Review Article

ENT and mucopolysaccharidoses

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Background

The mucopolysaccharidoses (MPS) are a heterogeneous group of inherited metabolic disorders, each associated with a deficiency in one of the enzymes involved in glycosaminoglycan (GAG) catabolism.[1] Over time, GAGs accumulate in cells and tissues causing progressive damage, a variety of multi-organ clinical manifestations, and premature death.[1]

- Head and neck disorders affect more than 90 % of MPS patients.[1]
- Hearing loss is almost a universal finding in children with MPS.[1]

Undiagnosed MPS patients are frequently referred to ENT surgeons due to the early onset of ENT MPS-related manifestations.[1]

Ear, nose and throat (ENT) manifestations in MPS are due to the accumulation of GAGs in the head and neck region.[1] ENT disease in MPS can be divided into respiratory disorders and otological or hearing problems.[1]

Respiratory disorders in MPS

Airway problems result from tissue storage of GAGs that produce a distortion of airway anatomy and function.[1] The respiratory disorders in MPS can be divided into:[1]

- Airway abnormalities (extrathoracic and intrathoracic) and,
- Alterations in respiratory and sleeping mechanics[1]

Table 1. Respiratory disorders in MPS

Extrathoracic[1]	Intrathoracic[1]	Alterations in respiratory and sleeping mechanics

• Abnormal cervical vertebrae
• Short neck
• High epiglottis
• Deep cranial fossa narrowing the nasopharynx
• Hypoplastic mandible
• Temporomandibular joint ankylosis
• Small thoracic cage
• Mucopolysaccharide infiltration of the nasopharyngeal, oropharyngeal, hypopharyngeal and laryngeal tissues
	• Tracheobronchial abnormalities e.g. trachea may be narrow, tortuous or occluded by the accumulation of soft tissue
	• Depending on the site and severity of obstruction, patients may present with:
	  • Stridor
	  • Dyspnoea
	  • Retractions
	  • Cough
	  • Cyanosis
	  • Feeding difficulties
		• Reduction in vital capacity[1]
		• Impaired O_2 uptake and CO_2 excretion[1]
		• Obstructive sleep apnoea[1]

Managing respiratory disorders in MPS

MPS patients with clinical symptoms of upper airway obstruction are often subjected to adenoidectomy and/or tonsillectomy.[1]

Adenoidectomy and/or tonsillectomy in 35–50 % of cases are performed prior to MPS diagnosis.[1] Despite adenotonsillectomy being a routine procedure in most children, the risks are usually higher in an MPS child, including post-operative haemorrhage, airway oedema, and failure to extubate.[1] The recurrence rate of adenoid hypertrophy after adenoidectomy in the MPS population is 56 %.[1]

When local airway procedures are no longer adequate or when there is significant tracheobronchial involvement, non-invasive continuous positive airway pressure (CPAP) may be employed by some patients during sleep.[1] Progression of upper airway obstruction when less invasive interventions are no longer adequate may often require a tracheotomy.[1]

Otological disorders

Conductive hearing loss is common, although many patients present with a sensorineural component.[1]

- The conductive component of hearing loss is attributed to the presence of seromucinous otitis or bone chain deformities, disruption in ossicular conduction by histopathological anomalies similar to otosclerosis or by arthropathy.[1]
- Sensorineural hearing loss is thought to be caused by the accumulation of GAGs in the cochlea, auditory nerve, and brain stem.[1]

In MPS II (Hunter syndrome), the most prevalent otolaryngological manifestations and interventions reported are otitis media, hearing loss and insertion of ventilation tubes, adenoidectomy and hearing aids.[1]

To summarise

MPS are rare, progressive and multisystem diseases with insidious signs and symptoms.[1]

Various ENT manifestations appear in the early stage of MPS.[1]

Early recognition of MPS requires careful attention to the presence of multiple signs and symptoms, many of which overlap with common childhood complaints.[1]

- Children with MPS have a high risk of hearing loss and this is an early symptom.[1]
- Clinical suspicion of the disease can be triggered by particular clusters of signs and symptoms that are unlikely in an unaffected child but that often occur together in the child with MPS II (Table 2).[1]

Table 2. "Red flag" signs and symptoms of MPS II that occur early in the disease course[1]

- Coarse facial features (may be subtle in the attenuated phenotype)
- Recurrent respiratory infections
- Chronic rhinorrhoea
- Upper airway restriction/noisy breathing/snoring
- Recurrent otitis media
- Hearing loss
- Heart murmur
- Hepatomegaly
- Umbilical and inguinal hernia
- Recurrent watery diarrhoea
- Joint stiffness
- Developmental delay and/or speech delay (in severe phenotype only)

Early treatment considerably improves patient outcomes during long-term therapy and is crucial to slow disease progression before irreversible damage occurs.[1]

Reference: 1. Bianchi PM, Gaini R, Vitale S. ENT and mucopolysaccharidoses. *Italian Journal of Pediatrics* 2018;44(Suppl 2):127. https://doi.org/10.1186/s13052-018-0555-0

sanofi-aventis south africa (pty) ltd., Reg. no.: 1996/010381/07, Floor 5, Building I, Hertford Office Park, 90 Bekker Road, Midrand, 2196. Tel: (011) 256 3700.
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For Medical Information Enquiries kindly contact ZA.Medinfo@sanofi.com

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