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Morquio Syndrome from a Dentist's aspect

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Abstract:- Morquio syndrome is a rare autosomal recessive inherited disease of lysosomal storage defect associated with multiorgan involvement and symptoms are seen due to excessive accumulation of Glucose-amino-glycans in the affected sites. Its characteristic features are extremely abnormal gait, short stature, short neck, and macrocephaly which can be accompanied with high level of GAG KS in urine during urine analysis and atlantoaxial subluxation and other characteristic radiographic features for proper diagnosis. Many oral manifestations are associated with this disease like hypoplastic enamel, abnormal tooth anatomy, macroglossia, temporomandibular joint defect, therefore dental intervention is necessary at an early stage but there are many features which might interfere in normal dental treatment, that's why detailed knowledge about this syndrome will help dentists to handle these patients more efficiently.

Keywords:- *Morquio Syndrome, Lysosomal Defect, Mucopolysaccharidosis, Multiorgan Involvement, Oral Manifestations.*

I. INTRODUCTION

Mucopolysaccharidosis (MPS) type IV A, also called Morquio Syndrome, is a rare genetic progressive lysosomal storage disorder (mucopolysaccharidosis) with autosomal recessive inheritance [1], characterized by multiorgan system involvement associated with wide range of symptoms with life expectancy less than 30 years.

According to 2020 report of National MPS Society, Morquio syndrome is caused by accumulation of GAG Keratan Sulfate (KS), which is primarily found in bone and connective, due abnormal excessive accumulation of GAG KS and chondroitin-6-sulfate in different areas of body which leads to cell death hence symptoms appear. [2]

There are 2 types of morquio syndrome: MPS IV A and MPS IV B

MPS IV A (more common) is caused by deficiency of N-acetylgalactosamine-6-sulfatase on chromosome number 16, primarily affects skeletal system but also affects other organs, while MPS IV B is caused by deficiency of beta-galactosidase on chromosome number 3, occurs only in 5% individuals, primarily affects skeletal system (skeletal dysplasia of long bones).

GM1 gangliodosis is also caused by mutation in same gene as MPS IV B, but unlike Morquio syndrome GM 1 gangliodosis patients have intellectual disability or degeneration of nerves.

II. SIGNS AND SYMPTOMS

General Symptoms	Endurance is decreased
Physical appearance	1. Coarse facial features (such as a flat bridged nose or square jaw) 2. Abnormal Gait 3. Severely short stature 4. Very short neck 5. Macrocephaly
Musculoskeletal system	1. Skeletal deformities (dysostosis multiplex with odontoid hypoplasia) 2. Abnormal hip formation (hip dysplasia) 3. Spine deformity (scoliosis, gibbus, kyphosis, atlantoaxial instability, cervical myelopathy, spinal cord compression [3] [4]) 4. Knee (knock knees or genu valgam) 5. Ankles (valgus deformity)
GIT	1. Hepatosplenomegaly 2. Umbilical and inguinal hernia
CVS	Heart valve problems (murmurs and heart failure)
CNS	Malrotation of cerebellum and brain stem [5]
Respiratory system [2]	1. Thoracic kyphosis 2. Sleep apnea 3. Reduced lung function 4. Frequent upper respiratory infection (tonsillitis)

Ear, Nose, Throat [2]	1. Hearing loss 2. Frequent Otitis media
Eyes [2]	Vision problem like corneal clouding
Mouth and Teeth [6]	1. Dysostosis multiplex (large appearing head, mid-face hypoplasia, mandibular protrusion) [7] 2. Macroglossia 3. Abnormal teeth (widely spaced with small, sharp pointed cusps along with very thin enamel)

Morquio syndrome is diagnosed by high levels of GAG KS and chondroitin-6-sulfate in urine, GALNS activity testing, skin biopsy, genetic analysis and radiography. [2] Enzyme replacement therapy is the only effective treatment so far known for Morquio syndrome, but it only shows some results if started at infancy.[8][9]

III. ROLE OF PEDODONTIST IN MORQUIO SYNDROME PATIENTS

Most common orofacial anomalies of Morquio syndrome are broad mouth, malpositioned, unerupted, and spaced permanent teeth, short nose porous, loss of dental structure, anterior open bite due to macroglossia and flattened condyle, hypoplastic enamel, therefore high caries risk. (Hypoplastic type of amelogenesis imperfecta can be differential diagnosis) [10]

- *Evaluation:*

Close monitoring of dental development (at least annually) and regular dental care to prevent caries and attrition, using fluoride varnish and pit and fissure sealants and keep check on oral hygiene.

- *Management:*

If patient has already developed caries, then restoration should be done and metal crowns are preferred. Al-Jawad et al demonstrated that in patients with MPS, deficient keratin sulfate in dentinal tubules disrupts the proper integration of enamel and dentin of primary and permanent teeth and causes an irregular hydroxyapatite crystal orientation and geometry throughout enamel layer. As a result, in MPS affected children, the occurrence of failures in enamel acid etching is frequent affecting adequate bonding of adhesive restorations.[11]

- *Role of Orthodontist in Morquio syndrome patients:*

Orthodontists plays a major role in treating dental problems of these patients as these patients show anterior open bite, tapered posteriors and spaced and flared anteriors, short vertical facial height along with condylar head resorption leading to TMJ problems.[12]

- *Management:*

In these patients non bonded orthodontic appliances are preferred as their enamel is very weak, Hawley's appliance is used for long term retention, along with that patient and parent should be instructed to maintain strict oral hygiene due to high caries risk.

- *Role of Oral Surgeon in Morquio Syndrome patients:*

Oral surgeons play vital role in treating morquio patients:

- *Maxillofacial trauma:*

In case of maxillofacial trauma, before operation a thorough radiological investigations should be done and problems and complications should be discussed with radiologist and neurosurgeons, in elective surgery case.[13]

In case of emergency cervical collar should be given to stabilize the spinal cord as these patients are prone to atlantoaxial subluxation, but cervical collar compromises airway patency, care must be taken during intubation. To limit the neck movement, head and neck should be kept in neutral position to minimize flexion or extension of neck in order to avoid sudden nerve damage.

Anesthetic care should preferably be in assistance with pediatric anesthesiologist experienced in this disorder.[4][9]

Major problem in these patients is airway management as macroglossia, short neck, decreased neck mobility and GAG deposition in submucosal and cartilaginous area contribute to airway restriction, for these patients oral fiberoptic approach should be first choice for intubation (nasal route might also be used) as it is minimally invasive and less traumatic.[14][15]

- *Extraction:*

As there are high chances of impaction in these patients, patient might need to get those teeth extracted due to high chances of development of dentigerous cyst, therefore extraction should be least eventful as possible.

Due to TMJ problems these patients can't keep their mouth wide open so Extraction is a bit difficult to perform.

- *Malignancy:*

Morquio syndrome is rarely associated with malignancy, so far only two malignancies are reported in morquio syndrome patients.

First case was reported in 1991, an 18-year-old boy with morquio syndrome was diagnosed with high grade (stage II) osteosarcoma of diaphysis of right femur, and his mother had ovarian carcinoma.[16]

Second case was reported in 2017, a 30-year-old man died due to poorly differentiated adenocarcinoma, interestingly he also had family history of malignancy, his father had breast carcinoma, his sister had skin carcinoma and his paternal grandfather had esophageal carcinoma.[5]

Therefore, MPS may play role in carcinogenesis or metastasis of epithelial neoplasm. As concerned with oral surgery as there are high chances of development of dentigerous cyst, so it can definitely convert into some metastatic jaw tumor.

IV. DIFFICULTIES DENTISTS MIGHT FACE WHILE TREATING A PATIENT WITH MORQUIO SYNDROME

- Due to thoracic cage kyphosis and macroglossia and short neck, these patients have difficulty in lying in supine position, they might show symptoms like shortness of breath and anxiety, therefore we should keep short appointments and try to do treatment in semi supine position.
- As TMJ is severely affected patient can't open mouth wide and also patient has macroglossia, so limited access and visibility is there.
- In cases with atlantoaxial instability, one should be very careful in moving the patient into dental chair, use pillows or cervical collar to stabilize neck and increase patient comfort as directed by caregiver.
- In case of emergency, Tracheostomies are difficult, due to abnormal anatomic structures like short neck, pectus carinatum, and buckling of trachea.
- OPG in short necked people can cause lack of clarity in central portion of film, hence can't be used for diagnosis.

V. CONCLUSION

Morquio syndrome is a very rare disease, so as a dentist we don't deal with such patients in our routine, but in case if we face such patients we have to be prepared and keep few basic things about these patients in mind in order to provide better treatment and avoiding any iatrogenic injury from our side.

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