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Berufsverband Deutscher Anästhesisten e.V. (BDA)
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Organ: Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin e.V. (DIVI)

Andersen diseas

Collagen VI-related myopathy

orphananesthesia

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

SUPPLEMENT NR. 2 | 2020

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 Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

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 Anästhesisten damit keine Erfahrungen gesammelt haben, so dass 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 ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass 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.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

OrphanAnesthesia –
a common 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 and 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 international. Thus, all recommendations are published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommenations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). 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.

A survey of until now in A&I published recommendations can be found on:

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Anaesthesia recommendations for

Collagen VI-related myopathy

Disease name: Collagen VI-related myopathy

ICD 10: G71

Synonyms – Spectrum of phenotypes:

Mild:	Bethlem myopathy / benign congenital muscular dystrophy
Intermediate:	Limb-girdle muscular dystrophy; myosclerosis myopathy
Severe:	Ullrich myopathy / Congenital atonic sclerotic muscular dystrophy

Disease summary: First described by Ullrich in 1930 and Bethlem in 1976, respectively [1]. Caused by mutations in any of the 3 genes which code for collagen type VI synthesis, COL6A1, COL6A2 and COL6A3 [2]. Collagen VI is a major contributor to the stability of the extracellular matrix. The remaining function of collagen VI determines the clinical severity of the disorder [3,4]. Considered different entities in the past, Bethlem and Ullrich myopathy are now considered extremes in the spectrum of collagen VI myopathy. Both inheritance (mostly autosomal recessive) and de-novo mutations (mostly autosomal dominant) are possible, the latter is more common. Combined prevalence is estimated at approximately 1 in 100,000 births (varying data for subtypes). Diagnosis relies on muscle biopsy and molecular genetic testing. There exists no causative treatment.

In Bethlem myopathy, patients will experience moderate muscle weakness, peripheral joint laxity and proximal joint contractures. Onset of symptoms will take place in late childhood or adolescence. Mobility will diminish over the years but usually still be present in advanced years. No valid data on life expectancy. Overall benign course.

In Ullrich myopathy, muscle weakness and muscular contractures are noticed at birth or in early infancy. Neonates may present with congenital hip dislocation and general hypotonia, whereas infants may present with difficulty climbing stairs. Even where independent ambulation is achieved in childhood, most will be wheelchair-bound from early adolescence onward. Affection of respiratory muscles is frequent and ventilation support may be necessary, intermittently (nocturnal) or permanently. The clinical course may be complicated by recurrent pulmonary infections. The phenotype will be characterised by hypermobility of peripheral joints and contractures of proximal joints as well as scoliosis and kyphosis. Affected individuals may present with a round facies with long thin limbs and muscular wasting. Muscular weakness may also prevent adequate mastication and may lead to underweight.

Impaired collagen VI function can also lead to follicular hyperkeratosis resulting in impaired wound healing and keloid scar formation.

▶ **Citation:** Prottengeier J, Shammas K, Smith J: Collagen VI-related myopathy. Anästh Intensivmed 2020;61: S20–S26. DOI: 10.19224/ai2020.S20

Collagen VI is not found in the CNS and thus the cognitive ability is unaffected. There is no sensory component. Cardiac function seems to be normal in Ullrich disease. Data for Bethlem myopathy is conflicting with isolated reports of mild cardiomyopathy and an unclear relevance for anaesthesia practice [5]. Serum creatine kinase may be slightly raised as a biochemical marker.

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

Surgical correction of musculoskeletal, especially spinal deformities – e.g. scoliosis correction [6]. Distraction osteotomy – growth rod insertion. Contracture release.

Tracheostomy, gastrostomy and pressure ulcer repair in the most severe cases.

Scar revision surgery.

Type of anaesthesia

There is no data to indicate the superiority of either intravenous or volatile anaesthetics [7]. Literature and pathophysiology suggest no connection to malignant hyperthermia. Depolarising muscle-relaxants should, however, be avoided in the context of patient immobilisation.

Little information is available in literature regarding neuro-axial blockade and regional anaesthesia in these patients. The presence of a scoliosis and/or kyphosis can present a significant technical challenge. Regional anaesthesia may be beneficial in patients with impaired respiratory capacities, but also present with severe challenges due to contractures and difficulties in positioning and anatomical access. Be aware that some reports indicate that minimal tissue injury can cause severe subcutaneous haemorrhage.

Necessary additional pre-operative testing (beside standard care)

Respiratory function needs to be robustly assessed prior to the administration of general anaesthesia. Even more than a chest X-ray, lung function tests should be performed to assess respiratory impairment. This includes an arterial blood gas analysis.

Although cardiac function seems unaffected by the disease per se, there may be evidence of right heart failure as a consequence of prolonged respiratory involvement and therefore an ECG and an echocardiogram will be advisable if right heart involvement is suspected. The significance of single reports of very mild and clinically irrelevant cardiomyopathy in Bethlem myopathy is not yet clear.

Blood analysis may highlight polycythaemia (respiratory impairment) or concurrent (airway/pulmonary) infection. Urea, creatinine and electrolytes will help to rule out any renal end organ damage as a result of the pre-existing scoliosis and is helpful to refer to following surgery in the prone position.

Particular preparation for airway management

In cases accompanied by the typical facial stigmata, micrognathia and a high arched palate, can lead to difficult intubation conditions. Preparations for difficult airway management are advisable.

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Particular preparation for transfusion or administration of blood products

Literature does not indicate any increased requirements resulting from the myopathy per se. However, corrective spinal and extensive musculoskeletal surgeries have inherent procedural risks of major blood loss.

Particular preparation for anticoagulation

No information on specific disease-related pathophysiology. As mentioned above: Remember the procedural risks of major musculoskeletal/spinal surgery.

Particular precautions for positioning, transportation and mobilisation

Previous immobilisation, contractures and underweight may be marked and careful patient positioning is crucial in order to avoid pressure ulcers and nerve entrapment syndromes.

This condition is associated with respiratory insufficiency, and although the prone position (for spinal surgery) can be helpful with gas exchange, extra care should be taken for adequate positioning.

Ullrich myopathy is associated with follicular hyperkeratosis which leads to keloid scar formation, impaired wound healing and increased skin and soft tissue vulnerability. Extra caution is advisable with bandages, eye pads and other adhesives.

Interactions of chronic disease and anaesthesia medications

Children with Ullrich disease may be on prophylactic antibiotics, which may alter the choice of antibiotics used for surgical prophylaxis.

Cyclosporine A may be of benefit in Ullrich disease and children on this drug may display its side effects including gingival hyperplasia and hypertension.

Anaesthetic procedure

Inhalational and TIVA techniques may both be used. Little evidence surrounds the use of neuro-axial anaesthesia and regional anaesthesia. Invasive procedures may lead to significant cutaneous and subcutaneous bleeding.

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Particular or additional monitoring

Invasive arterial catheters seem useful to assess ventilation and gas exchange both during surgery and in the post-operative period.

In cases of pulmonary hypertension and/or right ventricular dysfunction, advanced haemodynamic monitoring (pulmonary artery catheter or Swan-Ganz catheter, intraoperative-TEE) should be considered.

Possible complications

Skins lesions and reactions may be seen as a result of the use of dressings, eye tapes and ECG pads.

Pressure ulcers may develop due to any difficulty with the positioning of patients.

Post-operative care

In severe cases (typically Ullrich myopathy), respiratory failure may complicate the postoperative course. Those patients should be handled in an intensive care or high-dependency environment.

Disease-related acute problems and effect on anaesthesia and recovery

Iatrogenic causes of respiratory failure should be avoided including the overuse of opiate analgesia, prolonged action of neuromuscular blocking drugs, hypothermia and residual anaesthetic agents.

Ambulatory anaesthesia

Due to the complex and rare nature of this disorder and the risk of possible postoperative respiratory failure in severely affected patients, ambulatory anaesthesia should only be considered in the mildest of phenotypes.

Obstetrical anaesthesia

Literature does not provide any data regarding parturient patients with collagen VI myopathies. Neuro-axial procedures may be complicated by anatomical difficulties and skin/soft tissue vulnerability (haemorrhage!).

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References

1. Bethlem J, Wijngaarden GK. Benign myopathy, with autosomal dominant inheritance. A report on three pedigrees. Brain 1976;99:91–100
2. Lampe AK, Flanigan KM, Bushby KM, Hicks D. Collagen Type VI-Related Disorders. Pagon et al., GeneReviews (R): University of Washington, Seattle; 1993
3. Bonnemann CG. The collagen VI-related myopathies: Muscle meets its matrix. Nat Rev Neurol 2011;7:379–930
4. Gilbreath HR, Castro D, Iannaccone ST. Congenital myopathies and muscular dystrophies. Neurologic clinics 2014;32:689–703,viii
5. Finsterer J, Ramaciotti C, Wang CH, Wahbi K, Rosenthal D, Duboc D, et al. Cardiac findings in congenital muscular dystrophies. Pediatrics 2010;126:538–545
6. Takaso M, Nakazawa T, Imura T, Okada T, Ueno M, Saito W, et al. Surgical correction of spinal deformity in patients with congenital muscular dystrophy. J Orthop Sci 2010;15:493–501
7. Grosu I, Truong D, Teodorescu S, Mousny M, Veyckemans F. Anesthetic management of a child with Ullrich myopathy. J Anesth 2012;26(4):636–637

Further Information are to be found on the following websites:

- CURE CMD (Support group based in the USA; content in English; containing links to further online resources for non-physicians in social media): http://curecmd.org
- MUSCULAR DYSTROPHY UK (Charity based in the UK; content in English; umbrella organisation for different conditions of muscular dystrophy): http://www.musculardystrophyuk.org/

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