Understanding Sanfilippo Syndrome: A Case Report with Contemporary Literature Review

N Espinal[1], J Esmaelsadah[1], K K Patterson[2]

1 Third Year Dental Student, Stony Brook University School of Dental Medicine, Stony Brook NY

2 Department of Orthodontics and Pediatric Dentistry, Stony Brook University School of Dental Medicine

ABSTRACT

Dementia is a word often associated with the elderly population however, a type of dementia can affect the pediatric population in a rare genetic condition known as Sanfilippo syndrome.

Sanfilippo syndrome, also known as mucopolysaccharidosis (MPS) type III, is an autosomal recessive metabolic disorder resulting in deterioration of the central nervous system due to lack of enzymes that break down heparan sulfate.

Accumulation of heparan sulfate can lead to clinical symptoms in children often disregarded or misinterpreted by healthcare providers as uncooperative behavior.

This case report describes a 16-year-old male affected by Sanfilippo syndrome manifesting hyperactive, aggressive, and agitated behavior combined with lack of motor skills.

Contemporary literature review regarding Sanfilippo syndrome is also presented.

SANFILIPPO SYNDROME OVERVIEW

Sanfilippo syndrome also known as mucopolysaccharidosis type III (MPS III) is a rare genetic disorder affecting the body's ability to break down heparan sulfate, a glycosaminoglycan, due to a deficiency in lysosomal enzymes.

MPS III Subtype	Phenotype MIM No.	Affected Gene			Deficient Enzyme		
		Name	Location	Locus MIM No.	Name(s)		EC No.
					UniProtKB	Alternative	
IIIA	252900	*SGSH*	17q25.3	605,270	*N*-Sulpho-glucosamine sulphohydrolase	Heparan-*N*-sulfatase; sulfamidase; sulfamate sulfohydrolase	3.10.1.1
IIIB	252920	*NAGLU*	17q21.2	609,701	α-*N*-Acetyl-glucosaminidase	*N*-acetyl-α-D-glucosaminidase	3.2.1.50
IIIC	252930	*HGSNAT*	8p11.21-p11.1	610,453	Heparan-α-glucosaminide-*N*-acetyl-transferase	Acetyl CoA:α-glucosamine-*N*-acetyltransferase	2.3.1.78
IIID	252940	*GNS*	12q14.3	607,664	*N*-Acetyl-glucosamine-6-sulfatase	Glucosamine-6-sulfatase	3.1.6.14
IIIE	NG[a]	*ARSG*	17q24.2	610,008	*N*-Glucosamine-3-*O*-sulfatase	Arylsulfatase G	3.1.6.15

Notes: [a]NG, not given. Phenotype MIM No. has not been given for MPS IIIE as this disease was identified to date only in the constructed mouse model, and no human patients were described yet.

Figure 1: Subtypes of Sanfilippo Syndrome (Mucopolysaccharidosis Type III; MPS III)[1]

Incidence of Sanfilippo syndrome varies depending on the subtype and geographic region, but on average is around 1:70,000 live births.[2]

Deficiencies in these enzymes result in buildup of heparan sulfate in the body's cells which, over time, causes progressive damage to brain and other organs and can lead to childhood dementia.[2]

Sanfilippo syndrome is characterized by developmental delay, hyperactivity, sleep disturbances, and speech impairment all appearing in early childhood. Other symptoms may include seizures, hearing loss, vision problems, and joint stiffness. Sanfilippo syndrome type A is considered the most aggressive form, with patients surviving until 15–18 years old on average.[2]

CASE REPORT: MEDICAL HISTORY

- 16-year-old Asian male, adopted at age 5 yrs
- Sanfilippo syndrome type C
- Presented with adoptive mother to SBUSDM June 2021
- Mother's chief complaint: "I cannot find a provider who will treat my son, he has some baby teeth that have not fallen out yet."
- 4'9" and 107 lbs = BMI 23.2, 78th percentile for age/sex, normal BMI for age

- macrocephalic
- ADHD
- developmental delay
- non-verbal
- aortic insufficiency
- dilated aortic root
- scoliosis
- heart murmur
- reactive airway disease

MEDICATIONS:
- acetazolamide
- Claritin
- Flonase
- Melatonin
- multivitamin

CASE REPORT: DENTAL HISTORY

- Mother reports brushing patient's teeth twice a day, cooperativity varies
- Ceased use of fluoridated mouthwash due to patient swallowing product
- Permanent dentition, no third molars erupted
- Generalized moderate edema
- Gross caries #E, 19-OB, 29-O, and 31-O
- Over-retained primary teeth #D, E, F, G
- Oral rehabilitation in the operating room setting under general anesthesia

Due to patient's inability to cooperate in the office setting, multiple caries and required extractions of over-retained primary teeth, treatment in the operating room setting using general anesthesia was required (Figure 2).

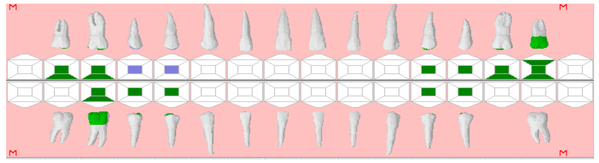


Figure 2: treatment rendered in OR setting with extractions of retained D, E, F, G

Radiographs revealed caries, calculus mesial tooth #30, moderately crowded maxillary anterior dentition, and developing third molars.

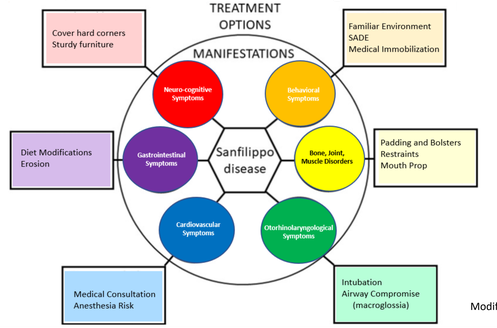
Patient was placed on prescription home fluoride dentifrice and 6 month recall and preventive plan.

LITERATURE REVIEW

Neurologic symptoms may appear as other diagnoses such as ADHD or autism. Misdiagnosis may be attributable to newborn screenings not being specific. Behavioral outbursts involving screaming, crying fits and aggressive behaviors may be response to sensitivity to touch, temperature changes or anxiety. A safe dental environment and routine in the dental office is beneficial for behavioral management.[3]

Dental manifestations may include obliteration of pulp chambers and irregular pulpal morphology.[4] Comorbidities with cardiac issues and airway compromise affect general anesthesia delivery.[3]

Oral hygiene aids such as a three-sided toothbrush, bite block and distraction techniques can be of benefit both at home and in office. Emphasis of care with caregivers is key.[3] A calming environment as in a Sensory-adapted dental environment (SADE) benefits in-office behavior guidance. [5]



Modified from Cyske et al.[1]

CONCLUSIONS

- **Multidisciplinary approach to case management**
  - consults with multiple specialties
  - proactive treatment planning
  - combined case treatment in OR setting
- **Preventive dental care key to long-term dental management**
- **Sensory Adapted Dental Environment (SADE) beneficial for behavior guidance in clinical setting[5]**

REFERENCES

[1] Cyske Z et al. Sanfilippo Syndrome: Optimizing Care with a Multidisciplinary Approach. 2022. J Multidiscip Healthc 15:2097-2110.

[2] Benetó N, Vilageliu L, Grinberg D, Canals I. Sanfilippo Syndrome: Molecular Basis, Disease Models and Therapeutic Approaches. Int J Mol Sci. 2020 Oct 22;21(21):7819. doi: 10.3390/ijms21217819. PMID: 33105639; PMCID: PMC7659972.

[3] Muschol, N et al, MPS III Guideline Development Group. Sanfilippo syndrome: consensus guidelines for clinical care. *Orphanet Journal of Rare Diseases*, 2022 *17*(1), 391.

[4] Hirst L, Mubeen S, Abou-Ameira G, Chakrapani A. Mucopolysaccharidosis (MPS): Review of the literature and case series of five pediatric dental patients. 2021. Clin Case Rep 9(3):1704-1710.

[5] American Academy of Pediatric Dentistry. The Reference Manual of Pediatric Dentistry. Chicago, Ill.: 2022-2023 p. 328.