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CLOVES syndrome

orphan**anesthesia**

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

SUPPLEMENT NR. 7 | 2025

OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

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orphananesthesia

Anaesthesia recommendations for CLOVES syndrome

Disease name: CLOVES syndrome

ICD 10: Q87.3

Synonyms: Congenital lipomatous overgrowth-vascular malformation-epidermal nevi-skeletal anomaly syndrome, Congenital lipomatous overgrowth-vascular malformation-epidermal nevi-spinal anomaly syndrome.

Disease summary: CLOVES syndrome is characterised by congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and spinal/scoliosis/skeletal deformities [1].

It results from a somatic mosaicism in the phosphatidylinositol 3-kinase catalytic subunit alpha (PIK3CA) gene and is a PIK3CA-related overgrowth spectrum (PROS) disorder that often presents at birth or childhood [2,3]. It is an extremely rare, nonhereditary disorder, with an estimated prevalence lower than 1:1,000,000 [4].

Skeletal abnormalities are in the upper and lower extremities and can include macrodactyly, sandal gap, leg-length discrepancy, hemihyperplasia, chondromalacia and furrowed soles [5]. Spinal abnormalities are common among affected individuals and can include tethered cord, scoliosis, and neural tube defects [6]. Other findings not included in the acronym include seizures, renal agenesis/hypoplasia, lymphatic malformations, splenic lesions, gastrointestinal involvement and an increased risk of developing Wilms tumours [6,7]. The vascular malformations typically present in childhood and include (venous, lymphatic and capillary) slow-flow and deeper (arteriovenous) high-flow vascular lesions [8]. Vascular and lymphatic lesions can lead to pain, haemarthrosis, bony abnormalities, bleeding, pulmonary embolism, thrombophlebitis, and even airway obstruction [9].

The prognosis of CLOVES syndrome depends on the severity of illness [5]. Mild disease tends to have a good prognosis. Treatment modalities for CLOVES syndrome includes supportive therapies, surgical interventions, and possible (mTOR) inhibitors [10].

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



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

Emergency information

A	AIRWAY / ANAESTHETIC TECHNIQUE	There is potential for airway difficulties related to malformations of lymphatic and vascular tissues. Many of the procedures require general anaesthesia. If regional anaesthesia is possible, consider ultrasound guidance given the vascular and tissue abnormalities. Consider spinal imaging for AVMs prior to neuraxial.
B	BLOOD PRODUCTS (COAGULATION)	There is an increased risk of perioperative anaemia related to arteriovenous malformations (AVM) and unrecognised GI bleeding. There is also an increased risk of blood loss during surgeries around AVMs and considerations for multidisciplinary preoperative strategies should be completed.
C	CIRCULATION	There is a potential for significant physical limitations and compression of cardiovascular structures related to the masses. There is also the potential for significant scoliosis and alteration in respiratory mechanics affecting right ventricular pressures and function.
D	DRUGS	These patients may be on mechanistic target of rapamycin (mTOR) inhibitors, which may increase their risk of surgical site infections and wound breakdown.
E	EQUIPMENT	Potential need for difficult airway equipment. Ultrasound for vascular and regional techniques may be warranted. Assistance may be required during positioning as a significant number of patients are wheelchair users.

Typical surgery

MRI, endoscopic procedures, haemiorrhaphy, orchidopexy, sclerotherapy, embolisation, resections of truncal and limb masses, orthopedic surgery (amputation, resections, osteotomies), and neurosurgical interventions (spinal fixation, spinal cord detethering) [11,12].

Type of anaesthesia

There are very few case reports of anaesthetic management in CLOVES syndrome [13]. General anaesthesia would be required for many of these procedures and a balanced anaesthesia with volatiles, opioids, and/or propofol would be appropriate.

Paraspinal arteriovenous malformations (AVM), scoliosis, spinal cord tethering, and potential perioperative anticoagulation increase the risk of neuraxial anaesthesia in these patients. The use of ultrasound during peripheral regional anaesthesia should be considered given the potential for altered anatomy.

Necessary additional pre-operative testing (beside standard care)

A careful airway examination is essential. Any prior cervical spine and upper airway imaging should be reviewed to identify any possible lymphatic or vascular malformations that may make airway management difficult. Neurologic examination and documentation of pre-existing peripheral neuropathies is recommended.

Full blood count, coagulation profile, type and screen should be obtained. Standard liver and renal function tests should be ordered when appropriate. Glucose levels should be monitored to assess for hypoglycaemia [14].

Patients with known pulmonary AVM, scoliosis, or masses affecting pulmonary mechanics may warrant pulmonary function testing, room air arterial blood gas, and/or an echocardiographic study. Exercise tolerance may be difficult to assess as many patients are wheelchair users [5]. Further testing to assess cardiopulmonary status may be warranted. Patients are at an increased risk of venous thromboembolism and consideration of imaging to rule out thrombosis may be warranted prior to invasive procedures.

A pre-operative haematology consultation may be beneficial to guide perioperative blood management.

Particular preparation for airway management

Patients with CLOVES syndrome may be at risk of difficult intubation. Truncal abnormalities may make positioning for airway manipulation challenging. Vascular and lymphatic abnormalities can affect the airway and cervical spine [15]. A thorough airway examination is indicated. Adjuncts should be immediately available for safe tracheal intubation.

Particular preparation for transfusion or administration of blood products

Evaluation of anaemia and coagulopathy should be determined preoperatively as they may have unrecognized anaemia secondary to angiodysplasia-related or phlebectasia-related gastrointestinal bleeding [16]. Blood transfusion risks should be taken into consideration, including transfusion related immunomodulation effects because of the increased risk of postoperative infection in these patients [4].

Blood conservation strategies are likely to be beneficial. Excision of truncal vascular malformations has resulted in significant blood loss, large-volume transfusions and non-invasive surgical treatments (embolisation, sclerotherapy) should be considered prior to

surgical resection [17]. Topical and intravenous tranexamic acid may be helpful although not described in this population [18].

Particular preparation for anticoagulation

There is an association between phlebectasia and thromboembolism. This seems to apply above all to phlebectasia of the upper half of the body and operations in the prone position, because of decreased venous return, dependency, and direct compression [8]. Perioperative prophylaxis with anticoagulation and vena cava filters should be considered in patients with central and thoracic phlebectasia and should be addressed in a multidisciplinary fashion [8].

Prophylactic endovenous closure of ectatic veins in patients with CLOVES syndrome before major surgery has been recommended to reduce the risk of pulmonary embolism [19].

Particular precautions for positioning, transportation and mobilisation

Truncal and limb deformities can make positioning difficult. There is a significant proportion of patients who are wheelchair users [5].

Interactions of chronic disease and anaesthesia medications

Not reported.

Anaesthetic procedure

There are few cases describing anaesthesia management in CLOVES syndrome [13]. Neuraxial anaesthesia may carry an increased risk due to the potential paraspinal AVM, scoliosis, and perioperative anticoagulation.

Intercostal nerve blocks and cryoneurolysis as well as paravertebral blocks have been used with success for chronic nociceptive and neuropathic chest wall pain [20, 21]. The use of ultrasound during regional techniques is likely beneficial considering the patient's potential for altered anatomy.

Particular or additional monitoring

Standard monitors should be used as appropriate (e.g., electrocardiogram, non-invasive blood pressure, pulse oximetry, capnography, gas analyzer). Neuromuscular monitoring is essential when patients require neuromuscular blocking agents. If intraoperative transoesophageal echocardiography is indicated, consideration must be given to the possibility of esophageal phlebectasia or angiodysplasia [16].

The intraoperative use of thromboelastography has not been described but is likely helpful for managing acute hemorrhage.

Certain patients may be at high risk for pulmonary embolism, compromised cardiac function, and bleeding. Depending on the type of procedure, extended haemodynamic monitoring postoperatively may be warranted.

Possible complications

The majority of the reported perioperative complications occurred postoperatively with few complications occurring during the intraoperative period. Therefore, only a small proportion of reported complications are directly associated with anaesthesia.

One episode of intraoperative airway obstruction has occurred [13]. There is an increased risk of wound breakdown, infection, thromboembolism, and bleeding that continues into the postoperative period [4,16]. These patients may be on mechanistic target of rapamycin (mTOR) inhibitors, which may cause immunosuppression and impair wound healing. Therefore, a multidisciplinary discussion should be considered regarding the ongoing management of the condition.

Post-operative care

Thrombosis and coagulopathy risk assessment by haematology should be considered after any surgery, especially those with vascular malformations [3]. One single-centre cohort study demonstrated a 9% risk of post-operative pulmonary embolism [19].

Post-operative stridor has been reported in three patients [4].

Patients with significant scoliosis and pulmonary dysfunction may require prolonged ventilatory support in the intensive care unit.

Disease-related acute problems and effect on anaesthesia and recovery

Perioperative pulmonary embolism is a particular concern for these patients [19]. A multidisciplinary discussion with a focus on perioperative anticoagulation strategies is advised.

Ambulatory anaesthesia

Minor procedures can be considered as day cases, particularly in patients with limited systemic manifestations with CLOVES syndrome.

Obstetrical anaesthesia

There is no reported literature on obstetrical anaesthesia in patients with CLOVES syndrome. Neuraxial anaesthesia may be difficult and a high risk (AVM, scoliosis, tethered cord, anticoagulation).

General anaesthesia may be necessary. Additional airway adjuncts should be available, given possible airway difficulties in CLOVES syndrome and pregnancy.

These patients are also at increased risk of thromboembolism events, which may be compounded in pregnancy.

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