

Anaesthesia recommendations for **Chanarin-Dorfman Syndrome**

Disease name: Chanarin-Dorfman Syndrome

ICD 10: E75.5

Synonyms: Neutral Lipid Storage Disease with ichthyosis

Disease summary:

Chanarin-Dorfman syndrome (CDS) is an autosomal recessive, multisystemic metabolic disorder. The characteristic feature of congenital ichthyosis is the deposition of lipids in cells. The first case was described by Dorfman in 1974 (1). Although the actual metabolic defect in CDS patients is unknown, available data suggest an abnormality in intracellular triglyceride metabolism. Mutation of the CGI-58 gene (also known as ABHD5) on chromosome 3p-21 causes triglyceride accumulation (2). ABDH5 constitutes a multimeric protein pivotal in activating intracellular lipases, notably adipose triglyceride lipase (ATGL), a key participant in the lipolysis process. Computational simulations employing machine learning-driven homology modeling approaches have proposed that mutations in the E41, R116, and G328 genes disrupt hydrogen bonding networks, resulting in a consequential inhibition of ATGL activation (3,4).

The presence of lipid vacuoles in neutrophil granulocytes in peripheral blood smears in patients with ichthyosis is diagnostic. It is a rare but interesting condition that should be considered when evaluating an isolated elevation of alanine aminotransferase (ALT) (5). Myopathy is observed in 60% of these patients. The objective of this article was to improve comprehension regarding anaesthesia management for patients with CDS.



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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

Emergency information

A	AIRWAY / ANAESTHETIC TECHNIQUE	Given the possibility of muscle spasms and limited joint movement in ichthyosis patients, prioritize difficult airway management. Be mindful of using flexible intubation methods (laryngeal mask, videolaryngoscope, fiberoptic, and emergency cricotracheotomy). / If there are no contraindications, choose regional anesthesia, otherwise be prepared for TIVA.
B	BLOOD PRODUCTS (COAGULATION)	Thoroughly examine the bleeding tendency, and have blood and plasma products prepared prior to the operation.
C	CIRCULATION	Given the potential cardiac complications linked to hyperlipidemia, conduct a comprehensive cardiac consultation prior to the operation and utilize both noninvasive and invasive cardiac monitoring during the procedure.
D	DRUGS	Avoid using succinylcholine and, if you need inhalation anesthesia, choose low-flow inhalation anesthesia.
E	EQUIPMENT	Exercise caution during the transfer to prevent potential skin trauma and closely monitor the patient in the Post Anesthesia Care Unit (PACU) after the operation.

Typical surgery

Patients' complaints are usually multisystemic. Therefore, patients may require surgery for cataracts, hearing problems, skin involvement, muscle involvement, and cardiomyopathy (6). Ocular manifestations have been identified in 46% of documented cases and are characterized by the development of cataracts. Furthermore, occurrences of nystagmus, strabismus, or ectropion may also be observed (7).

Muscular involvement may manifest through elevated creatine kinase levels and lipid accumulation within muscle fibers. Ocular manifestations can manifest as cataracts, nystagmus, and strabismus. Additional findings potentially observed in this clinical disorder include hearing loss, cardiomyopathy, intellectual disability, growth retardation, microcephaly, and intestinal involvement (8,9).

Type of anaesthesia

There is no clear recommendation for general or regional anesthesia. Regional or local anesthesia may be used. Because general anesthesia decreases liver perfusion, it may exacerbate preexisting liver injury in these patients. Liver toxicity should be considered when selecting anesthetics. Like all drugs, inhalational anesthetics undergo processes of distribution, metabolism, and elimination in the body. Anesthetics undergo significant metabolism, and in many cases, reactive and potentially toxic products are formed. These metabolic and chemical processes may depend on age, interactions with other drugs, and genetic predisposition. Halothane, isoflurane, and desflurane undergo oxidative metabolism mediated by cytochrome P450 to produce trifluoroacetyl (TFA). In all exposed patients, these modified tissue proteins (haptens) are formed. In susceptible individuals, these modified liver proteins can lead to liver damage and patient death as a result of an immune response for reasons that are still unclear (10). Total intravenous anesthesia (TIVA) may be a reasonable option in patients with CDS.

Caution should be exercised, as hepatic perfusion is compromised by hypotension, hypercapnia, and sympathetic stimulation. Normocapnic ventilation should be used throughout the procedure to avoid hepatic encephalopathy (11). In recent years, TIVA has become an alternative to inhalation anesthesia due to its target-controlled applicability. Oh SK et al. (12), in their study involving 730 patients, observed that TIVA application demonstrated a higher level of safety among patients with elevated transferase levels.

The potential for cutaneous trauma arising from ichthyosis and its associated susceptibility to infections warrants consideration. Furthermore, anticipation of coagulopathic tendencies,

potentially stemming from incipient liver dysfunction, is prudent. Consequently, caution is advised in the selection of regional anesthesia.

Necessary additional pre-operative testing (beside standard care)

A comprehensive evaluation, including complete blood count and blood biochemistry encompassing measurements of urea, creatinine, potassium, sodium, and creatine kinase (CK), is warranted. This assessment is imperative given the presence of progressive adult proximal weakness, episodes of rhabdomyolysis characterized by myoglobinuria potentially induced by vigorous exercise and extended fasting, recurrent episodes of weakness, and indications of muscle weakness and clinical observation. An EMG should be performed. T2°monitors the effects of dyslipidemia on the cardiovascular system, and a cardiology consultation with ECG and ECO should be performed.

Hepatomegaly, steatosis, and worsening liver function tests may be observed. An abdominal USG may be performed to determine liver enzymes, function tests, and hepatomegaly. If muscle weakness is present and regional anaesthesia is planned, consultation is helpful for legal reasons. Vigilant observation of cutaneous manifestations is imperative, and any potential skin infection should be meticulously investigated without disregard.

Particular preparation for airway management

Since spasm of the masseter muscle and limitation of joint movement may be observed in these patients due to ichthyosis, attention should be given to difficult airways and conditions for difficult airways (flexible intubation style, laryngeal mask, videolaryngoscope, fiberoptic, emergency cricotracheotomy). Since liver failure can lead to bleeding disorders, intubation should be performed more carefully in these patients, and damage to the larynx and trachea should be avoided. Moreover, a meticulous assessment of the airway is essential, particularly in patients presenting with characteristics such as a small oral cavity, enlarged tongue, and restricted neck mobility.

Particular preparation for transfusion or administration of blood products

These patients may require increased blood transfusions due to bleeding disorders resulting from liver failure. Blood type and crossmatch must be correct. Blood and blood products should be prepared before surgery. Extensive coagulation tests (bleeding time, fibrinogen level) should be performed before surgery.

Particular preparation for anticoagulation

There is no evidence to support the need for particular anticoagulation.

Particular precautions for positioning, transportation and mobilisation

In these patients, the skin structures are fragile due to ichthyosis. The use of endotracheal tubes and ECG pallets can damage the skin. Because patients with ichthyosis tend to lose heat, heating pads can be used on the couch to maintain normothermia during anesthesia. Because weak muscle strength weakens the bone structures in myopathies, it is sensitive during transport and surgery, and softening silicone or gel pads can be used during positioning.

Interactions of chronic disease and anaesthesia medications

Increased serum creatine phosphokinase may occur due to myopathies. The use of succinylcholine should be avoided in these patients because it may cause hyperkalemia and malignant hyperthermia (13). Nondepolarizing agents should be preferred as muscle relaxants. Hepatotoxic agents should be avoided whenever possible. For this reason, it may be more appropriate to use TIVA rather than inhalational anesthetics in the induction and maintenance of general anesthesia.

Anaesthetic procedure

TIVA may be used in conjunction with general anesthesia. Because the skin is sensitive due to ichthyosis, care should be taken to avoid ichthyosis and cellulitis in the area of application when regional anesthesia is performed.

Succinylcholine, a neuromuscular blocking agent that depolarizes muscle, is contraindicated in individuals with Chanarin-Dorfman syndrome owing to the potential to worsen metabolic and muscular complications inherent in this disorder. Chanarin-Dorfman syndrome, a rare genetic condition, is typified by irregularities in lipid metabolism, notably the accumulation of triglycerides in diverse bodily tissues. Succinylcholine's mechanism can induce the release of potassium from muscle cells, potentially leading to hyperkalemia, marked by elevated levels of potassium in the bloodstream. Nondepolarizing muscle relaxants may be used.

Antagonization of neuromuscular blockade with pyridostigmine or neostigmine appears to be possible.

There are (no) reports of successful administration of sugammadex.

Particular or additional monitoring

Neuromuscular blockade monitoring is strongly recommended when a neuromuscular blocker is used. It is useful to obtain baseline values before injecting the nondepolarizing neuromuscular blocker. Moreover, insufficient neuromuscular blockade could result in skin sensitivity and discomfort during the surgical procedure. Monitor body temperature to avoid chills and increased oxygen requirements. In cases of cardiomyopathy, transesophageal echocardiography is very useful.

Neuromuscular monitoring

Depth of anaesthesia: BIS Body temperature

Transesophageal echocardiography

Due to ichthyosis on the eyelids, it is recommended to wear eye protection and use tearless solutions during surgery.

The careful monitoring and preservation of liver function during anesthesia administration are fundamental prerequisites for enhancing patient safety and refining drug management strategies within the perioperative context. A comprehensive preoperative assessment of

hepatic biomarkers, alongside diligent intraoperative surveillance of these markers, holds paramount importance. These measures are particularly critical in customizing anesthesia approaches, precisely modulating drug metabolism, and mitigating potential complications, especially in patients with underlying hepatic pathophysiology. A collaborative effort among medical specialists, underpinned by an interdisciplinary approach, establishes an optimal framework for navigating the complexities of anesthesia, ultimately leading to favorable perioperative outcomes.

Possible complications

Inhalation anesthetics may cause hepatotoxicity.

Difficult mask ventilation and difficult intubation may occur due to myopathies.

Because skin structures are sensitive, there is a risk of bleeding during procedures.

Sedatives (benzodiazepines) may cause respiratory failure (11). Anesthesia-associated rhabdomyolysis is an infrequent surgical complication that manifests postoperatively with myalgia, weakness, and potential renal failure if not promptly addressed. Underlying predisposing conditions such as muscular dystrophies and myopathies may contribute to the onset of this complication (14).

Post-operative care

The extent of postoperative monitoring and possible admission to the intensive care unit depend on both the surgical procedure and the patient's preoperative condition.

Prolonged immobilization was avoided. Concomitant muscle atrophy may worsen the condition.

Prolonged immobilization and bed confinement may increase tissue damage in ichthyosis.

May be an acute psychiatric disorder

May be an epileptic status.

Disease-related acute problems and effect on anaesthesia and recovery

TIVA should be preferred over inhaled anesthetics during general anesthesia.

Succinylcholine should be avoided because of liver toxicity. Nondepolarizing muscle relaxants should be used as muscle relaxants (11,15).

Because ichthyotic skin is sensitive, cellulitis-like skin infections may occur.

Ambulatory anaesthesia

Like general anesthesia preparation

Obstetrical anaesthesia

Like general anesthesia preparation

There are no reliable data available.

References

1. Özkale Y, Erol İ, Canan O, Durdu M . Chanarin Dorfman Syndrome: A case report Cukurova Medical Journal 2015;40:614-18. <https://doi.org/10.17826/cutf.71286>
2. Bruno C, Bertini E, et al. Clinical and genetic characterization of Chanarin-Dorfman syndrome Biochemical and Biophysical Research Communications Elsevier 6 May 2008.
3. Shahoei R, Pangei S, Sanders MA, Zhang H, Mladenovic-Lucas L, Roush WR, Halvorsen G, Kelly CV, Granneman JG, Huang YM. Molecular Modeling of ABHD5 Structure and Ligand Recognition. Front Mol Biosci. 2022 Jun 28;9:935375. doi: 10.3389/fmolb.2022.935375.
4. Mangukiya N P, Kaleem S, Meghana D, et al. Chanarin-Dorfman Syndrome (CDS): A Rare Lipid Metabolism Disorder. Cureus August 21, 2023 ; 15(8): e43889. doi:10.7759/cureus.43889
5. Di Donato S, F. Taroni F. "Disorders of lipid metabolism" in Myology, A. G. Engel and C. Franzini-Armstrong, Eds., 1587-1621, McGraw Hill, New York, 2004.
6. Bolattürk F, Göl Ö, Yetkin M. Chanarin Dorfman Sendromu: Olgu sunumu. Bozok Tıp Dergisi. 2018;10.16919/bozoktip.349928.
7. Kalyon S, Gökden Y, Demirel N, Erden B, Türkyılmaz A. Chanarin-Dorfman syndrome. Turk J Gastroenterol. 2019;30(1):105-108. doi:10.5152/tjg.2018.18014).
8. Emre S, Unver N, Evans SE, et al. Molecular analysis of Chanarin-Dorfman syndrome (CDS) patients: Identification of novel mutations in the ABHD5 gene. Eur J Med Genet. 2010;53(3):141-144. doi:10.1016/j.ejmg.2010.03.002
9. C. Pena-Penabad, M. Almagro, W. Martinez, J. Garcia-Silva, J. Del Pozo, M.T. Yebra, C. Sanchez-Manzano, E. Fonseca Dorfman-Chanarin syndrome (neutral lipid storage disease): new clinical features Br. J. Dermatol., 144 (2001), pp. 415-418

10. Martin JL. Volatile anesthetics and liver injury: a clinical update or what every anesthesiologist should know. *Can J Anesth.* 2005;52:125-9.
<https://doi.org/10.1007/BF03027715>
11. Butterworth JF, Mackey DC, Wasnick JD. *Morgan & Mikhail Klinik Anesteziyoloji* 2021;33/717
12. Oh SK, Lim BG, Kim YS, Kim SS. Comparison of the Postoperative Liver Function Between Total Intravenous Anesthesia and Inhalation Anesthesia in Patients with Preoperatively Elevated Liver Transaminase Levels: A Retrospective Cohort Study. *Ther Clin Risk Manag.* 2020;16:223-232
13. Ogawa M, Doi K, Mitsufuji T, Satoh K, Takatori T. Drug induced hepatitis following sevoflurane anesthesia in a child]. *Masui.* 1991;40:1542-5.
14. Veropalumbo, C., D'Aniello, R., Sangermano, M., Paoella, G., & Vajro, P. (2013). Hypertransaminasemia: is it always liver disease? The case of subclinical myopathies and macroenzymes. *Global Journal of Gastroenterology and Hepatology*, 1(1), 8-17.
15. Koç A, Eren N. Anesthesia management in patient with Chanarin Dorfman Syndrome. *JARSS.* 2019; 27(2): 151-154

Date last modified: October 2023

This recommendation was prepared by:

Author(s)

Alparslan KOÇ¹

Nurhan EREN¹

¹*Erzincan Binali Yildirim University Mengucek Gazi Training and Research Hospital
Anesthesiology and Reanimation Clinic, Erzincan, Turkey*

Disclosure The authors **have** no financial or other competing interests to disclose. This recommendation was unfunded.

This recommendation was reviewed by:

Reviewers

Hayrettin DAŞKAYA

Mehmet TOPTAŞ

Disclosure The reviewers have no financial or other competing interest to disclose.
