orphanaesthesia

Anesthesia recommendations for patients with

Cornelia de Lange syndrome

Disease name: Cornelia de Lange syndrome

ICD 10: Q87.1

Synonyms: De Lange Syndrome, Brachmann – de Lange Syndrome, Typus degenerativus amstelodamensis

Cornelia de Lange syndrome (CdLS) is a genetic disorder caused by mutations in the cohesin complex and its regulators with hypoplasia of the mesenchyme as the suggested main pathophysiology. The majority of cases are sporadic. The clinical characteristics include growth retardation, gastrointestinal transport problems, hirsutism, limb abnormalities and facial abnormalities, such as brachycephaly, short neck, high arched eyebrows, short nose, low-set ears, wide nasal bridge, sometimes cleft palate, laryngeal anomalies and micrognathia [2]. The mental development is compromised and might be accompanied by aggressive, autistic or self-destructive tendencies [8]. Epilepsy and congenital cardiac defects are sometimes associated, as well as immunodeficiency. Anesthetic management concentrates on airway management (which can be challenging) and in prevention of aspiration, the leading cause of death in CdLS.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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

Typical surgery

Typical major surgery is needed for the gastrointestinal problems associated with CdLS: gastrointestinal reflux (fundoplication/gastrostomy tube placement), pyloric stenosis, intestinal malrotation, volvulus, congenital diaphragmatic hernia [2,8]

Common minor surgery includes orchidopexia for cryptorchidism, herniotomy, nasolacrimal duct stenosis, orthopaedic surgery of the limbs, bronchoscopy, and vesicoureteral reflux.

Type of anesthesia

In CdLS, all types of anaesthesia have been reported to be safely performed: general anaesthesia as well as spinal [7] and epidural anaesthesia [3, 9], both in adult and paediatric patients.

Necessary additional diagnostic procedures (preoperative)

Careful evaluation is needed with regard to the airway management. There is no single good predictor for the anticipation of a difficult airway in CdLS, but the clinical features (e.g. micrognathia, short neck, impaired mouth opening) could give the anesthesiologist a hint [13].

Preoperative laboratory workup should at least include a blood count, as immunodeficiency and thrombocytopenia [1] have been described.

The cardiac status should be evaluated with regard to associated congenital heart defects [2]. Associated heart defects such as ventricular septum defects, right ventricular hypertrophy, pulmonary stenosis [4, 15] and chronic pericarditis [21] have been reported, with pulmonary stenosis being the most frequent with an incidence of approximately 39% [15].

Almost all patients with CdLS suffer from gastroesophageal reflux and are prone to aspiration. Antiacid treatment or sodium citrate could attenuate adverse outcomes, should aspiration occur despite preventive efforts.

Particular preparation for airway management

In CdLS, the majority of articles report problems with airway management [10]. Difficult airway should thus be anticipated in every case of CdLS and proper preparations for airway management should be conducted. Direct laryngoscopy has been described as difficult in up to 50% of patients [23]. Intubation using “fiberoptic over laryngeal mask” [6, 20], McCoy laryngoscope [11] and Airwayscope® [5, 17] or blind nasotracheal intubation [24] have been shown to be successful in case reports.

Awake fiberoptic intubation can sometimes be an appropriate technique for airway securement, but it has also been described as difficult or impossible [22] due to a lack of cooperation in mentally impaired patients with CdLS [19].

There is no single good predictor available for the assessment of airway problems in CdLS.

Particular preparation for transfusion or administration of blood products

In rare cases, immunodeficiency has been reported, as well as one lethal case of cytomegalic virus infection. Transfusion could thus be directed to CMV-negative blood products, whereas no laboratory tests or aids for decision making for detection of specific immunodeficiency in CdLS have been reported yet.

Particular preparation for anticoagulation

No special issues.

Particular precautions for positioning, transport or mobilisation

Emphasis should focus on the psychological disorders. A familiar environment and presence of parents could ease the psychological guidance and reduce problems in the patient – caretaker interaction [12].

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

Neuroleptic medication is common in adult patients with CdLS. One case report described malignant neuroleptic syndrome after increasing the dose of loxapine [13].

Anaesthesiologic procedure

General anaesthesia and neuraxial anaesthesia have been successfully performed according to literature.

The anaesthesist should be aware of immature organ function, resulting in possibly lower doses than usually necessary [14]. Emphasis should be put on careful and individually titrated drug dosing in order to avoid over- or underdosing. In two case reports, even regular doses of metoclopramide [14] or midazolame [16] led to oversedation.

As a consequence of the incalculable effect of sedative drugs, careful premedication should be performed only if necessary and best in monitored areas due to risk of overdose.

CdLS is not associated with malignant hyperthermia (MH) and balanced anesthesia using volatile anesthetics [18] has been performed frequently. One case report discusses neuroleptic malignant syndrome in one patient with CdLS, a causal association with MH has not been established [13]. Succinylcholine has been used safely in patients with CdLS. Neuromuscular blockade has been performed using depolarizing and non-depolarizing drugs. Reversion of muscle relaxation has been effective in case reports [21].

Short neck, cervical webs and other anatomical features may lead to problems in placing catheters or central lines [21]. Ultrasonography could aid in catheter placement by visualization of the anatomy.

Particular or additional monitoring

Due to incalculable effect of drug, monitoring of anaesthesia depth (for instance using BIS monitoring) could be discussed in order to avoid overdosing, although coexisting neurological disease, epilepsy, neuroleptic medications and intellectual disability could potentially bias the monitoring. Reference values for this specific population are not existent.

Possible complications

Leading cause of death and the main anaesthesia risk is aspiration and the resulting pneumonia. Complicated airway management, in combination with gastrointestinal passage problems, gastroesophageal reflux as well as neurological disease with dysphagia and vocal cord dysfunction further increases the underlying risk of aspiration.

Hypoxia from prolonged airway management is an additional risk, which stresses the emphasis on proper preparation.

Postoperative care

After difficult intubation, careful extubation after the surgery is suggested; perhaps involving a Cook catheter, allowing for rapid reintubation should the efforts fail.

Postoperative ICU admission is suggested. For prevention of aspiration, readiness of suction and special attention is needed throughout the postoperative period.

Information about emergency-like situations / Differential diagnosis

Malignant neuroleptic syndrome has been described once in a patient with CdLS.

Emergency situations mainly arise from sudden intestinal disease, such as volvulus.

Airway management should be performed following a locally adapted guideline of the “anticipated difficult airway”. Moreover, proper techniques and additional personnel must be readily available at the time of anesthesia induction.

Ambulatory anaesthesia

Ambulatory anaesthesia is not recommended.

Obstetrical anaesthesia

To date, no obstetrical anesthesia cases have been reported in the literature to the knowledge of the authors. Pregnancy is very well possible, and there are inherited cases of CdLS.

Literature and internet links

1. Cavalleri V, Bettini LR, Barboni C et al. (2016) Thrombocytopenia and Cornelia de Lange syndrome: Still an enigma? Am J Med Genet A.170A(1):130-4.doi:10.1002/ajmg.a.37390
2. Deardorff MA, Noon SE, Krantz ID (Last Update: 2016) GeneReviews: Cornelia de Lange Syndrome
3. del Rio, E Reyes Espinosa, Cordero Luna D, Vasquez Montes MT, et al. Caudal block and sedation for bilateral herniorrhaphy in an infant with Cornelia de Lange syndrome (Bloqueo caudal y sedacion para herniorrafia bilateral a un lactante con sindrome de Cornelia de Lange). Revista Española de Anestesiologia y Reanimación 2004;51(7): 403-404
4. Filippi G. The de Lange syndrome. Report of 15 cases. Clinical genetics 1989;35(5):343-363
5. Furuya A, Suzuki S, Kondo S, et al. The use of dexmedetomidine and Airwayscope in airway management of a child with Cornelia de Lange syndrome. Masui. The Japanese Journal of Anesthesiology 2014;63(7):810-813
6. Hirai T, Nitahara K, Higa K; et al. Anesthetic management of an infant with Cornelia de Lange syndrome. Masui. The Japanese Journal of Anesthesiology 2006;55(4):454-456
7. Kachko L, Sanko E, Freud E, et al. Spinal anesthesia in a child with Brachmann-de Lange (Cornelia de Lange) syndrome. Journal of Anesthesia 2010;24(6):942-944. doi: 10.1007/s00540-010-1026-y
8. Lacombe D. Orpha.net: Cornelia de Lange syndrome
9. Lumb AB, Carli F. Respiratory arrest after a caudal injection of bupivacaine. Anaesthesia 1989;44(4):324-325
10. Moretto A, Scaravilli V, Ciceri V, et al. Sedation and general anesthesia for patients with Cornelia De Lange syndrome: A case series. American Journal of Medical Genetics 2016;Part C, Seminars in medical genetics 172(2):222-228.doi:10.1002/ajmg.c.31493
11. Moschini V, Ambrosini MT, Sofi G. Anesthesiologic considerations in Cornelia de Lange syndrome (Considerazioni anestesiologiche nella sindrome di Cornelia de Lange). Minerva Anestesiologica 2000;66(11):799-806
12. Nagai H, Noda Y, Mase K, et al. Anesthetic management of a pediatric patient with Cornelia de Lange syndrome. Masui. The Japanese Journal of Anesthesiology 1996;45(1):99-101
13. Papadimos TJ, Marco AP. Cornelia de Lange syndrome, hyperthermia and a difficult airway. Anaesthesia 2003;58(9):924-925.doi:10.1046/j.1365-2044.2003.03362_17.x
14. Sargent WW. Anesthetic management of a patient with Cornelia de Lange syndrome. Anesthesiology 1991;74(6):1162-1163
15. Selicorni A, Colli AM, Passarini A, et al. Analysis of congenital heart defects in 87 consecutive patients with Brachmann-de Lange syndrome. Am J Med Genet A 2009;149A(6):1268-72
16. Stevic M, Milojevic I, Bokun Z, et al. Unpredictable drug reaction in a child with Cornelia de Lange syndrome. International Journal of Clinical Pharmacy 2005;37(1):1-3. doi: 10.1007/s11096-014-0050-7
17. Sugiyama T and Okutani R. Difficult tracheal intubation in a child with Cornelia de Lange syndrome using a paediatric Intlock installed in a Pentax Airway Scope. Anaesthesia 2012;67(12):1411-1412.doi:10.1111/anae.12070
18. Takeshita T, Akita S, Kawahara M. Anesthetic management of a patient with Cornelia De Lange syndrome. Anesthesia Progress 1987;34(2):63-65
19. Torres MD, Calvo E, Fernandez Espla F, et al. Anesthetic management of an adult patient with Cornelia de Lange Syndrome. Minerva Anestesiologica 2010;76(3):229-231
20. Tsukazaki Y, Tachibana C, Satoh K et al. A patient with Cornelia de Lange syndrome with difficulty in orotracheal intubation. Masui. The Japanese Journal of Anesthesiology 1996;45(8):991-993
21. Veall GR. An unusual complication of Cornelia de Lange syndrome. Anaesthesia 1194;49(5):409-410
22. Vestergaard L, Dey N, Winding R. Anesthetic considerations in a patient with Cornelia de-Lange syndrome. Journal of Anaesthesiology, Clinical Pharmacology 2015;31(3):419-420. doi: 10.4103/0970-9185.161732
23. Yo T, Noguchi I, Kimura T, et al. General anesthesia in a patient with Cornelia de Lange syndrome with restricted opening of the mouth. Masui. The Japanese Journal of Anesthesiology 1998;47(5):611-614
24. Yokoyama T, Tomoda M, Nishiyama T, et al. General anesthesia for a patient with Cornelia de Lange syndrome. Masui. The Japanese Journal of Anesthesiology 2000;49(7):785-787.

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Please note that this guideline has not been reviewed by two anaesthesiologists, but two disease experts instead.