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Prader-Willi syndrome

Proteus syndrome

orphanaesthesia

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

SUPPLEMENT NR. 4 | 2018

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 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.

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

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orphananesthesia

Anaesthesia recommendations for patients suffering from

Proteus syndrome

Disease name: Proteus syndrome

ICD 10: Q87.3

Synonyms: Wiedemann syndrome, Elephant man disease

Proteus syndrome (PS) is a rare hamartoma disorder in which there is asymmetric overgrowth of multiple body tissues causing severe disfigurement. Its global incidence is estimated to be less than 1 in a million. The syndrome, first described by Cohen and Hayden in 1979, was named by Wiedemann in 1983 after the Greek sea god 'Proteus' who had the ability to transform into any shape.

It has been hypothesised recently that PS is caused by post-zygotic mosaic mutation of somatic genes. Researchers have recently identified a mutation of the AKT1 gene (14q32.33) as the cause of unregulated growth of cells involving the three germ layers. The p.Glu17Lys mutation triggers a constitutive activation of AKT1 kinase, which results in signal transduction at the site of the tyrosine kinase receptor, in turn, causing accelerated growth of cells with inhibition of apoptosis. This mutation is not inherited and is lethal in its non-mosaic variant. The severity of PS depends on how early the mutation has occurred during embryonic development and in which cell line. Only the progeny cells from the mutated cell display the disease hallmark, i.e. unregulated growth, thus the individual grows with a combination of normal and mutated cells.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

▶ **Citation:** Sethi D: Proteus syndrome. Anästh Intensivmed 2018;59:S85-S92. DOI: 10.19224/ai2018.S085

Disease summary

The syndrome is sporadic in its occurrence, non-familial and has a progressive course. The affected individual is born without any deformity, with the abnormal body growth becoming apparent only in the first few years after birth. Accelerated overgrowth is seen during childhood and tends to plateau after adolescence as the growth plate activity slows down.

The most common and striking feature of PS is disproportionate skeletal overgrowth causing hemi hypertrophy, asymmetric limbs with disproportionate length, macrodactyly and vertebral anomalies. Other features include asymmetric muscle development, lipomas or lipoatrophy, hyper-pigmented skin lesions, epidermal nevi, cerebriform connective tissue nevi, vascular malformations, tumours of ovary or parotid glands and visceral involvement such as cystic lung disease.

As there is massive heterogeneity in the clinical presentation and the severity of clinical features is highly varied, accurate diagnosis of PS can be challenging. The differential diagnosis of PS includes several disorders such as hamartomatous tumour syndrome, neurofibromatosis type 1, hemihyperplasia, multiple lipomatosis, Klippel Trenaunay syndrome, Maffucci syndrome or CLOVE syndrome (congenital lipomatous overgrowth, vascular anomalies and epidermal nevi).

For establishing the diagnosis of PS, the criteria laid down by the National Institute of Health are followed (1998). These require the presence of three general (mandatory) features including mosaic distribution of lesions, progressive course and sporadic occurrence together with identifying some of the specific clinical features. The clinical diagnosis can be supplemented by genetic analysis and identifying AKT1 gene mutation. In addition, genetic analysis can be a useful tool in patients in whom the clinical features are mild and the symptoms are ambiguous. For genetic testing, DNA from the biopsy samples of affected tissues is analysed; typically, a punch biopsy of an affected skin area is used.

Typical surgery

These patients often need to undergo orthopaedic or reconstructive surgeries for management of overgrowth and physical rehabilitation. Epiphysiodesis, osteotomy, scoliosis correction, joint replacement, correction of digital gigantism or limb length discrepancies and debulking of overgrown connective tissue are the most frequently performed procedures.

Orthodontic treatment of dental abnormalities and malocclusion due to asymmetric overgrowth of maxilla and mandible are also often required.

Patients may undergo gastrointestinal surgery for complications like rectal prolapse, gastric outlet obstruction, acute intestinal obstruction and intussusception secondary to hamartomas or lipomas of the gut wall. Patients with lung involvement including large bullous lesions may require bullae resection surgery.

Otolaryngological surgery is needed for excision of hyperplastic tonsils and adenoids, or correction of hearing loss caused by hyperostosis of the external auditory canal.

These individuals may require tumour excision surgeries, as they are prone to tumours such as ovarian cystadenomas, testicular tumours, and meningioma and parotid adenomas.

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Type of anaesthesia

General or regional anaesthesia may be used depending on the surgical procedure. For orthopaedic and reconstructive surgery in patients with PS, use of regional anaesthesia with central or peripheral neuro-axial block, as opposed to general anaesthesia, has the advantage of avoiding possible problems of a difficult airway, respiratory complications and reducing the incidence of DVT (deep venous thrombosis). There have been concerns about performing regional anaesthesia blocks due to the frequent presence of neural and vascular malformations; however, the use of ultrasound has mitigated this problem and blocks have been performed successfully.

Necessary additional diagnostic procedures (preoperative)

The basic diagnostic work-up of patients with PS includes skeletal survey with radiographs, CT or MRI imaging of all clinically affected areas (e.g. chest and abdomen). Preoperatively, these should be reviewed carefully and any skeletal, neuro-vascular or visceral abnormalities should be recorded.

As cystic lung malformations and restrictive lung disease secondary to scoliosis are common, a chest X-ray should be done routinely. Sometimes a severe distortion of the chest wall may mask a clear view of the lung fields. Therefore, high-resolution CT chest is useful in the cases where there is suspicion of an underlying lung disease. In addition, the true severity of lung problems can be masked by paucity of respiratory symptoms due to decreased physical activity and restricted mobility of patients. In such cases, pulmonary function testing will be needed.

Although cardiac involvement is rare, hypertrophic cardiac rhabdomyomas and conduction abnormalities have been reported. Thus a baseline ECG should be done. Patients with signs and symptoms of cardiac disease or an abnormal ECG should have an echocardiography and a cardiology review.

Hemimegalocephaly and white matter abnormalities of the brain in PS can cause developmental delay, mental retardation or seizures. Such patients require evaluation by a neurologist, often with an MRI of the CNS and electroencephalography.

CT / MR imaging of the spine should be done if a neuraxial block is planned in patients with vertebral anomalies.

Particular preparation for airway management

Overgrowth of soft tissues of the airway, enlarged epiglottis, asymmetric hyperplasia of the tonsils and adenoids are common in PS; these conditions can lead to airway obstruction and difficult intubation. Hyperostosis and enlarged cervical vertebrae can cause external airway compression apart from restricting the head and neck movements. Craniofacial disfigurement from abnormal growth of skull and facial bones can make airway management challenging.

Thus these patients need a thorough clinical evaluation of their airway which can be supplemented with radiographs and imaging studies of head and neck. In patients with a history or clinical examination suggestive of a difficult airway, sedative premedication should be avoided and a difficult airway cart must be kept ready in the operation theatre. Be aware that difficulties may occur during any stage of mask ventilation, laryngoscopy, intubation or

placement of supraglottic device. There are case reports of managing difficult airway in PS by using a McCoy laryngoscope and fibre-optic scopes.

Particular preparation for transfusion or administration of blood products

There can be increased surgical site bleeding due to underlying vascular malformations necessitating blood transfusion. Peri-operative angiography and radiological interventional procedures may be needed to prevent massive blood loss from vascular malformation bleeding. It is prudent to use blood conservation strategies and intraoperative blood salvage devices when a massive blood loss is expected.

Particular preparation for anticoagulation

Although the coagulation pathway is normal, patients with PS are at high risk of developing DVT (deep venous thrombosis) and PE (pulmonary embolism) due to vascular malformations in their body. There are reports of fatal embolisms and sudden early deaths due to this complication. Patients are particularly at risk during the period of convalescence after surgery. Therefore, DVT prophylaxis should be considered in surgeries predisposing to DVT, or if prolonged postoperative immobilisation is likely .

Particular precautions for positioning, transport or mobilisation

Difficulty in positioning, transport and mobilisation of patients may arise from skeletal overgrowth, enlarged limbs and restricted joint mobility. Additional supports and padding for overgrown body parts are needed for appropriate positioning of patients on the operating table.

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

Patients may be on antiepileptic medications, which will be needed to continue perioperatively. Patients with a history of DVT will be on long term anticoagulants; their doses need to be adjusted and timed carefully to avoid intra-operative bleeding and haematoma formation during neuraxial block.

Anaesthesiologic procedure

Technical difficulties can arise in performing regional blocks due to anatomical abnormalities. Spine deformities including asymmetric vertebral bodies and kyphoscoliosis are frequently seen in PS. Ultrasound guidance is especially useful to safely perform peripheral and neuro-axial blocks and to avoid any neurovascular complications.

Neurological compromise due to spinal canal infiltration by angiolipomatous mass or canal stenosis from vertebral hypertrophy is also reported. If such abnormalities are seen on an MRI of the spine, or if a patient has pre-existing neurological deficits, then central neuro-axial blocks are best avoided.

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There are case reports of encountering an unanticipated difficult airway while anaesthetising patients with PS. Hence the anaesthesiologist should be prepared with a difficult airway cart in OT and manage difficult airway scenarios as per e.g. the ASA algorithm.

Although muscular overgrowth is commonly seen, PS is not primarily a muscular disease and hyperthermic responses to various malignant hyperthermia triggers have not been reported. Therefore, no particular anaesthetic agent is contraindicated.

In patients with cystic lung disease, nitrous oxide and high airway pressures during positive pressure ventilation should be avoided. The anaesthetist should be alert to any sudden rise in airway pressures and difficulty in ventilation, which may arise from spontaneous pneumothorax.

Particular or additional monitoring

Standard monitoring is imperative including capnography. Airway pressures should be monitored during positive pressure ventilation in patients with cystic lung disease for early detection of pneumothorax.

Peripheral perfusion must be monitored after insertion of arterial catheters, owing to possible vascular malformations.

Possible complications

Cystic lung malformation or restrictive lung disease secondary to scoliosis or both can predispose patients to reduced respiratory function and mucous clearance impairment. The poor respiratory reserves in these patients can lead to perioperative respiratory failure and secondary, persistent bacterial pneumonia.

Pulmonary vascular malformations can be complicated by pulmonary haemorrhages or PE. DVT leading to PE has been reported as a cause of early death in PS.

Postoperative care

The postoperative care for these patients should be carried out in an appropriate high care setting, especially when there is a suspicion of airway or respiratory compromise.

Incentive spirometry, aggressive chest physiotherapy and pulmonary care for clearing the respiratory tract secretions are needed in patients with an underlying cystic lung disease or scoliosis in order to prevent respiratory complications.

Early mobilisation should be encouraged in these patients; perioperative prophylaxis for DVT with anticoagulants should also be considered in these patients when early ambulation after surgery is unlikely.

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

DVT and PE in these patients can lead to sudden cardiorespiratory compromise.

Ambulatory anaesthesia

There is paucity of literature on ambulatory anaesthesia in patients with PS. As multisystemic involvement is common, most patients are not suitable candidates for ambulatory anaesthesia. Also, routinely performed surgical procedures may be more complex and time-consuming due to musculo-skeletal and visceral anomalies in these patients. Thus use of ambulatory anaaesthesia should be restricted only to some minimally invasive procedures.

Due to the high incidence of a difficult airway in these patients, they are at increased risk of peri-operative airway problems. There are reports of severe, near fatal airway complications in PS. Therefore, ambulatory anaesthesia should be carried out only by an anaesthesiologist who is skilled in managing difficult airway scenarios. Furthermore, the availability of all difficult airway aids should always be ensured. Monitoring must include capnography. For intravenous sedations, drugs allowing for maximal airway protection (e.g. dexmedetomidine) and having titrable effects (e.g. remifentanil) are preferable.

Obstetrical anaesthesia

There is scant literature on pregnancy in patients with PS. However, it should be considered a high-risk pregnancy and obstetric care for these patients should be carried out in a high care setting. The specific problems that the anaesthetist should be prepared for while planning the anaesthetic management include difficult neuro-axial block, difficult airway management, risk of increased intra-operative blood loss and post-operative DVT.

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