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Goodpasture syndrome

Inclusion body myositis

orphan**a**nesthesia

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

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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 Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und 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 Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass 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 eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass 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.

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 recommendations 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.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

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orphananesthesia

Anaesthesia recommendations for Goodpasture syndrome

Disease name: Goodpasture syndrome

ICD 10: M31.0

Synonyms: Goodpasture's syndrome (GS), anti-glomerular basement membrane disease, crescentic glomerulonephritis type 1, GPS

Disease summary: Goodpasture syndrome is a rare and organ-specific autoimmune disease (Gell and Coombs classification type II). It is mediated by anti-glomerular basement membrane (anti-GBM) antibodies [7]. The disease was first described by Dr Ernest Goodpasture in 1919 [6], whereby the glomerular basement membrane was first identified as an antigen in the 1950s. More than one decade later, researchers succeeded in defining the association between antibodies taken from diseased kidneys and nephritis [7].

The disorder is characterised by autoantibodies targeting at the NC1 domain of the $\alpha 3$ chain of type IV collagen in the glomerular and alveolar basement membrane with activation of the complement cascade, among other things [7,17]. The exclusive location of this $\alpha 3$ subunit in basement membranes in lung and kidney only is responsible for the unique affection of these two organs in GPS [7].

Nevertheless, the aetiology and the triggering stimuli for anti-GBM production remain unknown. Due to the fact that patients with specific human leukocyte antigen (HLA) types are more susceptible, a genetic HLA-associated predisposition seems possible [4,7]. However, because this strongly associated allele is frequently present, there seem to be additional behavioural or environmental factors influencing immune response and disease expression. The latter may include respiratory infections (e.g., influenza A2), exposition to hydrocarbon fumes, organic solvents, metallic dust, tobacco smoke, certain drugs (i.e., rifampicin, allopurinol, cocaine), physical damage to basement membrane (e.g., lithotripsy or membranous glomerulonephritis) as well as lymphocyte-depletion therapy (such as alemtuzumab), but unequivocal evidence is lacking [4,7,9,17].

The incidence is estimated to be about 0.5 to 2 cases per million per year in European Caucasoid and Asian populations [7,19,20]. Uncommon for autoimmune diseases, Caucasians males are more affected than females, however, the disease is even more common among the Maori people of New Zealand [19]. It is also a cause of acute renal failure in approximately 10–20 % of all cases of rapidly progressive or crescentic glomerulonephritis. The age distribution shows two peaks: the first occurs between 20 and 30 years (with more frequent haemorrhagic features) and second between 60 and 70 years of age. Regarding age patterns, men have a higher prevalence in the younger age group, whereas it is higher for women in the older age group [4,7].

GPS typically presents as acute renal failure caused by a rapidly progressive glomerulonephritis. This is often accompanied by pulmonary haemorrhage that may be life-

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threatening, especially without prompt diagnosis and treatment [7,17]. Symptoms may begin slowly and become rapidly progressive in a matter of days [1]. Fatigue, weakness, lethargy, nausea, vomiting, diarrhoea, pruritus, loss of appetite and weight, malaise, chills, fever, headache, arthralgias, a pale appearance and general discomfort or even seizures may be rather unspecific and initial symptoms [4,7,21,22,23]. About 60–80 % of the cases display clinically apparent renal and pulmonary manifestations, whereas 20–40 % have renal disease alone, and in less than 10 % of the patients, manifestation is limited to the lungs [4,7,19]. Pulmonary symptoms include haemoptysis, dry cough, shortness of breath, inspiratory crackles over lung bases, chest pain, cyanosis, dyspnoea, tachypnoea up to respiratory failure [7]. Regarding children, they do not present commonly with pulmonary findings before puberty [15]. Affection of the kidney may lead to haematuria, foamy urine, swelling of the hands and feet, high blood pressure, oedema, uraemia, oliguria, anuria and back pain in the kidney area [4,7,9]. Autoimmune inner ear disease (AIED) may be associated and present with vertigo, a ringing, hissing or roaring sound in the ear up to a sudden hearing loss in one ear progressing rapidly to the second ear (within weeks or months) [7].

More than 90 % of the patients with GPS have circulating serum anti-GBM antibodies [2]. A definitive diagnosis is substantiated by percutaneous kidney biopsy (preferred in comparison to a lung biopsy) and confirmed by immunofluorescent techniques and tested by an enzyme-linked immunosorbent assay (ELISA) for the presence of pathognomonic circulating anti-GBM serum antibodies [7].

There is a lack of systematic data of this rare syndrome. As yet, no causal therapy or, at least, controlled therapeutic trials are available. Nevertheless, rapid recognition and treatment is crucial in GPS. The three principles in therapy of GPS are (1) rapid removal of circulating antibodies (primarily by plasmapheresis), (2) stopping any further production of antibodies by drug-induced immunosuppression (high-dose corticosteroids and cyclophosphamide represent the standard therapy, but other immunosuppressive agents like azathioprine or rituximab are also established) and (3) removal of offending agents that may have initiated the antibody production [7]. Renal-replacement therapy as well as renal transplantation may help to replace renal function. Most centres therefore recommend a 6-month period of sustained negative testing for anti-GBM antibodies before undertaking transplantation surgery [14]. There are several case reports of necessary extracorporeal membrane oxygenation (ECMO) due to refractory hypoxemic respiratory failure in GPS with severe pulmonary haemorrhage [1,3,9,12,15].

GPS has a poor prognosis and it largely depends on the diagnosis and treatment timeline of this rapidly progressive disease. Untreated, the lethality of GPS ranges from 77 to 96 % [9]. Under the triple therapeutic regime comprising corticosteroids, immunosuppressive therapy and plasmapheresis, a survival of 70–90 % in one year and up to 80 % in five years may be obtained [4,7]. Besides, in patients with dialysis due to end-stage renal disease in New Zealand and Australia, the median survival was nearly six years [20]. In addition to age, a history of pulmonary haemorrhage is associated with an increased risk of mortality on dialysis [12,20]. Dialysis dependency at presentation rarely generates full recovery of renal function. Nevertheless, patients requiring temporary dialysis may recover a good renal function and only less than 30 % of the surviving patients require long-term dialysis [4,7,12,13]. Double positivity for serum ANCAs and anti-GBM is another indicative of a worse renal prognosis and higher mortality [4]. Pulmonary patients can also often fully recover from lung damage with fast and adequate treatment [3,19]. The long-term outcome of GPS might be better in children than in adults [15].

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

Emergency information

	AIRWAY / ANAESTHETIC TECHNIQUE	No special airway malformations, but GA may be challenging (due to respiratory status) – availability of tracheal suction (pulmonary bleeding) – anaesthesia only in cases of stable disease if applicable – be aware of severe / refractory hypoxaemic failure due to pulmonary haemorrhage with necessity of VV-ECMO – consider neuraxial / peripheral RA as a feasible alternative if applicable
B	BLOOD PRODUCTS (COAGULATION)	Be prepared for recurring transfusions in case of persistent intrapulmonary bleeding (sufficient storage of blood products) – be aware of low platelets and fibrinogen in patients undergoing plasmapheresis
C	CIRCULATION	Anticipate haemodynamic deviation due to pre-existing hypertension when undergoing anaesthesia – consider IBP (blood gas analysis) and (non-)invasive haemodynamic (to avoid fluid overload)
D	DRUGS	No risk for MH – be aware of secondary insufficiency of the adrenal glands (long-term corticosteroid-therapy) and infectious complications (immunosuppressive therapy) – consider drug dose adaption in case of renal impairment
E	EQUIPMENT	Use ultrasound for vessel cannulation / peripheral RA (oedema, swollen limbs) – perioperative availability of dialysis may be necessary

Typical surgery

Percutaneous kidney biopsy and alternatively transbronchial or (rarely) open-lung biopsy for diagnosis [7]

Bronchoscopy/(rarely) thoracoscopy for diagnostic issues [7]

Renal transplantation [7,11]

Arteriovenous fistula for dialysis.

Type of anaesthesia

A general recommendation regarding an ideal anaesthetic approach cannot be given as there is a lack of data for anaesthesia in patients with GPS. As usual, and whenever possible, anaesthesia should only be considered in cases of a stable disease.

Anaesthetists/intensive care physicians are often involved in securing the airway in instable GPS patients with pulmonary haemorrhage.

General anaesthesia might be challenging due to the respiratory status of a patient with GPS.

Neuraxial (epidural) anaesthesia has been used in a patient with GPS undergoing bilateral nephrectomy and has been described as uneventful [16].

Peripheral regional anaesthesia techniques should be applicable to most patients. Due to possible generalised oedemas especially located in the extremities, a landmark-guided approach may be difficult and ultrasound-guided regional anaesthesia recommended.

Necessary additional preoperative testing (beside standard care)

Chest radiography: May show normal findings (18 %) as well as infiltrates and patchy parenchymal consolidations which are usually bilateral, symmetric perihilar and bibasilar [1,7,19]

Chest radiography / ultrasound: Pleural effusions are unusual but can occur [7,19].

Computed tomography: May reveal localised/nodular/diffuse/extensive/bilateral infiltrates with a pattern of alveolar damage [1]

Pulmonary function test: May help to better characterise or identify further progress of pulmonary impairment before scheduled surgery

Blood testing: May show anaemia of variable degree (due to pulmonary bleeding or often secondary to iron deficiency as well as renal failure), high level of waste products as well as elevated blood urea nitrogen (BUN) and serum creatinine levels

Urine analysis: Proteinuria and/or haematuria may be observed.

Particular preparation for airway management

As far as is known, there are no anatomic peculiarities due to GPS itself. Nevertheless, a standardised approach to airway examination and the detection of airway challenges is recommended. A thorough preparation for airway management should be based on the examination results.

In case of pulmonary bleeding, urgent endotracheal intubation might be performed. Depending on the degree of haemoptysis and pulmonary bleeding in the individual patient, intubation performed with video-assistance or the application of a fiberoptic technique may be considered. Of course, direct laryngoscopy should also be available, and for some anaesthetists and in individual (bleeding) situations it may be the more reliable option.

As pulmonary bleeding is usually a bilateral phenomenon, lung separation techniques are normally not helpful when it comes to "distinguishing a good lung from a bad". In refractory bleeding with the development of severe hypoxemia, urgent transfer to an ECMO centre might be the only life-saving approach as a VV-ECMO might serve as a bridge to recovery in combination with the underlying medical therapy of the GPS.

Particular preparation for transfusion or administration of blood products

No specific recommendations have been given. No typical bleeding disorders were reported for GPS patients. Nevertheless, problems may arise during plasmapheresis when platelets drop and fibrinogen is removed.

However, patients with GPS often show significant anaemia (due to persistent intrapulmonary bleeding) with appropriate recurring transfusions [7,9]. Therefore, depending on scheduled surgery as well as the degree of haemoptysis/pulmonary bleeding, an adequate amount of blood products should be available.

Particular preparation for anticoagulation

Especially in cases of pulmonary haemorrhage, dialysis or plasmapheresis, the method and intensity of anticoagulation should be calculated by weighing the risks and benefits in each individual patient and should depend on surgery.

Particular precautions for positioning, transportation and mobilisation

There are no specific recommendations for patients with GPS.

Interactions of chronic disease and anaesthesia medications

Long-term medication with corticosteroids should be considered due to secondary insufficiency of the adrenal glands. Thus, additional "stress-dose corticosteroid dosing" might reduce the risk of perioperative adrenal insufficiency [24].

Immunosuppressive therapy might be related to a higher risk of infectious complications.

Anaesthetic procedure

Preoperative evaluation: See details above.

Premedication: might be performed by weighing the benefits and risks in individual patients.

Patient positioning: No specific recommendations.

IV line: Placement might be difficult due to swelling/oedema of the limbs [3,7].

Invasive blood pressure measurement: Facilitates frequent arterial blood gas analysis, especially in case of pulmonary and renal (i.e., potassium levels) impairment.

(Mechanical) ventilation: Pulmonary restriction and reduced diffusing capacity are characteristics in patients with GPS. Moreover, lung-protective ventilation should be performed with adequate low tidal volumes to avoid baro-/volutrauma. Frequent tracheal suction due to pulmonary bleeding may be necessary [16].

Anaesthesia: Total intravenous or balanced anaesthesia using volatile anaesthetics can be performed safely. The use of fentanyl, remifentanyl and propofol is reported as uneventful for induction and maintenance [5,16]. An increased oxygen tension in the anaesthetic gas mixture may be necessary due to pulmonary impairment, especially due to a pathologic degree of ventilation-perfusion [16]. There are no absolute or known relative contraindications for anaesthesia-related drugs just because of the disease GPS, but drug doses should be adapted depending on the degree of the patient's renal impairment. There is no specific risk for malignant hyperthermia.

Regional anaesthesia can be performed as described above.

Particular or additional monitoring

Haemodynamic monitoring (invasive or noninvasive): may be reasonable to avoid fluid overload in patients with GPS [7].

Possible complications

Pulmonary bleeding/haemorrhage and resulting respiratory failure/hypoxemia as well as anaemia.

Necessity of (long-term) dialysis due to renal failure.

Haemodynamic deviation due to pre-existing hypertension when undergoing anaesthesia.

Infections in case of fulminant immunosuppression.

Postoperative care

Postoperative care should be based upon the patient's pre-existing conditions as well as the surgical or interventional procedure.

Especially respiratory and renal function as well as blood pressure should be monitored in an appropriately extended stay in PACU, IMC or ICU before transfer to the normal ward (or discharge at home) is acceptable.

Disease-related acute problems and effect on anaesthesia and recovery

Emergency-like situations: diffuse alveolar or pulmonary haemorrhage with necessary ventilation, recurring re-intubations up to implantation of (VV-)ECMO in refractory hypoxaemia due to pulmonary bleeding [3,7,19,21].

Differential diagnostics: Wegener granulomatosis, systemic lupus erythematosus, microscopic polyangiitis, other forms of systemic vasculitides (i.e., Churg-Strauss syndrome, essential mixed cryoglobulinaemia, Henoch-Schönlein purpura, microscopic polyarteritis, drug-induced vasculitis), pulmonary embolism, other disorders or infections (i.e., pneumocystis carinii pneumoniae, rheumatoid arthritis) [4,7,19].

Ambulatory anaesthesia

Specific recommendations for or against ambulatory anaesthesia cannot be given as there is no published literature on this topic. In stable GPS disease, ambulatory procedures will be possible if patients are ASA status I–III and do not show relevant contraindications for ambulatory anaesthesia.

Obstetrical anaesthesia

Patients with GPS are fertile, thus an obstetrical anaesthetist might have to deal with female GPS patients with for labour analgesia. During pregnancy, the disease can seriously threaten the lives of both mother and child. Apart from prematurity, abortion (on account of the teratogenic effect of an indispensable therapy) will be possible. Gestational diabetes may occur due to steroid therapy. Therefore, an appropriate clinical management of pregnant women with GPS will require intensive care, a centre with an adequate expertise and a multidisciplinary co-operation among the attending medical specialists [8,10,22].

Hypertension and proteinuria are the most common findings in pregnant GPS patients. Although difficult during pregnancy, it is important to determine whether these symptoms are caused by preeclampsia or a renal abnormality due to GPS [10]. For definitive diagnosis, serologic studies and renal biopsy should be considered, whereby the latter does not seem to be associated with an increased risk during pregnancy [22]. Apart from blood-pressure monitoring, the management of pregnant women with GPS should include a serial assessment of renal function, haematologic values and pulmonary function tests for an assessment of a restrictive pattern or hypoxaemia [23]. Deterioration in renal function may potentially exacerbate by hypertension related to pregnancy [22].

Vaginal delivery as well as caesarean section are both reported in parturient with GPS [10,18,23].

In general, neuraxial as well as general anaesthesia might be performed in this patient population. Severe complications due to anaesthesia have not been reported. However, the lack of reports on obstetrical anaesthesia should result in proper shared decision-making regarding the selection of anaesthesia techniques for specific women.

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Wichtiger Hinweis

Für Angaben über Dosierungsanwei-
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vom Verlag und den Herausgebern keine
Gewähr übernommen werden. Derartige
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Allein aus Gründen der besseren Les-
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weiterer Sprachformen verzichtet. Sämt-
liche Personenbezeichnungen gelten für
alle Geschlechterformen. Dies impliziert
keinesfalls eine Benachteiligung der je-
weils anderen Geschlechter, sondern ist
als geschlechtsneutral zu verstehen.

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