orphanaesthesia

Anaesthesia recommendations for patients suffering from

Erdheim-Chester disease

Disease name: Erdheim-Chester disease

ICD 10: C96.1 (ICD-9-CM: 202.3)

Synonyms: ECD is also called lipoid granulomatosis; non-Langerhans cell histiocytosis; Erdheim-Chester syndrome; polyostotic sclerosing histiocytosis

Erdheim-Chester disease is an extremely rare multisystem neoplasm characterized 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 characterized by 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). On immunohistochemistry, ECD histiocytes are positive for CD68, CD163, and Factor XIIIa, and negative for CD1a, S100 protein and Langerin (CD 207). ECD is a clonal disorder with recurrent BRAFV600E mutations in more than half of the patients, in which chronic uncontrolled inflammation is an important mediator of disease pathogenesis, due to frequent hyperactivation of mitogen-activated protein kinase signaling.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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

Disease summary

Nearly 550 cases have been described in literature. It is usually a disease presenting in adulthood, between the 4th and 7th decades 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 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 axial skeleton, although this is not universally present. 99mTc bone scintigraphy typically demonstrates symmetric and abnormally strong 99mTc labeling 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 patients, which can manifest as diabetes insipidus, exophthalmos, cerebellar ataxia, panhypopituitarism and papilledema.

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 anesthesia administration, which may prove challenging in a patient with ECD.

A thorough systemic examination with evaluation of individual organ systems is mandatory. These patients can also come for correction of hydroureteronephrosis, which may require a cystoscopy or an 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. 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 specially 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 postoperative pain relief. All standard ASA monitors must be instituted in every patient. Special precautions for eye cover must be utilized.

Anaesthetic implications of positioning may be exaggerated in these patients due to associated skeletal and systemic affliction by the disease. Anesthesia 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 trendelenberg position used in most robotic surgeries, may be associated 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 paucity of literature for robotic surgery in the ECD population.

Particular preparation for airway management

Standard preparations for airway management must be made in the form of preoxygenation, working suction, aspiration prophylaxis, availability of resuscitation equipment, basic and advanced airway adjuncts as well as standard ASA (American Society of Anaesthesiologists) 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. videolaryngoscopes, fiberoptic bronchoscope, McCoy blade, gum elastic bougie, airway exchange catheter, supraglottic airway devices etc.) must be readily available.

In cases of difficult airway, awake fiberoptic intubation can be done under dexmeditomidine (alpha-2 receptor agonist) sedation or a supraglottic airway device (e.g. laryngeal mask airway, I gel, intubating LMA) can be used. 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 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 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.

Particular precautions for positioning, transport or 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 mobilization must be cautious in order to avoid falls.

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

There have been no randomized 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.

Anaesthesiologic procedure

Anaesthesiologic 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 musculo-skeletal deformities. Ultrasound-guidance must be sought in securing invasive monitoring lines in 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 perioperative 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, SPO2, Pulse, NIBP, ETCO2 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 monitor (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, nature and extent of surgery.

Possible complications

The most important complication is the triggering of Macrophage Activation Syndrome (MAS). It is characterized by accumulation of genetically altered mast cells and abnormal release of their mediators, affecting functions in every organ system. Other complications are due to specific-organ involvement by the disease.

Postoperative care

Postoperative care involves continued extensive organ-system monitoring, gentle handling of the patient and keeping a high vigil for development of complications like MAS. Apart from routine practices like preventing hypothermia, PONV prophylaxis and measures for prevention of DVT, ophthalmological assessment may be done in addition for patients with severe orbital involvement.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

Emergency-like situations can arise in the form of disease reactivation or development of MAS. In this rare syndrome, macrophages engulf the hematopoietic 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, xanthelesma, pleural effusion, pulmonary fibrosis, pericardial effusion, cardiac failure, renal failure, hydro-ureteronephrosis, diabetes insipidus, ataxia, paraplegia, neuro-psychiatric manifestations and retro-peritoneal 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 all standard precautions are followed.

Obstetrical anaesthesia

There is 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 the intervertebral spaces may be fused and the ligaments 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 Caesarian sections. Literature is sparse for anaesthetic management of pregnant women with this rare disease.

Literature and internet links

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