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Erdheim-Chester disease

Haemophilia A

orphanaesthesia

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

SUPPLEMENT NR. 4 I 2022

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 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 recommenations 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.

Find a survey of the recommendations published until now on:

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Anaesthesia recommendations for

Erdheim-Chester disease

Disease name: Erdheim-Chester disease

ICD 10: C96.1

Synonyms: ECD, Lipoid granulomatosis; Non-Langerhans cell histiocytosis; Erdheim-Chester syndrome; Polyostotic sclerosing histiocytosis

Disease summary: Erdheim-Chester disease is an extremely rare multisystem neoplasm characterised by excessive production and accumulation of histiocytes within organs and tissues. It was discovered in 1930 by Jacob Erdheim and William Chester. The term was coined by Jaffe in 1972 to describe this rare disorder characterised by the infiltration of bone marrow with histiocytes, macrophages, lymphocytes and multi-nucleated giant cells. In nearly half of patients, there is mutation of the BRAF gene (V600E). Immunohistochemistry revealed that ECD histiocytes are positive for CD68, CD163, and factor XIIIa, and negative for CD1a, S100 protein and langerin (CD207). ECD is a clonal disorder with recurrent BRAFV600E mutations in more than half of the patients in whom chronic uncontrolled inflammation is an important mediator of disease pathogenesis, due to frequent hyperactivation of mitogen-activated protein kinase signalling.

Nearly 550 cases have been described in the literature to date. It is usually a disease presenting in adulthood, between the 4th and 7th decade of life (40–70 years of age), with slight male preponderance. It can also, rarely, present in childhood. The major sites of involvement include the long bones (with epiphyseal sparing), cardiovascular system, lungs, orbit, brain, retroperitoneum and the skin. The commonest presenting complaint is bone pain.

Non-osseous involvement includes fibrotic infiltration of the cerebral, retroperitoneal, retro-orbital, pericardial and pulmonary tissues. Other general symptoms include fever, polyuria, polydipsia, weight loss, weakness, night sweats and fatigue. Children may present with failure to thrive, though it is rare in the paediatric population. The characteristic radiographic feature of ECD is bilateral and symmetrical osteosclerosis in the di-metaphyseal region, with sparing of epiphyses and the axial skeleton, although this is not universally present. 99mTc bone scintigraphy typically demonstrates symmetric and abnormally strong 99mTc labelling of the distal ends of the long bones. A similar finding can be observed in a positron emission tomography scan. Central nervous system involvement occurs in nearly half of all patients and can manifest as diabetes insipidus, exophthalmos, cerebellar ataxia, panhypopituitarism and papilloedema. A macrophage activation syndrome (MAS) is a dreaded complication which can be triggered in patients of severe ECD due to various stressors like infection and surgery.

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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

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Typical surgery

Patients with ECD can present to the anaesthesiologist for a variety of elective and emergency procedures. In particular, these patients may undergo orthopaedic procedures commonly in view of the predominant osseous involvement. Their bones are prone to fractures with minimal trauma. Reduction of fractures (either open or closed) may require emergency anaesthesia administration, which may prove challenging in a patient with ECD.

A thorough systematic examination with evaluation of individual organ systems is mandatory. These patients can also come for correction of hydroureteronephrosis, which may require cystoscopy or exploratory laparotomy. Patients may also present for ophthalmic surgery in view of the damage caused by the growing retro-orbital deposits (e.g., glaucoma surgery, retinal detachment surgery, corneal surgeries and nasolacrimal duct surgery).

Type of anaesthesia

Anaesthetic management depends on the degree of systemic involvement by the disease and the nature of the surgery. The type of anaesthesia will be determined by the surgical site and the urgency of the procedure. The main anaesthetic goals include: maintaining adequate oxygenation, normocarbia, normothermia, preventing secondary organ damage and neurovascular injury.

In emergency surgeries, general anaesthesia is fraught with the risk of aspiration due to possibility of full stomach. Elaborate pre-anaesthetic workup may not be possible in emergency situations. Basic biochemical investigations, electrocardiogram and a chest radiograph must be done for assessing organ system functions.

For extremity surgeries, especially fracture reduction, regional anaesthesia is preferred. It provides excellent analgesia as well as reduces the risk of deep vein thrombosis. In elective procedures, a coagulation profile and platelet count must be done to rule out coagulopathies and platelet dysfunction. Ultrasound-guided nerve blocks are especially recommended in these patients due to possibility of disturbed anatomy and to improve accuracy. Continuous infusion catheters can be threaded into the nerve sheath using ultrasound guidance for ensuring post-operative pain relief. All standard ASA monitors must be instituted in every patient. Special precautions for eye cover must be utilised.

Anaesthetic implications of positioning may be exaggerated in these patients due to associated skeletal and systemic affliction by the disease. Aneasthesia for robotic surgery in these patients can prove challenging as the patient is placed away due to a huge robotic console. In addition, a steep Trendelenburg position, used in most robotic surgeries, may be associated with greater physiologic alterations and risk of neurovascular injury in patients with ECD. These procedures are associated with rise in intraocular pressure, which can be deleterious in patients with exophthalmos secondary to ECD. There is a paucity of literature on robotic surgery in the ECD population.

Necessary additional pre-operative testing (beside standard care)

As ECD is a multisystem disease, with both osseous and non-osseous involvement, a thorough evaluation of all organ systems is required before elective surgeries. Apart from routine investigations (like complete blood count, renal function tests, Serum electrolytes, Blood sugar, liver function tests, coagulation profile, chest X-ray, and electrocardiogram),

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orthopaedic and neurologic evaluation should be done pre-operatively. Radiologic tests of involved bones and brain scanning for possible extension may be considered, wherever required. An ophthalmologic evaluation and fundoscopy can be done in case of eye involvement. In case of surgery in patients with an extensive disease, blood grouping and cross-matching are required should peri-operative blood transfusion be needed. 99mTc bone scintigraphy and PET (positron emission tomography) scanning can be done to assess the extent of disease in ECD. If difficult airway is suspected, cervical spine X-rays (anteroposterior & lateral views) can be done to assess the patient's neck mobility.

Particular preparation for airway management

Standard preparations for airway management must be made in the form of pre-oxygenation, working suction, aspiration prophylaxis, availability of resuscitation equipment, basic and advanced airway adjuncts as well as standard ASA (American Society of Anesthesiologists) monitoring devices. Patients with ECD may have difficult airway which will mandate the setting up and accessibility of a difficult airway cart. Apart from availability of all sizes of airways, tubes and laryngoscope blades, advanced airway equipment useful for difficult airways (e.g. video laryngoscopes, fibre-optic bronchoscope, McCoy blade, gum elastic bougie, airway exchange catheter, supraglottic airway devices etc.) must be readily available.

In cases of difficult airway, awake fibre-optic intubation can be done under upper airway local anaesthesia and intravenous dexmedetomidine (alpha-2 receptor agonist) infusion/sedation. An experienced anaesthesiologist should be available in such cases. A supraglottic airway device (e.g., laryngeal mask airway, i-gel®, intubating LMA) and other difficult airway adjuncts should be kept ready. Theoretically, there can be affliction of the laryngeal cartilages in patients with ECD and there can be instances of airway trauma complicating difficult airway management. Care must also be taken to limit neck movements during intubation in view of the possible cervical spine involvement in ECD.

Particular preparation for transfusion or administration of blood products

There are no particular preparations for transfusion or administration of blood products in patients with ECD. Platelet transfusions may be required in patients with thrombocytopenia. Care must be taken to prevent allergic reactions during blood transfusions as they can trigger histamine release and lead to the activation of MAS. Another problem especially with massive or rapid transfusions is the development of hypothermia, which can be deleterious in patients with ECD. Mismatched transfusions must be avoided at all costs.

Particular preparation for anticoagulation

There is no particular preparation for anticoagulation in patients with ECD. In patients with ECD presenting with intracranial lesion or intraocular masses, extreme caution should be taken while instituting anticoagulant therapy, as there is a possibility of sudden intracranial or intraocular haemorrhage. Anticoagulant therapy in the face of MAS is not recommended as MAS presents with thrombocytosis which can compound the risk of bleeding. Regular monitoring of coagulation parameters and platelet counts is recommended when ECD patients are subjected to anticoagulation.

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Particular precautions for positioning, transportation and mobilisation

Patients with ECD are more prone to develop positioning-related neurovascular injuries. Extremes of surgical positioning for prolonged periods must be avoided. In view of their fragile skeletal system, transportation must be gentle. Post-surgical mobilisation must be cautious in order to avoid falls and injuries.

Interactions of chronic disease and anaesthesia medications

There have been no randomised studies to highlight the interaction of the patient's long-term medication with the anaesthetic agents. Nevertheless, it is known that long-term steroid and immunosuppressant medication administration can have important anaesthetic implications.

Anaesthetic procedure

The anaesthesiological procedure is according to the surgical requirement and stage of the disease. Generally, elective procedures are scheduled only during the remission phase. Intravenous cannulation can be difficult in patients with severe musculoskeletal deformities. Ultrasound guidance must be sought for securing invasive monitoring lines to improve ease and accuracy. Face mask application during induction of general anaesthesia must be extremely cautious in patients with exophthalmos to prevent further eye injuries.

In patients with respiratory involvement of ECD, regional anaesthesia is preferable to reduce peri-operative pulmonary complications. Central neuraxial blocks may prove difficult in patients with spinal deformities. Ultrasound-guided peripheral nerve blocks can go a long way in reducing patient morbidity and mortality.

Particular or additional monitoring

Standard ASA monitoring with ECG (electrocardiogram), SPO2 (pulse oximetry), pulse, NIBP (non-invasive blood pressure), ETCO2 (end-tidal carbon-dioxide) and temperature must be done in all cases. Additional monitors are required in patients with ECD in the form of peripheral neuromuscular monitoring (for assessing depth of neuromuscular blockade and assisting extubation) and depth of anaesthesia monitoring (e.g., bi-spectral index monitoring for preventing awareness and titrating anaesthetic dose requirements). In patients with respiratory involvement, airway pressures, tidal volume, inspired oxygen concentration, arterial blood gas analysis and other ventilatory parameters must be monitored. In patients with renal involvement of ECD ("hairy kidney"), hourly urine output, urinary sodium excretion and specific gravity may be monitored. In patients with cardiac involvement of ECD, invasive arterial, central and, in some instances, pulmonary artery monitoring may be required. Monitoring is dependent on specific organ involvement, as well as the nature and extent of surgery. Post-operatively, apart from vital parameters, monitoring must focus on the development of organ system dysfunction and a macrophage activation syndrome.

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Possible complications

The most important complication is the triggering of macrophage activation syndrome (MAS). It is characterised by the accumulation of genetically altered mast cells and an abnormal release of their mediators, affecting functions in every organ system. Other complications are due to the disease-specific involvement of organs, e.g. renal failure.

Post-operative care

Post-operative care involves continued extensive organ-system monitoring, gentle handling of the patient and a high vigilance for the development of complications like MAS. Apart from routine practices like preventing hypothermia, PONV (post-operative nausea vomiting) prophylaxis and measures for prevention of DVT (deep vein thrombosis), ophthalmological assessment may be additionally done for patients with severe orbital involvement. Intensive care unit (ICU) admission is required after major surgeries.

Disease-related acute problems and effect on anaesthesia and recovery

Emergency-like situations can arise in the form of disease reactivation or development of MAS. In this rare syndrome, macrophages engulf the haematopoietic cells in the bone marrow due to dysfunctional natural killer cells or cytotoxic T lymphocytes, resulting in uncontrolled macrophage activation. MAS can be seen with both ECD and LCH (Langerhans cell histiocytosis). Differential diagnosis of ECD include LCH, juvenile xanthogranuloma, Hand- Schuller-Christian disease, xanthoma disseminatum and Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy).

Extra-skeletal complications of ECD include vision loss, corneal abrasions, xanthelasma, pleural effusion, pulmonary fibrosis, pericardial effusion, cardiac failure, renal failure, hydro-ureteronephrosis, diabetes insipidus, ataxia, paraplegia, neuropsychiatric manifestations and retroperitoneal fibrosis.

Ambulatory anaesthesia

There is no contraindication to ambulatory anaesthesia in patients with ECD. There is paucity of literature on ambulatory anaesthesia for ECD patients. PONV (post-operative nausea vomiting) prophylaxis must be administered to all patients for ambulatory surgeries. Post-anaesthetic discharge criteria are the same as for standard ambulatory anaesthesia. It must be made sure that there is a responsible person accompanying the patient home and that all standard precautions are followed.

Obstetrical anaesthesia

There is a paucity of literature on obstetric anaesthesia in patients with ECD. Organ system dysfunction due to ECD can compound the physiologic effects of pregnancy. Regional anaesthesia may prove to be difficult as intervertebral spaces may be fused and ligaments

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may be fibrosed. Administration of general anaesthesia in a pregnant patient carries a greater risk of aspiration and difficult airway in patients with ECD. Since these patients may have associated bone marrow dysfunction, the chances of obstetrical haemorrhage are higher. Hence, it is recommended to arrange for cross-matched blood during Caesarean sections. Literature on the anaesthetic management of pregnant women with this rare disease is sparse. These patients will require post-operative intensive care unit observation and monitoring.

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