Scientific Article

Looking a gift horse in the mouth: effects of cornstarch therapy and other implications of glycogen storage disease on oral hygiene and dentition

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Glycogen, as a storage form of glucose, is an important energy source as well as a vital reservoir for maintaining blood glucose levels. The pathways for synthesis and degradation of glycogen are enzymatically mediated and subject to numerous regulatory factors in order to balance release of free glucose with resynthesis of glycogen. The essential quality of blood glucose support provided by glycogen degradation is nowhere better illustrated than in glycogenosis, type I (von Gierke's disease). This genetic disorder, transmitted as an autosomal recessive trait, results in severe hypoglycemia with fasts of short duration as the consequence of an inability to release free glucose from liver glycogen. Thus, in response to catabolic regulatory stimuli, the liver produces large quantities of glucose-6-phosphate from glycogen, which remain confined to the cell. This phosphorylated compound can be disposed of only by glycolytic cleavage or direct resynthesis of glycogen. The former results in a significant lactic acidemia, the latter in progressive liver enlargement.

At least two distinct genotypes exist within the same general phenotypic presentation of type I glycogenosis. The defect in classic von Gierke's disease is defined as a deficiency of the enzyme glucose-6-phosphatase, which mediates cleavage of the phosphate bond with production of free glucose. This disorder is classified as type IA glycogenosis. The second abnormal genotype, termed type IB, is now well-described and results in deficiency of a protein called translocase,[1,2] which is responsible for the transport of glucose-6-phosphate across the microsomal membrane where it becomes accessible to phosphatase. Affected patients share the clinical features of type IA disease, and also suffer from increased susceptibility to pyogenic organisms and bleeding tendencies due to leukocyte[3] and platelet[4] dysfunctions, respectively.

The basis for the granulocytic dysfunction is the cumulative effect of impairments in respiratory burst activity, oxygen consumption, and hexose monophosphate shunt activity.[5] The basis for the platelet dysfunction is poorly understood, but alteration in cellular glycoprotein synthesis has been suggested.[6]

The chief principle of treatment is maintaining a constant source of blood glucose other than endogenous glycogen, ideally as close to absolute requirements as possible in order to minimize additional glycogen synthesis. In very young infants, this is achieved by frequent daytime feedings and continuous overnight nasogastric feedings.[7] Overall, the diet should be adjusted to provide decreased lipid and increased carbohydrate.[8] In children older than 2 years, current therapy is cornstarch supplementation of the diet to provide a source of free glucose, liberated slowly in the gastrointestinal tract by the action of pancreatic amylase.[9] The quantity used is determined by the need to equal or slightly exceed hepatic glucose production rates. Cornstarch is mixed with water or a sucrose- and lactose-free liquid and consumed as a beverage at 3-hr intervals around the clock. Cornstarch use in young infants is not recommended because of unreliable pancreatic amylase secretion.

Cornstarch therapy is known to be efficacious in preventing hypoglycemia, while eliminating the need for the physical and emotional trauma of nasogastric intubation on a nightly basis. However, such treatment in the presence of compromised resistance to pyogenic organisms can have significant implications for oral hygiene and dentition. This report relates our experience with a child with type IB glycogenosis, in whom the combination of frequent pyogenic infections and cornstarch treatment created major oral health problems.

Case report

Medical history

The patient is a white female, diagnosed clinically at the age of 6 months as having type I glycogen storage disease. Enzymatic confirmation of this diagnosis was achieved at age 16 months, with specific studies documenting type IB disease. The delay in enzymatic diagnosis was intentional, in order to allow time for growth and therapeutic stability, since an open-liver biopsy was required for tissue sampling. The glucose-6-phosphatase must be assayed before and after detergent treatment of the tissue homogenate in order to differentiate between types Ia and Ib. Thus, approximately 1g of liver tissue is required.

Initial treatment consisted of frequent daytime feedings, with continuous nasogastric feeding of a lactose- and sucrose-free formula for 8 hr over night. From the age of 8 months, she began experiencing recurrent otitis media, possibly a result of the partial obstruction introduced by the nasogastric tube. This was treated with a variety of antibiotics; at that time, six primary anterior teeth were present and in excellent condition. Growth remained excellent, with height and weight at 11 months at the 20th and 50th percentiles, respectively. Due to problems maintaining the continuous nasogastric feeds, cornstarch therapy was initiated at 18 months, earlier than recommended. Nonetheless, she did well on this regimen, experiencing very few hypoglycemic episodes for the next several months. Since diagnosis, the caloric distribution of her diet has been as follows: 65–70% carbohydrate, 10–13% fat, and 20–25% protein.

From 18–21 months, the child suffered from acute and chronic bouts of otitis media, requiring almost constant antibiotic therapy and resulting in multiple episodes of oral thrush. This adversely impacted her oral intake, resulting in poor weight gain. By 23 months of age this cycle had begun to cause significant gingivitis, compounded by ineffectual leukocytic response. She underwent bilateral myringotomy at 25 months for relief of the middle ear problems, with a dramatic improvement in her general health, appetite, and growth, which persisted until 42 months when she began experiencing increased mouth breathing and breathing obstruction. At 51 months she underwent a tonsillectomy and adenoidectomy with removal of "huge, obstructing" tonsils. Her general health and development subsequently have been good. At this writing she is 9 years, 9 months old and attending school regularly in an age-appropriate class.

Dental history

The child was initially referred to the dental service at 18 months of age because of oral pain and recurrent oral soft tissue ulcers. The latter were present on the gingiva, mucobuccal folds, and palate. By history, the ulcers recurred in 30-day cycles. An oral suspension of equal parts of milk of magnesia, elixir of Benadryl™ (Parke-Davis, Morris Plains, NJ) and viscous Xylocaine™ (Astra Pharmaceuticals, Westboro, MA) (triple rinse) was applied topically with a cotton applicator to the lesions several times each day to relieve pain. Within one week the lesions had diminished and the tissue was healing. The diagnosis of herpetic etiology was not confirmed by culture.

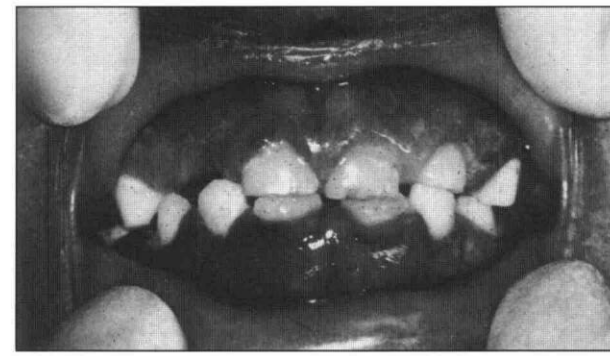

Fig 1. Plaque and materia alba around gingival margin of teeth with resultant decalcification and smooth surface caries development.

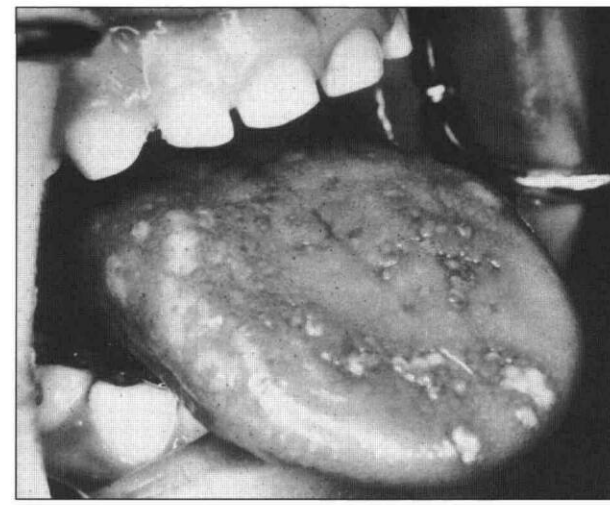

Fig 2. Herpetiform lesions on the tongue.

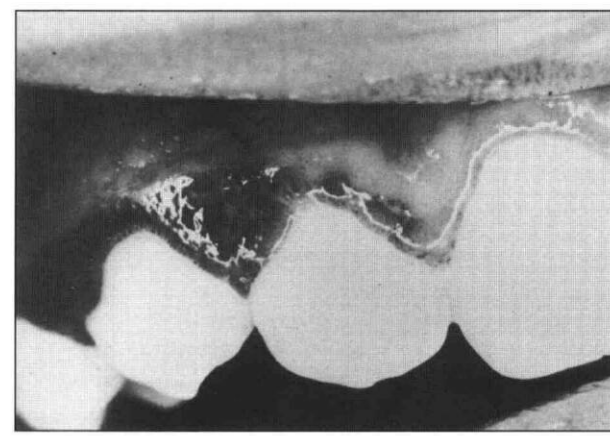

Fig 3. Acute marginal gingivitis and herpetic-type lesions noted above the marginal tissue.

At 21 months, the child was again seen because of oral ulcers and a right-sided facial swelling. Numerous ulcers were present on the lips, gingiva, tongue, mucobuccal fold, and palate extending to the midline (Figs 1–3). The child was febrile and uncomfortable. A 7-day course of amoxicillin was started and triple rinse again prescribed for topical use on the lesions. A 7-day topical course of acyclovir was initiated empirically. Within 3 days the lesions were healing and the facial swelling had decreased. At that time, although oral hygiene was poor and the teeth continually coated with white milky plaque from cornstarch, there was no evidence of dental caries.

At 30 months the child experienced swelling and inflammation in the area of the erupting second primary molars. A 7-day course of amoxicillin was begun because of the possibility of a secondary infection. At this time the teeth were covered with a white plaque of cornstarch. Plaque removal revealed extensive areas of enamel decalcification (Fig 1) appearing as white bands on the smooth surfaces of teeth at the gingival margin. Several posterior teeth had occlusal and interproximal decay.

The child's behavior, the extent of the treatment, previously reported cases of prolonged and severe bleeding following dental extraction,[4] and concern for medical management of the child in the clinic under heavy sedation mandated admission to hospital and general anesthesia. She tolerated the procedure well and postoperative recovery was uneventful. Three weeks later a hard swelling was noted in the left cheek and intraoral rednesss and swelling noted in the left mucobuccal fold in the area of the maxillary left primary canine and first primary molar. These teeth were extracted and the child placed on penicillin V for 10 days.

The child has been seen regularly at 3- to 4-month intervals and care has been provided in the dental clinic using nitrous oxide analgesia during restorative treatment. The oral ulcers continue to recur in approximately 30-day cycles. Acyclovir applied topically has been effective in reducing the severity of the lesions and is applied as soon as the ulcers make their appearance. With age, the child has become better able to identify their onset, which has made this therapy more effective. She also is able to use the triple rinse as a rinse and expectorant, which provides better coverage of the lesions before each meal.

At age 9 she is still very timid regarding dental appointments but is cooperative for treatment. Oral hygiene is improved and although new carious lesions have occurred, rampant decay has been prevented.

Discussion

Due to the increased susceptibility to pyogenic organisms, the need for antibiotic therapy, the inherent difficulties in maintaining oral hygiene in a young child, and the predictable consequences for the dental health of the child, type IB glycogenosis presents a difficult therapeutic dilemma as illustrated by this case. While these factors, practically implicit in the diagnosis, contribute to development of gingivitis, periodontal disease, and bone loss, the current therapeutic regimen of frequent high-carbohydrate meals and cornstarch supplementation compounds the problem by encouraging dental caries. Although sucrose is the carbohydrate usually implicated in caries formation, cornstarch is hydrolyzed to a fermentable carbohydrate. The frequency of exposure and the adhesiveness of the carbohydrate substrate were clearly major factors that influenced the clinical course of this child. In our patient, these problems progressed to the point of requiring extensive restorative dental care and otolaryngologic surgery to alleviate the need for persistent antibiotic therapy.

Any decision to proceed with surgical intervention in patients with type IB glycogenosis must be tempered by considering the inherent platelet dysfunction and the propensity to develop severe and life-threatening hypoglycemia. Although our patient underwent several such procedures successfully, the potential for intraoperative bleeding and/or severe hypoglycemia with cerebral edema always must be considered. It should be pointed out that this potential would preclude any routine dental office procedure that requires interrupting the usual dietary regimen. Restoration and maintenance of dental integrity requires constant vigilance and scrupulous attention to oral hygiene, an effort that can only be successful with full parental understanding and participation.

When the child was first seen, although large amounts of materia alba and plaque were seen on the teeth, decay was not a problem. Due to the extensive cervical decalcification and decay, primary molars were restored with stainless steel crowns. Anterior teeth were restored with composite resins for aesthetic reasons. The frequent feedings and problems with oral hygiene make full coverage of teeth in the primary dentition the treatment of choice. The added technical difficulty and cost of full-coverage restorations in the permanent dentition make an aggressive oral hygiene program all the more important. Home care has been difficult because the high starch diet leaves the teeth covered with a white film most of the time. The child's tooth brushing has greatly improved but brushing is not feasible after every starch dosage. Custom fluoride trays have been made to permit home application of topical fluoride. The frequent use of fluorides is intended to reduce enamel decalcification and to improve enamel remineralization. Dental sealants have been applied to the occlusal surfaces of the molars to prevent decay in these areas.

To our knowledge, this is the first report of the dental implications of cornstarch therapy in glycogen storage disease. Since survival after diagnosis is generally long term,[10,11] pediatricians and dentists need to be alert

to this aspect of medical care. Moreover, this case clearly illustrates the absolute need for close cooperation between general pediatrician, dentist, otolaryngologist, and anesthesiologist in order to safely accomplish otherwise fairly routine procedures. In such patients, prolonged dental chair anesthesia poses a threat to survival. Thus, in management of cases where such close interaction is not easily accomplished, we recommend that the patient be referred to an academic center whenever anesthesia and/or surgery is contemplated.

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From the Archives

The cost of cognitive activity

Cerebral Origin of Dental Decay. Hard-working students force the growth of their intellectual capacity at the expense of their teeth.... It is said that the teeth undergo a rapid alteration in students who labor long, and that on the cessation of the hard work the dental disease dies away..... It is thought that the brain when overworked, steals all the phosphates, and leaves none for the teeth, or else that a deterioration of the general health is brought about by the excessive study. Now, it is certainly a matter for consideration whether excessive mental work per se is capable of inducing serious disease. Side by side with natural mental life there probably goes on more or less unhealthy action, which bears pretty much the same relation to the former as the latter does to the friction on a steam engine. What is friction in the engine is anxiety or worry in the man. So, then, all cerebral action is accompanied by the inevitable residue of anxiety or whatever else we choose to call it, but this residue may be lessened by various circumstances, and may be augmented by many conditions; and so it is that of two men of equal original health and equal original powers, but of dissimilar environment, the one succumbs because the heat of frictional anxiety has consumed him, the other lives longer because the obstacles to his vital acceptation of the first law of motion have been reduced to a minimum.

from *Lancet*, 1883