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Sanfilippo syndrome type III B – medical clinical and dental implications: Case report

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Abstract

The Sanfilippo Syndrome subtype IIIB is an autosomal recessive disorder caused by deficiency of the lysosomal enzyme alpha N-acetylglucosaminidase. This syndrome comes under the umbrella of Mucopolysaccharidosis (MPS), a group of seven inherited metabolic disorders characterized by the deficiency catalysing the degradation of Glycosaminoglycans (GAG) or Mucopolysaccharides. MPS Type III is otherwise known as Sanfilippo Syndrome, with five subtypes. Two male siblings, aged 9 and 10, from consanguineous marriage of an Arab family, attended the Pedodontic Clinic at Al Ahsa Dental Centre, Hofuf, Saudi Arabia. On examination, the dental findings were strikingly similar, inclusive of enamel breakdown, multiple carious teeth with pulpal involvement, macroglossia, to name a few. This case report documents the medical findings, clinical features and dental findings affected with the rare Sanfilippo Syndrome (MPS IIIB).

Keywords: Sanfilippo syndrome, Genetic Disorder, Glycosaminoglycans, Childhood disability

Introduction

Mucopolysaccharidosis (MPS) are a group of genetic metabolic disorders resulting from the absence or defect of acid hydrolase, a lysosomal enzyme that is required to breakdown sulphated Glycosaminoglycans (GAG) or Mucopolysaccharides. GAGs are a series of long chains of sugar carbohydrates that are present on both cell surfaces and in the extra cellular matrix in all tissues such as heparan sulphate, keratin sulphate, chondroitin sulphate etc. Due to the deficiency of lysosomal enzymes, GAGs accumulate in the cells, blood and

connective tissue and subsequently result in cellular damage and tissue/organ dysfunction.[5].

According to the National Organization for Rare Disorders (NORD), there are nine subdivisions of MPS, namely: 1. MPS I H/S (Hurler/Scheie Syndrome), 2. MPS I H (Hurler Syndrome), 3. MPS II – Hunter Syndrome, 4. MPS III A, B, C, D, E (Sanfilippo Syndrome), 5. MPS I S (Scheie Syndrome), 6. MPS IV A&B (Morquio Syndrome), 7. MPS IX (Hyaluronidase deficiency), 8. MPS VII (Sly syndrome), 9. MPS VI (Maroteaux-Lamy Syndrome).[12]

The following case report aims to present and discuss about MPS III B (Sanfilippo Syndrome - OMIM number - #252920). Discovered in 1963 by Dr. Sylvester Sanfilippo, this syndrome is found to be an inherited autosomal recessive disorder caused by a deficiency of one of four enzymes involved in the degradation of the glycosaminoglycan heparan sulphate. As mentioned above, there are five subtypes – A, B, C, D and E[7]. Sanfilippo type A was the most frequent subtype accounting for 1 in 114,000 live births, followed by type B[15]. All MPS disorders are said to be caused by a recessive gene inheritance with the exception of MPS II (Hunter Syndrome), which is X-linked.[4]

MPS IIIB is caused by a deficiency of the lysosomal enzyme alpha- N- acetylglucosaminidase (NAG), which catalyses the removal of terminal alpha-N-acetylglucosamine residues from heparan sulphate. In the absence of NAG, the partially degraded heparan sulphate accumulates in the tissues and is excreted in the urine[2].

Case report

Here we report the case of two siblings from an Arab family, who visited the Pedodontic Clinic at Al Ahsa Dental Centre, Hofuf, Saudi Arabia.

Patient 1, aged 9, visited the clinic in 2016, with the chief complaint of bleeding from the gingiva. On examination, poor oral hygiene, carious primary molars, enamel breakdown on almost all teeth as well as moderate gingival hyperplasia were observed. According to the anamnesis obtained, the patient had been diagnosed with Sanfilippo Syndrome IIIB, similar to his older brother. The mother had a normal delivery and the child was reportedly normal until about 2.5 years. Later his condition deteriorated steadily. He underwent several hospital admissions in the past due to hypoactivity, reduced oral intake, hypertension, seizures, moderate mental retardation, dysplastic aortic valve with moderate aortic regurgitation. He was under treatment for all the above and came to the Clinic only once. Due to extreme uncooperative behaviour as well as considering the debilitated condition of the patient, we performed only hand scaling under antibiotic prophylaxis. The parent was instructed to perform meticulous oral hygiene practices, including use of minimal amount of tooth paste on a gauze piece and wiping the tooth surfaces subsequently. He is currently on Lasix 30mg bid and Captopril 12.5mg bid, along with oxygen support and NGT feeding.

Patient 2, aged 10, visited the clinic in 2016, was the older of the 2 siblings, more cooperative and active than his younger brother. According to the anamnesis reported, this child also had a normal delivery and his milestones were relatively normal till age 3, after which it slowly declined. By age 5, he became immobile and required wheel chair. He has been reported to have ADHD, VSD, profound language impairment, epilepsy, limited mobility, joint malformations and hepatosplenomegaly. His chief complaint was multiple carious teeth and generalized gingivitis. Scaling was performed as well as glass ionomer restorations on molar

teeth. Oral hygiene instructions were explained to the parent, verbally as well as in the form of booklet. He is currently under Depakene 125 mg (Sodium valproate).

Both children presented with similar physical characteristics, typical of Sanfilippo syndrome. Intra oral examination revealed severe gingivitis, malocclusion, macroglossia, open bite and multiple decayed teeth. The children were periodically recalled; however, Patient 1 became oxygen-dependent soon after a complex respiratory distress and hence was unable to visit the Clinic further. Patient 2 frequented the Clinic on a 6 monthly basis and we performed further preventive regimens including sealants on all first molars as well as hand scaling. His last visit was in July 2020. Parent was instructed to use Chlorhexidine gluconate 0.2% on a dipped gauze piece and applied onto the gingiva once every day, followed by wiping with plain water-soaked cotton.

Discussion

Sanfilippo syndrome (MPS III) refers to one of five autosomal recessive neurodegenerative lysosomal storage disorders (LSD), where the symptoms are attributed to the incomplete lysosomal degradation of heparan sulfate. The subtypes are caused by the deficiency of: a) sulfamidase (MPS III A)., b) alpha N-acetylglucosaminidase (NAGLU, MPS III B)., c) heparin acetyl Co A: alphaglucosaminide N-acetyltransferase (HGSNAT, MPS III C)., d) N-acetylglucosamine 6-sulfatase (GNS, MPS III D)., e) N –glucosamine 3 -0-sulfatase (arylsulfatase G or ARSG, the currently considered MPS III E)[7.] All subtypes are inherited by an autosomal recessive trait; signs, symptoms and the course of the disease in the different subtypes are almost indistinguishable[1].

The primary characteristic of Sanfilippo syndrome is the degeneration of the central nervous system, resulting in mental retardation and hyperactivity[7]. Most of the affected children exhibit a normal development until one year of age, sometimes till 3 years[8], followed by motor and speech delay, behavioural problems (similar to Autism) and facial dysmorphisms[1]. The clinical course of MPS III can be divided into 3 phases, the first starting between 1&4 years of life, manifesting in developmental delay after an initial normal development[2]. This was true in case of both our patients. The second phase starts around 3 to 4 years and is characterized by severe behavioural problems and progressive mental deterioration. In the third phase, behavioural problems slowly disappear, but motor degradation with swallowing difficulties and spasticity emerge[2]. Our Patient 2 is currently in the third phase of MPS III. Patient 1 is in a thoroughly debilitated stage at present.

As early as 1977, Webman et al had described dental abnormalities, inclusive of obliterated pulp chambers and canals, in this disorder[13]. Since then, a wide range of craniofacial and dental abnormalities have been described[4]. The main observation thus far on all the LSDs are that of poor oral hygiene, high prevalence of caries, gingivitis and significant loss of teeth[6]. In the present cases also, similar findings were noted. Administrations of pureed food substance that easily adhere to tooth surfaces accelerate cariogenicity in these children. In addition, these patients also suffer from retching, choking and gastro oesophageal reflux with regurgitation of the gastric contents into the mouth. Exposure to constant gastric acid may be the cause of damage to the enamel surfaces. Reduced dietary option may lead to further nutritional deficiency. Abnormalities in facial skeleton, cleft lip & palate, missing/abnormal/extra teeth have also been observed[6].

The main medical/clinical features of this syndrome include short stature, macrocephaly, coarse facies,

umbilical and inguinal hernias, developmental delay, skeletal dysplasia with dysostosis multiplex, limited joint mobility, hearing loss, ocular involvement, neurodegeneration with dementia, heart diseases, respiratory distress and hepatosplenomegaly. Oral features commonly reported are thick lips, microdontia, anterior open bite, tongue protrusion, enlargement of alveolar process, gingival hyperplasia, diastema, macroglossia, high arched palate and condylar defects. Also, malocclusions, delayed eruption of teeth, cystic lesion or enlargement of the dental follicle have been recorded[10]. In the present case report, the Patient 1 had been found to be hypoactive, whereas in patient 2, hyperactivity had been observed. We could not follow up much on Patient 1, as he took a downhill course quickly and became oxygen-dependent. But Patient 2, has been a regular visitor to the Clinic and we had performed restorations and preventive applications.

Since these patients do require special care, it is essential to educate the parents to provide good oral hygiene, regular dental visits as well as preventive applications[10]. As there are difficulties with intubation in these patients, due to a Mallampatti score of 4, Sedoanalgesia has been carried out successfully, according to literature[11]. Complex procedures requiring general anaesthesia tend to be high risk in these patients.[10]. In conclusion, patients with Sanfilippo Syndrome suffer from poor dental and gingival status as well as inadequate oral hygiene. The severity of these problems is often directly proportional to the degree of disability associated [6].

Thus far, there are no effective treatments for Sanfilippo Syndrome. But to name a few, enzyme replacement therapy, Genistein treatment[16], hematopoietic cell transplantation, gene therapy and substrate deprivation therapy have been tried[11].

Conclusion:

Patients with an MPS disorder represent a challenge to treat due to the complicated medical and physical disabilities. The management of dental and periodontal diseases in these patients can be extremely laborious in the conscious patient and as such presents a decreased quality of life. It is therefore imperative for paediatric dentists, to have an in-depth comprehension regarding various rare syndromes, their medical manifestations, further progression, as well as the dental implications, in the hope of providing adequate oral care for such children.

Figure: 1

Figure: 2

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