orphanaesthesia

Anaesthesia recommendations for patients suffering from

Deletion 9p Syndrome

Disease name: Deletion 9p Syndrome

ICD 10: Q93.5

Synonyms: Alfi's Syndrome, 9p minus syndrome, chromosome 9p deletion syndrome

In 1973, Alfi et al. reported three infants with partial deletion of the short arm of chromosome 9 distal to band 9p22 who had several clinical features in common. In 1976, after identifying three additional patients with the same chromosomal deletion, this group described the deletion 9p syndrome.

The deletion 9p syndrome is very rare. It is estimated to occur in one in 50,000 newborns. Since its first description, well over 100 patients have been described in the literature, but there are likely many more people affected who have either not been diagnosed or not been reported. New cases have been published occasionally that describe new features associated with deletion 9p syndrome. Whether these new features are truly part of the syndrome or only accidentally occur together remains unclear.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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

Disease summary

This syndrome is defined by deletion of the short arm of the 9th chromosome. In most cases, the breakpoint is reported in the bands from 9p21 to 9p24. The majority of cases are de novo deletions but parental translocations are also reported. The phenotype of deletion 9p is heterogenous and no clear correlation between breakpoint and clinical features has been established. Common features of the syndrome include mental deficiency, psychomotor and speech delay, craniofacial dysmorphism, and and other congenital malformations. The syndrome appears to be balanced between males and females.

Clinical features of deletion 9p syndrome:

Common features of this syndrome include trigonecephaly with prominent forehead, small upslanting palpebral fissures, flat nasal bridge, orbital hypertelorism, long philtrum, low set dysplastic ears and long phalanges with excess of whorls. In a case series of 11 patients, the mean IQ of the patients was 48. However, the intellectual disability can range from mild to severe. Additional malformations include, choanal atresia, midface hypoplasia, high arched palate, small mouth, micrognathia, and short webbed neck. Obstructive sleep apnea may complicate these midfacial malformations. Beyond the craniofacial anomalies, the most common congenital malformations are cardiac defects (ventricular septal defect, patent ductus arteriosus and pulmonary stenosis), inguinal and diaphragmatic hernias, pylorus stenosis, omphalocele, genital and/or gonadal dysgenesis, scoliosis and/or kyphosis, and pectus excavatum. EEG changes, seizure disorders, and developmental delay of speech and motor development with truncal hypotonia are also frequently reported.

Terminal deletions of the short arm of chromosome 9 have been associated with XY sex reversal, with or without additional features of the deletion 9p syndrome. The degree of the sex reversal is variable.

Recurrent ear, respiratory and urinary tract infections are reported frequently in this patient population. Recurrent aspirations can be attributed to muscular hypotonia with impaired swallowing and coughing, gastroesophageal reflux, diaphragmatic hernias, and pylorus stenosis. Allergies and asthma are common, but specific immunological impairments are rarely identified.

Typical surgery

Correction of craniosynostosis, repair of choanal atresia, inguinal hernia, diaphragmatic hernia, omphalocele, scoliosis, insertion of ear tubes, correction of anomalies of external genitalia.

Type of anaesthesia

Although no specific agents or type of anaesthesia can be recommended for all patients, general anaesthesia might be the most feasible anaesthetic regimen given the nature of the common surgical interventions and the young age these procedures are usually performed. However, because of craniofacial dysmorphism, anesthesiologists must prepare to manage a difficult airway.

Neuroaxial anaesthesia or analgesia may be indicated for certain surgical procedures, but spinal deformities might limit its relevance.

In addition, as with any patient with a seizure disorder, cerebral toxicity threshold of local anaesthetics may be lower. Therefore, if neuroaxial or peripheral regional anesthesia is proposed in patients with deletion 9p syndrome with a seizure disorder, doses of agents must be adjusted to decrease peak plasma concentrations, especially in the newborn and young infant.

Necessary additional diagnostic procedures (preoperative)

Since deletion 9p is a syndromic disorder and congenital anomalies should be expected, the past medical history must be investigated carefully.

Because ventricular septal defect, patent ductus arteriosus and pulmonary stenosis frequently accompany this disorder, a cardiac evaluation is usually performed when the diagnosis of the deletion 9p syndrome is confirmed. These records as well as recent cardiac evaluations and current status should be reviewed preoperatively.

If cardiac defects are present, the need for pre-procedural antibiotic endocarditis prophylaxis must be assessed and prescribed in accordance with society guidelines.

Because of the frequent pulmonary infections in these patients, the respiratory system should be evaluated closely. In most cases, a meticulous physical examination and history is sufficient for a preoperative evaluation. In the setting of new or significant findings, a chest x-ray or other imaging might be indicated. Close communication with the child's paediatrician, primary care physician, or pulmonologist may provide critical insight into the patient’s current status.

If asthma, pulmonary malformations and/or severe scoliosis further impair respiratory function, preoperative pulmonary function tests may provide important data to define anesthetic management.

Gastroesophageal reflux and pyloric stenosis increase the risk for aspiration during induction of general anesthesia. Administering a proton pump inhibitor and/or citric acid/sodium citrate preoperatively might be indicated. The need for a rapid sequence induction should be carefully assessed.

Patients with deletion 9p syndrome who also have EEG abnormalities and/or seizure disorders may have an increased risk for perioperative seizures. Antiepileptic drug levels should be reviewed. If levels have not been measured recently, obtaining a preoperative value should be considered. In addition, in consultation with the neurologist, an IV regimen should be established, especially in the setting of vomiting, strict fasting, or anticipated NPO status postoperatively.

Radiologic evaluation for rib and vertebral anomalies is recommended if a neuroaxial anaesthetic or analgesic technique is considered.

Particular preparation for airway management

Because the common features of the deletion 9p syndrome include craniofacial anomalies such as craniostenosis, midfacial hypoplasia, cleft palate/high arched palate, migrognathia, small mouth, short neck and choanal atresia, these patients incur a risk for a compromised airway, especially during induction of general anesthesia. The risk of a difficult airway

situation must be carefully weighed against the need for a rapid sequence induction (e.g., due to pylorus stenosis, gastroesophageal reflux).

In the only case report focused on anaesthetic management of a patient with deletion 9p syndrome, Cakmakkaya et al described a 5-year-old girl, with micrognathia and a short neck as well as gastroesophageal reflux who underwent laparoscopic Nissen fundoplication under general anaesthesia. The critical aspect of this case was a difficult intubation. Laryngoscopy revealed a Cormack and Lehane Grade III view. In addition, inserting the endotracheal tube (ET) placement was complicated by a trachea much narrower than expected for age.

In patients with craniofacial dysmorphism, reviewing the anaesthetic history followed by a meticulous preoperative airway examination are critical. This process should be considered to anticipate and plan for a difficult mask ventilation, laryngoscopy and/or intubation. The difficult airway algorithm should be communicated to all participating providers.

Difficult airway equipment including supraglottic devices, different sized ET tubes and a size appropriate fiberoptic 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

As appropriate for physical condition and comorbidities.

Particular precautions for positioning, transport or mobilisation

As appropriate for physical condition and comorbidities.

Probable interaction between anaesthetic agents and patient’s long-term medication

Antiepileptic medications often either induce or inhibit cytochrome P450 isoenzymes in hepatic metabolism and, therefore, can decrease or increase plasma concentrations of several drugs used perioperatively, such as beta-blockers, calcium channel antagonists, antibiotics, or warfarin.

Anaesthesiologic procedure

The intraoperative anaesthetic management should be based on the patient's cardiac, pulmonary, renal and neurologic comorbidities.

Asthma, recurrent pulmonary infections and chronic aspiration may lead to a hyper-reactive airway and difficult ventilation during induction and intraoperatively. Sevoflurane is an appropriate anesthetic agent for induction as well as maintenance of anaesthesia.

In patients with seizure disorders, the epileptogenic properties of anaesthetics and other medications used perioperatively should be considered. Premedication with a benzodiazepine might be warranted. Hyperventilation should be avoided, especially in newborns/infants during an induction with sevoflurane, as this may decrease the threshold for seizures.

Literature suggests a decreased MAC of volatile anaesthetics as well as overall lower BIS values in children with intellectual disabilities. In addition, pre-existing muscular hypotonia might reduce the amount of muscle relaxants needed.

Particular or additional monitoring

As appropriate for physical status, extend of surgery and comorbidities.

Possible complications

Summary of possible peri-anaesthetic complications (for more detailed explanation see above and below chapters):

Anesthesia induction:

- Difficult airway management
- Regurgitation, aspiration
- Seizures

Intraoperative:

- Ventilation difficulties

Emergence:

- Delayed emergence
- Upper airway obstruction
- Regurgitation, aspiration
- Seizures

Postoperative care

Due to residual effects of anaesthetic and analgesic agents, patients with craniofacial anomalies incur a higher risk for upper airway obstruction, especially in the early post-anaesthetic period. In addition, hypotonia can contribute to impaired post-anaesthetic respiratory function, and gastroesophageal reflux increases the risk of postoperative aspiration. Therefore, prolonged postoperative monitoring may be necessary.

Patients with intellectual disability and speech delay often cannot express their needs, including the level of pain. A family member or caretaker with close relationship to the patient at the bedside may not only calm the patient but also help the post-anaesthetic care team to better understand the patient's needs.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

Recurrent ear, urogenital or respiratory infections are common in patients with deletion 9p syndrome. In case of perioperative infection signs, the possibility of other than surgery-related infections should be kept in mind.

Delayed recovery from anaesthesia can be related to an increases sensitivity to anaesthetic medications. However, pre-existing muscular hypotonia might mimic prolonged anaesthetic effects. It is important to evaluate and document the preoperative functional status to be able to recognize the return to normal function for each individual patient.

Ambulatory anaesthesia

In general, procedures should be performed in a medical centre with multidisciplinary resources and experience in managing syndromic patients.

The feasibility of ambulatory anaesthesia largely depends on the individual patient's comorbidities. Since difficult airway management and/or delayed or complicated recovery are common, in general, we do not recommend ambulatory anaesthesia .

Obstetrical anaesthesia

In cases of deletion 9p syndrome described in the literature, the syndrome was diagnosed at birth or later in life. Abnormal pregnancy or delivery are rarely reported in retrospect. Although often small for gestational age, Apgar scores seem within normal range.

Literature and internet links

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Last date of modification: February 2017

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Table 1: Common features of the deletion 9p syndrome with references

Craniofacial appearance	▪ Trigonocephaly ▪ Craniosynostosis ▪ Mid-facial hypoplasia ▪ Flat nasal bridge ▪ Long philtrum ▪ Micrognathia ▪ High-arched palate ▪ Upslanting palpebral fissures ▪ Epicanthus ▪ Hypertelorism ▪ Highly arched eyebrows ▪ Low hair line ▪ Webbed neck ▪ Short neck [1-3]
Organ Systems	
Nervous System	▪ Mental retardation ▪ Motor development delay ▪ Speech delay ▪ Muscular hypotonia ▪ EEG changes/seizures [2, 4, 5]
Cardiovascular System	▪ Ventricular septal defect, ▪ Patent ductus arteriosus ▪ Pulmonary stenosis [6-8]
Respiratory System	▪ Choanal atresia ▪ Pulmonary hypoplasia ▪ Laryngomalacia [3, 9, 10]
GI System	▪ Diaphragmatic hernia ▪ Gastroesophageal reflux ▪ Duodenal stenosis ▪ Umbilical/İnguinal hernia ▪ Omphalocele [5, 8, 9]
Urinary System	
Genital System	▪ Impairment of gonadal development ▪ Abnormal external genitalia development ▪ Hypospadias ▪ Ambiguous genitalia [2, 8, 11, 12]
Musculoskeletal System Vertebrae Extremities	 ▪ Scoliosis[2, 9] ▪ Long middle phalanges of the finger ▪ Long fingers and toes ▪ Increased number of whorls on the fingers ▪ Foot positioning defects ▪ Simian crease [1, 2]

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