



Importance of Early Dental Care in a Child with Niemann-Pick Disease, Type C

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Abstract

Niemann Pick disease is an autosomal recessive neurodegenerative disorder produced by an accumulation of intracellular cholesterol in lysosomes and endosomes. It manifests in middle-to-late childhood and provokes ataxia, dysarthria, dysphagia (making oral nutrition difficult), hypotonia, spasticity, seizures and developmental abnormalities, which means that maintaining oral hygiene is difficult. A six-year-old girl diagnosed with Niemann Pick type C, currently treated with 2-hydroxypropyl-beta-cyclodextrin-intrathecal. Her oral health has been managed for 4 years applying the caries management by risk assessment (CAMBRA) preventive protocol. Through oral hygiene maintenance at home (good brushing technique, and 0.12% chlorhexidine mouthwash) and three-monthly plaque check-ups and fluoride varnish applications, the child has remained free of caries. From the outset, treatment has included psychological management with the help of the patient's mother. The use of preventative protocols makes it possible to manage the oral health of children with Niemann Pick disease. The help and participation of the family are essential to the oral health and psychological management of children with this disease.

Abbreviations

CAMBRA: Caries Management by Risk Assessment; NPC: Niemann-Pick Disease Type C; HPBCD: Hydroxypropyl-Beta-Cyclodextrin; ICDAS: The International Caries Detection & Assessment System; DMEM: Dulbecco's Modified Eagle's Medium

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Introduction

Niemann-Pick disease type C (NPC) is an autosomal recessive neurodegenerative disorder caused by the mutation of two genes. In 95% of families, it is caused by mutations in the NPC1 gene, whose cytogenetic location is 18q11.2, NPC type 1 (257220). In the remaining 5% of families, it is produced by mutations in the gene NCP2, with cytogenetic location 14q24.3, NPC type 2 (607625). Its minimum incidence is estimated to be 1:150,000 of newborn live babies in Western Europe, and usually manifests in middle-to-late childhood. The clinical manifestations are similar in both types of NPC, as they are produced by intracellular transportation of endocytosed cholesterol with sequestration of unesterified cholesterol in lysosomes and late endosomes. This provokes an accumulation of cholesterol and sphingolipids in particular organs. Niemann Pick Type D is a specific form of NPC 1 in patients of Nova Scotia Acadian ancestry. Niemann-Pick disease type A and B are different and provoked by deficits in sphingomyelinase activity [1]. The accumulation of lipids in the liver can provoke severe hepatic disease with hepatosplenomegaly and cirrhosis. If they accumulate in the lungs they can cause respiratory failure. The accumulation of glycosphingolipids is typical in cases with neurological disorders such as ataxia, dysarthria, dysphagia (making oral nutrition difficult), hypotonia, spasticity, seizures and developmental abnormalities that can lead to dementia. Death occurs in the late second or third decade of life but may occur sooner [2,3]. Caries is a multifactorial disease and its development is determined by the teeth themselves, the bacterial ecosystem, diet and oral hygiene habits. Any change in these factors can affect individual susceptibility, risk, and caries activity [4]. As in the case of special patients, prompt dental care of patients with rare diseases will help them to enjoy a better quality of life. This will allow early diagnosis of oral diseases, and the use of preventative protocols can avoid the appearance of pathologies and facilitate and simplify the clinical management of these patients.



Figure 1: Front and lateral radiographs of the head were it can see the Ommaya reservoir. The intrathecal treatment with hydroxypropyl-beta-cyclodextrin (HPBCD) is placed.



Figure 2: Protrusion in upper jaw and gingivitis in lower jaw. The child has frequent tartar formation on the second molars.



Figure 3: As soon as the deciduous teeth, 7.1 and 8.1, were extracted, they were submerged in Dulbecco's Modified Eagle's medium (DMEM) for later investigation of Niemann-Pick type C disease.

Case Presentation

Medical history

A Caucasian girl of 6 years of age was first referred to the University of Murcia Dental Clinic 4 years ago. Without family antecedents, she was diagnosed with Niemann Pick disease type C at the age of two at the Virgen de la Arrixaca University Hospital (Murcia, Spain).

She presented encephalopathy, seizures controlled by medication, psychomotor retardation, dysphagia, and spastic tetraparesis. The girl received enteral nutrition via a gastronomy tube.

Since diagnosis the patient had been medicated with miglustat (glucosylceramide synthase inhibitor). Due to the poor neurological evolution of the disease, authorization was requested from the Spanish Ministry of Health to begin compassionate treatment with intrathecal hydroxypropyl-beta-cyclodextrin (HPBCD). She has been treated with this experimental drug since April 13th 2012, which she receives 400 mg every 15 days, in an Ommaya reservoir (Figure 1) with local analgesia without sedation; the patient has suffered no incident or complications arising from sedation, or secondary effects or allergy to the medication. During the last few months, the child has begun to take small amounts of puréed food, although not every day.

Dental history

Clinical examination found that the child presented dental development compatible with her age, acute gingivitis (Figure 2), hyposalivation with thick saliva, and frequent tartar formation on the second molars. The International Caries Detection & Assessment System (ICDAS) was used to diagnose caries, finding that she did not present caries. The CAMBRA method was also used to evaluate the risk of caries and to elaborate a treatment plan.

Discussion

For children with systemic disease that make oral hygiene maintenance difficult it is important to manage dental health care from an early age, using preventative dental protocols to avoid future restorative treatment and to provide a better quality of life. These systemically compromised patients attend frequent hospital appointments in which they undergo numerous clinical tests, a situation which compromises their behavior when it comes to dental health care. At the first appointment, it was decided not to use any type of drug-based management but to use psychological management as a technique for managing her behavior. Although the child suffered neurological deterioration and could not speak, her understanding was sufficient to permit this approach. The presence and help of her mother was fundamental to attending to the patient, as she was able to assist communication with the patient.

The patient remained in her wheelchair, which avoided any need for her to get used to a new 'environment' that might affect her behavior. The behavior management techniques used included a combination of desensitization, 'tell-show-do,' non-verbal communication, and voice control. The fact that the child did not need invasive treatment facilitated management, although there were moments when she broke down in tears.

According to the CAMBRA protocol, the child is considered a high-risk patient [4]. For the last 4 years, since she was first referred to the clinic, she has received preventative dental treatment every three months. She and her parents have been instructed in oral health care, correct tooth brushing techniques and 0.12% chlorhexidine application to manage gingivitis [5]. Manual prophylaxis is performed manually with curettes and fluoride varnish is applied every 3 months.

Caries management is carried out by visual examination, as no

bite plate radiograph has been taken due to the family's unwillingness for their daughter to undergo any more X-rays as she has undergone numerous general X-rays over the years.

Four years on, the girl has remained free of caries, although gingivitis management has produced less positive outcomes due to the fact that the patient is not fed by mouth and presents a low saliva production, accompanied by a Angle Class II malocclusion.

As the patient presents dysphagia, to prevent possible aspiration deciduous teeth were extracted as soon as the parents noticed slight mobility of a tooth. A chronological disorder has occurred in exfoliation; the first tooth lost was 6.1, followed by 5.1. The last teeth to be extracted were 7.1 and 8.1 (Figure 3). As soon as they had been extracted they were submerged in Dulbecco's Modified Eagle's Medium (DMEM) for later investigation of Niemann-Pick type C stem cells. On the same day, the normal eruption of 1.1 and 2.1 was observed. Extractions were performed infiltrating 2% Lidocaine and epinephrine 1:100.000, after topical anaesthesia with Hurracaine®. The extractions were performed without difficulty as the child was attending the clinic every three months and was always seen by the same dentist, which has helped her to get used to the clinic and staff. Although the child does not speak, she recognizes the dentist, and her facial expressions and reactions are interpreted by the mother.

Conclusions

1. Child patients with rare diseases that cause physical impairments must attend the pediatric dental clinic as young as possible to receive three-monthly program of preventative measures, as these patients are at high risk from caries.

2. Oral preventative protocols are of fundamental importance to the avoidance of more complicated restorative treatment; they will also help patients to have a better quality of life. The participation and help of parents in oral hygiene maintenance is essential and parents should be instructed to this end.

3. In children with Niemann Pick type C disease, extraction of deciduous teeth should be performed as soon as the mobility of each tooth is noticed in order to avoid possible aspiration due to the dysphagia that these patients present.

Declarations

Ethics approval and consent to participate

The Research Ethics Committee of the University of Murcia considers that this case report is exempt from ethical approval (Ref: 1361/2016).

The girl's mother signed the informed consent of the Dental Clinic of the University of Murcia before starting the implementation of the CAMBRA protocol.

Acknowledgement

We are grateful to child's family for trusting us. She died January, 3, 2017 with 7 years old.

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