European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2015

Letter to the Editor

ORAL MANIFESTATIONS OF GLYCOGEN STORAGE DISEASES

P.F. Carls

Consultant, Oral-Maxillofacial Surgeon, Oxford, UK

Correspondence to:
Dr Peter F. Carls
Consultant, Oral-Maxillofacial Surgeon,
69 Banbury Road,
Oxford, UK
e-mail: carls@doctors.org.uk

Glycogen storage disease was described as autosomal recessive, and sixteen different mutations have been identified in the gene that encodes hepatic glycogen synthase. Glycogen storage disease type I (GTI) is a rare autosomal recessive disorder that leads to deficiencies of glucose-6-phosphatase catalytic activity (Type Ia) and glucose-6-phosphate translocase (Type Ib) (1); this reduces glycogen storage in the liver of GTI patients, due to a lack of glycogen synthase activity, which causes a marked decrease in liver glycogen content. The characteristic element in GTI is the absence of the hepatic isoform of the glycogen synthase enzyme, and it is responsible for the liver transformation of glucose-6-phosphate in the form of a deposit: glycogen (2).

Unlike other forms of glycogen storage diseases, GTI does not involve the storage of excessive or abnormal glycogen: the glycogen stores are moderately decreased in the liver. The symptoms range from asymptomatic hyperglycaemia to recurrent hypoglycaemic seizures. GTI has an extremely low prevalence, currently around 40 cases documented worldwide.

The clinical history in patients with GTI is that of an infant or child who begins to sleep for an uninterrupted night when he or she no longer receives evening or night meals. Patients with GTI also show acute gastrointestinal disorder or other periods of low food intake. Hypoglycaemia is the primary manifestation of hepatic GTI and can have different degrees, from subclinical to sometimes seizures in the morning before breakfast, even though most of the time, children may be asymptomatic. Mild hypoglycaemic episodes may be clinically unrecognized in patients with GTI; other symptoms of subclinical hypoglycaemia are pallor, drowsiness, sweating, and lack of attention. Uncoordinated eye movements, disorientation, seizures, and coma may accompany severe episodes of GTI. Since glucose cannot be stored as liver glycogen, dietary carbohydrate is converted to lactate, and this results in postprandial hyperglycemia and hyperlactacidemia, alternating with fasting hypoglycaemia and hyperketonemia. The liver is not enlarged, and the short stature of GTI patients is common. Gluconeogenesis from amino acids (alanine) and lipid (glycerol) precursors is also altered in GTI patients, contributing to the prolongation and exacerbation of glycemic imbalance (3).

Under prolonged fasting, the patient with GTI can manifest lethargy, loss of consciousness, nausea, vomiting, seizures, and hypoglycaemic coma. The biochemical profile of GTI patients is represented by the specific fasting

Received: 02 June 2015
Accepted: 15 July 2015

ISSN: 2038-4106

hypoglycaemia accompanied by hyperketonemia and normal lactate, hyperglycaemia (with glucosuria) and postprandial hyperlactacidemia. In addition, GTI patients show incapacity to transform glucose into glycogen and redirection to lactate conversion but also hyperlipidemia. After prolonged fasting, the increased concentration of free fatty acids lowers the alanine concentration of GTI patients.

In clinical examination, the only distinctive element of patients with GTI is growth retardation and, consequently, short stature. In addition, discrete hepatomegaly (liver steatosis) and osteopenia were recorded in GTI patients. Recurrent hypoglycaemic episodes can cause developmental delay, cognitive deficits, personality deformities and mental retardation in GTI patients.

Diagnosis methods of GTI are the administration of glucose or galactose and observed elevation of blood lactate and lipid after intake for the definitive diagnosis of GTI liver biopsy that has been replaced by gene mutation analysis, a non-invasive diagnosis method (3).

The management of GTI is simple, accessible, and effective in preventing symptoms and acute and chronic complications. Treatment of GTI consists in keeping a balanced and diversified diet and an organized meals program, with breaks no longer than 2 to 4 hours, rich in complex carbohydrates with low glycemic index and proteins during the day and low in simple carbohydrates, accompanied by a meal of unpacked starches before sleeping or during the night (4)

Oro-maxillo-facial aspects

Oro-maxillo-facial aspects of patients with GTI show a physically and psychologically balanced patient, a slight mismatch between biological and chronological age, with the first dental eruption in deciduous teeth at a normal age but with normal development and a slight delay in the occurrence of 6-year-old molars correlated with delayed bone age. Oral manifestations of the GTI disease present extensive generalized inflammation of the gingiva, erythema, ulceration, and generalized deep periodontal pocketing with bleeding on probing. Generalized severe horizontal bone loss could be noted radiographically. Current evidence indicates that the neutrophil is protective in the periodontium (5). Thus, GTI patients with aberrant neutrophil production or behaviour often have early-onset, severe forms of gingivitis and/or periodontitis, particularly evident in patients whose neutrophils are chemotactically defective. In patients with GTI, dental care should be focused on primary prevention and early recognition of dental and periodontal diseases. Understanding the pathophysiology of GTI will enhance the ability for its clinical management and, hopefully, for the future development of a cure.

Primary prophylaxis of GTI patients involves observing rigorous oral hygiene by performing a dental brush with an electric brush and fluoride kinds of toothpaste (over 1000ppm F) at least twice daily, the duration of a brush being 2 minutes. Antiseptic mouthwashes, dental floss, interdental brushes, or other antimicrobial drugs are also recommended. Considering the child's feeding habits during the night, it is recommended to rinse the oral cavity with clean water immediately after the meal. With the eruption of 6-year-old molars, dental sealings and local fluoridation are indicated to prevent cavities. In conclusion, since children with GTI are much more susceptible to developing periodontal disease, prevention is an effective tool for maintaining good oral health.

REFERENCES

1. Hicks J, Wartchow E, Mierau G. Glycogen Storage Diseases: A Brief Review and Update on Clinical Features, Genetic Abnormalities, Pathologic Features, and Treatment. *Ultrastructural Pathology*. 2011;35(5):183-196. doi:10.3109/01913123.2011.601404
2. Chen Y, Burchell A. *Glycogen Storage Diseases. In the Metabolic and Molecular Bases of Inherited Disease*. (Scriver C, Beaudet, A, Sly W, Valle D, eds.). McGraw-Hill, Inc.; 1995:935-965.
3. Özen H. Glycogen storage diseases: New perspectives. *World Journal of Gastroenterology*. 2007;13(17):2541. doi:10.3748/wjg.v13.i18.2541
4. Heller S, Worona L, Consuelo A. Nutritional Therapy for Glycogen Storage Diseases. *Journal of Pediatric Gastroenterology and Nutrition*. 2008;47(Suppl 1):S15-S21. doi:10.1097/mpg.0b013e3181818ea5
5. Ley K, Laudanna C, Cybulsky MI, Nourshargh S. Getting to the site of inflammation: the leukocyte adhesion cascade updated. *Nature Reviews Immunology*. 2007;7(9):678-689. doi:10.1038/nri2156