balanced diet may prevent the production of excess amounts of lactic acid. In addition, the use of uncooked corn starch probably provided the patient with satisfactory glucose supplementation, especially during sleep, since glucose derived from corn starch is slowly and continuously absorbed from the bowel into the blood.

During the follow-up period, delayed tooth development and neutropenic ulceration of the oral mucosa and gingiva appeared. Unexpectedly, no dental caries was observed. Oral lesions were treated by local antiseptic irrigations to prevent secondary bacterial or fungal infections.

Conclusion

In summary, type 1b glycogen storage disease may pose difficult management problems both to the dental surgeon and the anesthesiologist. Careful attention to aseptic techniques, normoglycemia, and acid base status, and awareness of the possibility of bleeding and hematomata formation are needed to overcome these difficulties.

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