orphanaesthesia

Anaesthesia recommendations for

Goldenhar syndrome

Disease name: Goldenhar syndrome

ICD 10: Q87.0

Synonyms: Craniofacial microsomia, Oculo-auriculo-vertebral (OAV) spectrum/ syndrome/ sequence/dysplasia, facio-auriculo-vertebral syndrome /sequence/ dysplasia, Goldenhar-Gorlin syndrome.

The *European Guideline Craniofacial Microsomia* published in November 2020 recommends the use of the term Craniofacial microsomia exclusively and discourages the use of all other terms such as Goldenhar syndrome. In the literature, the term Goldenhar syndrome is often used for a severe variant of Craniofacial microsomia that includes vertebral anomalies.

Disease summary: In 1952, Maurice Goldenhar published a case collection of congenital mandibulo-facial malformations with or without epibulbar dermoids, auricular appendages and auricular fistulas. With the attempt to systematically classify these malformations, he described for the first time what later became known as the Goldenhar syndrome.

Goldenhar syndrome is grouped within the spectrum of craniofacial microsomia. It consists of hemifacial microsomia (HFM), epibulbar dermoids and vertebral anomalies. Major manifestations of HFM are orbital distortion, mandibular hypoplasia, ear anomalies, nerve involvement and soft tissue deficiency (OMENS). In addition, patients with Goldenhar syndrome can present with heart, kidney and lung malformations as well as spine and limb deformities. Depending on the organs affected and the severity of the malformations, the phenotype is highly variable. The OMENS-Plus classification system is most commonly used to describe the phenotype variability of craniofacial microsomia (Amendment 1).

The exact cause of Goldenhar syndrome is unknown but considered to be multifactorial, i.e. a combination of gene interactions and environmental factors that causes a maldevelopment of the first and second branchial arches during the first trimester of pregnancy. Males are affected more often than females (3:2). About 10–30 % of patients have bilateral, usually asymmetric facial microsomia. There is no agreement on the incidence of Goldenhar syndrome in the literature. Reports vary between 1:3,000–5,000 and 1:25,000–40,000. A recent population-based data linkage study of the epidemiology of rare craniofacial abnormalities in Western Australia found a birth prevalence of 15.8 (11.6–20.9) per 100,000 live and stillbirths in the decade from 2000 to 2010. This study found associations between maternal hypothyroidism and craniofacial microsomia. Craniofacial microsomia was also associated with twin or higher order multiples as compared to singleton births, and with preterm birth, low birth weight, and low Apgar scores. The relevance of these associations have yet to be determined.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

- Craniofacial surgery
- Orodental surgery
- Ear reconstruction
- Excision of periauricular skin tags
- Surgery for conductive or sensorineural hearing loss
- Ophthalmologic surgery
- Spine surgery

Type of anaesthesia

General anaesthesia might be the only feasible anaesthetic regimen given the nature of the most common surgical interventions and the young age.

Neuro-axial anaesthesia techniques might be difficult or contraindicated depending on individual spine malformations (hemivertebrae, block vertebrae, spina bifida).

Regional anaesthesia or local anaesthesia can be considered if the surgical procedure allows it. A recent case report described the successful use of an axillary nerve block for placement of a peripherally inserted central catheter (PICC) in a 2-month-old girl with severe Goldenhar syndrome. However, intraoperative urgent conversion to general anaesthesia with intubation carries significant morbidity in a patient with a difficult airway compared to an electively scheduled difficult airway management.

Sedation and premedication should only be done after very careful evaluation of the individual risk of airway obstruction, difficult ventilation, and difficult intubation.

Necessary additional pre-operative testing (beside standard care)

A difficult airway is of highest concern in patients with Goldenhar syndrome. Nargozian et al. showed in a retrospective evaluation a significant association of the severity of the mandibular hypoplasia and the degree of difficulty with intubation. Based on these findings, imaging of the mandibular hypoplasia could be considered prior to surgery as part of the individual difficult airway algorithm. Case reports suggest that pre-operative 3D computer tomography of the airway is helpful for difficult airway management.

Sleep-related upper and lower airway obstruction (obstructive sleep apnoea: OSA) due to anatomical and functional factors are common in patients with major craniofacial anomalies. Clinical indicators such as snoring should be taken seriously as they might predict difficult mask ventilation as well as airway obstruction upon emergence from anaesthesia. Further upper airway evaluation might be indicated pre-operatively as anatomical anomalies such as adenoid or tonsillar hypertrophy might contribute to airway obstruction and can possibly be approached surgically.

Congenital heart defects have been reported in 5–58 % of patients with Goldenhar syndrome. Septal defects and conotruncal malformations such as tetralogy of Fallot are the most commonly seen congenital cardiac malformations in this population. Situs inversus and looping defects are also reported. All patients with Goldenhar syndrome should undergo one-time

cardiac evaluation. Based on these results and a careful pre-operative clinical evaluation, additional cardiac function testing might be indicated before surgery.

Pulmonary function can be compromised by partial or complete unilateral lung hypoplasia. Pulmonary hypoplasia might increase the risk for respiratory infections, pulmonary hypertension and pneumothorax. In addition, severe spinal deformities might cause restrictive lung disease and further decrease pulmonary function. One-time pulmonary evaluation for possible malformations is, therefore, necessary. A careful preoperative clinical evaluation of respiratory function is recommended, and in conjunction with possible pulmonary malformations, further pulmonary function testing might be warranted.

One feature of Goldenhar syndrome is vertebral anomalies. Failure of vertebral segmentation of the cervical spine such as occipitalisation and cervical vertebral fusion can be relevant for anaesthesia as it might aggravate an already difficult intubation. Radiologic evaluation of the cervical spine should be considered as well as complete spine imaging in case a neuro-axial technique is planned.

Genitourinary malformations such as ectopic or fused kidneys, renal agenesis, ureteropelvic junction obstruction or vesicoureteral reflux might be associated with Goldenhar syndrome. Although the malformation might not necessarily impact renal function it might increase the risk for urinary tract infection (UTI). It might be helpful to be aware of possible kidney malformations prior to major surgery with expected large fluid shifts, prolonged urinary catheter placement and post-operative ICU admission.

Particular preparation for airway management

Anticipation of a difficult airway is of highest importance in patients with Goldenhar syndrome. In 1998, Sculerati reported a chart review of patients with major craniofacial bone anomalies that included 41 patients with the oculo-auriculo-vertebral sequence. Of those, 9 patients (22 %) required a surgical airway peri-operatively.

A detailed and relevant history and a pre-operative airway examination are crucial. The exam should include assessment of mouth opening, size of the tongue, dental status, palate and mandibular shape, intraoral soft tissue masses such as adenoids or protruding tonsils, and neck range of motion.

Possible difficult mask ventilation, difficult laryngoscopy and difficult intubation should be anticipated and discussed in advance. An individually designed difficult airway algorithm should be communicated to all participating providers. Difficult airway equipment including supraglottic devices and a size appropriate fibre-optic device should be readily available. A video laryngoscope has been proven to be useful in some cases of difficult airway management. Equipment and expertise to secure the airway surgically should be in place.

Particular preparation for transfusion or administration of blood products

No special considerations.

Particular preparation for anticoagulation

No special considerations.

Particular precautions for positioning, transportation and mobilisation

Vertebral anomalies such as cervical spine instability can be present. In those cases, special attention should be paid to head and neck positioning peri-operatively and especially during airway management.

Interactions of chronic disease and anaesthesia medications

No special considerations.

Anaesthetic procedure

There is no evidence that any anaesthetic regimen is safer than another. The administration of volatile anaesthetics with or without muscle relaxants as well as longer acting opioids should be carefully considered because of their potential to delay airway recovery. If post-operative pain is expected to be controlled without high levels of opioids, remifentanil-based anaesthesia may be a good choice. Complete reversal of muscle relaxation with sugammadex is recommended.

Propofol is not known to cause much muscle relaxation; however, it suppresses cardiac output and contractility and may not be a good option in patients with cardiac disease.

Particular or additional monitoring

Cardiac and/or pulmonary morbidity may warrant placement of an arterial line.

Possible complications

Cannot intubate, cannot ventilate situation:

The most important consideration for general anaesthesia in patients with Goldenhar syndrome is the difficult airway management. Factors that contribute to a difficult airway are mandibular hypoplasia, cleft lip/palate and craniovertebral anomalies. The difficulty of intubation increases with age and bilateral mandibular hypoplasia.

Sleep-related upper and lower airway obstruction (obstructive sleep apnoea: OSA) due to anatomical and functional factors are common in patients with major craniofacial anomalies. In combination with facial malformations, mask ventilation may be difficult.

Emergence from general anaesthesia can again be complicated by airway obstruction.

Post-operative care

Obstructive sleep apnoea in combination with volatile anaesthetics, muscle relaxants and opioids put patients with Goldenhar syndrome at high risk for post-operative hypoxic events. Before tracheal extubation, reversal of muscle relaxation and complete recovery of airway reflexes should be confirmed. Prolonged post-operative monitoring, especially during opioid administration for pain management, is strongly recommended. Post-operative recovery in the ICU may be indicated.

Disease-related acute problems and effect on anaesthesia and recovery

Obstructive sleep apnoea is common in patients with major craniofacial malformations. Anaesthetic agents and opioids likely aggravate airway obstruction in the early post-operative period. The publication of two case reports suggested that congenital malformations of the middle ear and auditory canals can cause recurrent infections of the middle ear, sinusitis and meningitis. These conditions should be included in the differential diagnoses for peri-operative fever and infection.

Ambulatory anaesthesia

Eligibility for ambulatory surgery strongly depends on the severity and localisation of malformations. In any case, possible post-operative upper airway obstruction and the need for prolonged monitoring after general anaesthesia should be taken into account when evaluation for ambulatory anaesthesia.

Obstetrical anaesthesia

No special considerations.

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Amendment 1

Classic Goldenhar Triad:	
Hemifacial microsomia (HFM) **OMENS** classification	**O**rbital distortion
	Mandibular hypoplasia
	Ear anomalies: ▪ Microtia ▪ Low set ears ▪ Preauricular skin tags/pits ▪ External auditory canal agenesis/stenosis ▪ Middle ear malformations with conductive hearing loss
	Nerve involvement: ▪ Facial nerve palsy ▪ Auditory nerve dysfunction with sensorineural hearing loss
	Soft tissue deficiency [1]
OMENS-Plus classification	Associated extra craniofacial anomalies are present additional to the OMENS Classification [2,3]
Ocular and auricular malformations	▪ Ocular dermoids ▪ Eyelid coloboma ▪ Microphthalmia ▪ Blepharoptosis ▪ Anotia [4–8]
Vertebral anomalies	▪ Cervical spine instability ▪ Spinal fusion ▪ Hemivertebra with scoliosis ▪ Spina bifida [9–13]
Additional malformations associated with Goldenhar syndrome:	
Cardiovascular system	▪ Atrial and ventricular septal defects ▪ Conotruncal defects ▪ Targeted growth defects ▪ Situs and looping defects ▪ Obstructive lesion ▪ Patent ductus arteriosus [14–17]
Respiratory system	▪ Pulmonary hypoplasia/aplasia/agenesis ▪ Total anomalous pulmonary venous connection ▪ Costal agenesis ▪ Tracheobronchial abnormalities

	▪ Laryngomalacia ▪ Tracheoesophageal fistula ▪ Narrow airway ▪ Tracheal diverticulum ▪ Oesophageal atresia [18–25]
Urinary system	▪ Ectopic and/or fused kidneys ▪ Vesicoureteral reflux ▪ Ureteropelvic junction obstruction ▪ Ureteral duplication ▪ Renal agenesis ▪ Multicystic kidney [26–29]
Nervous system	▪ Intellectual disability ▪ Neuropsychomotor delay ▪ Developmental delay due to hearing impairment ▪ Anomalous Extratemporal Facial Nerve ▪ Neural tube defects [17,29–31]
Extremities	▪ Thump and radius anomalies ▪ Talipedes [13]
Orofacial	▪ Dental abnormalities ▪ Cleft lip/palate ▪ Macrostomia [42] ▪ Ankylosis of temporomandibular joint [32]

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