orphanaesthesia

Anaesthesia recommendations for

Gerstmann Sträussler Scheinker syndrome

Disease name: Gerstmann Sträussler Scheinker syndrome

ICD 10: A81.9

Synonyms: Gerstmann-Straussler-Scheinker syndrome, Gerstmann-Sträussler-Scheinker syndrome, GSS syndrome, GSS, Gerstmann-Straussler-Scheinker disease, Gerstmann-Sträussler-Scheinker disease, Gerstmann-Straussler syndrome

Disease summary: Gerstmann-Sträussler-Scheinker syndrome (GSS) is a very rare genetic human prion disease. The frequency of all inherited / genetic prion diseases is estimated at around 10–15% of all forms of human prion diseases and various mutations at the human prion protein gene are involved, some of them leading to GSS [8]. GSS is a slowly progressive neurodegenerative disease of the central nervous system [13]. Most cases are familial and follow autosomal dominant inheritance, but sporadic cases have been reported [7]. Besides genetic and sporadic prion diseases, some acquired (iatrogenic and zoonotic) forms are known. They are under suspicion to be occasionally transmitted by inoculation or ingestion of prion-contaminated material [1, 6].

GSS was first described by the physicians Gerstmann, Sträussler and Scheinker in 1936 (Gerstmann). To date the real prevalence is unknown, but is estimated with 1–10 per 100 000 000 humans. A total of 390 cases are reported until now [5,7,13]. With respect to the small number of cases as well as the frequency and distribution of different mutations, there doesn't seem to be a special pattern in global or geographic distribution of the disease itself. It appears equally in males and females [5].

Inherited/genetic prion-related disorders result from different mutations in the native prion protein gene (PRNP), whereat P102L is the most common one in GSS. PRNP encodes the normal cellular prion protein (PrPC) on human chromosome 20 [2,6,11]. Mutations alter its amino acid sequence and three-dimensional shape leading to the disease-associated form of the protein (prion protein scrapie, PrPSC) [14]. The PrPSc is rather insoluble and relatively protease resistant. It tends to aggregate and accumulate as amyloid plaques in tissues of the central nervous system [1,11]. Deposits of misfolded PrPC can be found in cerebellum, cerebral and cerebellar cortex, striatum, subcortical nuclei, basal ganglia, the wall of brain and meningeal blood vessels and lead to various neurological signs and symptoms [1,5,13]. Prion diseases including GSS may have certain morphologic and pathophysiologic similarities to other progressive dementing disorders, such as Alzheimer and Parkinson disease, but they typically occur at an earlier age [1,6]. Nevertheless, the precise mechanisms in the pathological changes are not fully understood yet.

The average onset of GSS is reported around the age of 50 (range 19–90 years) [4,7,10,13] with an average duration of 5 years (range 3 months to 19 years) [6,7,13]. Disease duration seems to depend on an underlying and causal mutation [13].

Some authors distinguish between different forms of GSS. The typical, classical type or “ataxic GSS” presents with slowly progressive cerebellar ataxia with difficulties in walking and keeping balance in the foreground as main feature, accompanied by cerebellar signs, gaze abnormalities, pyramidal signs such as spasticity, weakness, mild dementia, seizures, myoclonus, amyotrophy, areflexia or posterior column signs [2, 7].

Furthermore, the less typical or Creutzfeldt-Jakob disease (CJD)-like phenotype or “dementing GSS” presents with predominantly progressive dementia with pyramidal and extrapyramidal signs, parkinsonian and pseudobulbar symptoms and palsy. Ataxia is more a minor feature in this form [2,7,9,15].

Further symptoms may be spastic paraparesis, tetraplegia, limb rigidity, dysesthesia in thighs, stiffness in the legs, fine tremor and prominent parkinsonian features like cogwheel rigidity without tremor, extrapyramidal signs, myoclonic jerks, seizures, athetosis, apraxia, incontinence, hoarseness, dysarthria with progressive difficulty in word finding and language output as well as slurred speech, dysphagia, weight loss, progressive clumsiness, bradykinesia, optokinetic nystagmus, saccadic eye movements, sleep disturbances, apathy, psychotic manic-depression disturbances and presence of glabellar, grasp and palmomental reflex or generally brisk reflexes [1,2,7,9,12,13]. The disease may end in a bedridden state, akinetic mutism and totally dependent state and finally death [9]. The heterogeneity and peculiarity of neurological signs and symptoms may vary in dependence of different mutations, but also even within the same pedigree [2,11 13].

The definitive diagnosis of GSS is a neuropathologic one and requires a brain biopsy or autopsy from the patient and eventually affected family members with immunohistology and genotyping of PRNP [1,2,7]. Unique neuropathologic features of microscopic picture are widespread, large, multicentric PrP amyloid plaques, white matter degeneration, neuronal loss, gliosis and spongiform changes [2,6,8,9,13]. A Western Blot analysis may reveal protease-resistant prion protein fragment as a molecular hallmark of GSS [1]. Nevertheless, bioptic sample recovery and examination is only possible if adequate biosafety measures are ensured and can be recommended only to exclude the diagnosis of diseases in which therapeutic options are available [6].

Additional cerebrospinal fluid analysis, electroencephalography as well as imaging studies are less specific for diagnosing GSS than other prion diseases. Usual imaging findings include mild cerebral and cerebellar atrophy as well as other affected regions, that commonly correlate with the clinical signs and symptoms [1, 2,13].

Until now there is no proven treatment or prophylaxis for patients with GSS [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 general difficult airway, but airway management may be challenging due to myoclonus / muscle spasm (mouth opening?) – availability of suction (pseudobulbar palsy) – be aware of perioperative respiratory complications / aspiration – no general (dis)advantage for GA (TIVA / balanced) or RA – consider spasticity / contractures and lack of cooperation (cognitive disability) for neuraxial procedures as well as a potential (theoretical) prion-infection risk from CSF
B	**BLOOD PRODUCTS (COAGULATION)**	no specific recommendations
C	**CIRCULATION**	no specific recommendations
D	**DRUGS**	no risk for MH – consider risk of (silent) aspiration due to a present dysphagia when disposing sedative premedication
E	**EQUIPMENT**	adequate protective equipment needed for team members and use single-use instruments only (prion-infection risk!) – use ultrasound for vessel cannulation / RA – patient positioning / mobilisation with caution (spasticity, contractures, tremor, ataxia, lack of cooperation)

Typical surgery

The onset of disease usually is at the earliest reported in the second or more commonly fifth or a later decade, and GSS is not reported in children until now. Therefore, the patient clientele is usually adult.

With respect to ataxia or dementia and a lack of cooperation anaesthesia may also be necessary for imaging like magnet resonance tomography in diagnostic procedures. For definitive diagnosis a brain biopsy may be necessary.

With progression of the disease, progressive dysphagia may become a problem for patient's adequate nutrition. An open gastrostomy or percutaneous endoscopic gastrostomy (PEG) with implantation of a tube may be necessary to ensure patient's alimentation [15].

Ataxia and walking or balance difficulties can lead to trauma and fractures.

Patients with spasticity or contractures may need a professional pain management and support by an anaesthesia team.

Type of anaesthesia

There`s only one case report for general anaesthesia in a patient with GSS. Therefore, a general recommendation regarding an ideal anaesthetic approach cannot be given. General anaesthesia as well es regional anaesthesia may be applied and both may be associated with problems or risks.

Regional anaesthesia may be difficult due to possible cognitive and motor disability and consequently lower compliance. Furthermore, puncture and needle placement may be aggravated because of an increased muscle tonus, spasticity or contracture. An ultrasound examination may help to identify relevant anatomic structures, because a landmark-guided approach may fail in deformed or contracted extremities. With regard to neuroaxial regional anaesthesia, the potential (theoretical) infection risk from cerebrospinal fluid should be considered, especially if other infectious differential diagnoses are not excluded.

Finally, it is necessary to consider the degree of surgery as well as the patient's respiratory and cardiac status. The assessment of all these factors may help to find an individual and optimal anaesthetic procedure for a patient with GSS.

In patients with present dysphagia, there is often a long history of recurring pneumonia. This should be a concern when performing a general anaesthesia regarding the risk of aspiration before, during and after airway management.

Necessary additional pre-operative testing (beside standard care)

There are no general recommendations for additional diagnostic pre-operative procedures in patients with GSS.

The syndrome usually includes neurodegenerative signs and symptoms. Organs in thorax or abdomen are not impaired due to the disease itself. But especially actual vigilance, mobility, respiration status and swallowing should be evaluated well before undergoing anaesthesia.

Beside the disease's progress with all possible following and even present complications, the diagnostic procedure with anamnesis, clinical examination, laboratory and imaging tests should focus on heart, lung and other organs as done in other patients.

Electrocardiography or transthoracic echocardiography may help to evaluate the cardiac status if anamnesis or clinical examination indicate these tools. If there's no explicit cardiac comorbidity, electrocardiography may be normal [15]. Laboratory findings and chest radiography may help to uncover pneumonia, a frequent and recurring complication in patients with GSS.

Particular preparation for airway management

Prion proteins are resistant to inactivation by radiation, heat or harsh chemical treatments. In response to the possible risk of nosocomial transmission of prion-related disorders through

surgical or medical instruments, the use of single-use instruments is recommended [14]. As well as for surgical instruments this recommendation counts for anaesthetic expendable material. Besides central nervous system and appendix, prion proteins also occur in lymphoreticular tissues in some disease forms, such as bovine spongiform encephalopathy (BSE) associated variant CJD [6,14]. For GSS, the information on presence of pathological prion protein in lymphoreticular tissue is limited. Anaesthetists are nearly daily exposed to lymphoreticular tissue of the upper airway, for which reason reusable anaesthetic instruments should be avoided in high-risk patients [14].

This should especially be considered in cases of necessary fibreoptic intubation. Fibreoptic equipment is expensive and finding suitable accessories may be difficult in desperate emergency situations [3].

There is no evidence of a generally more difficult airway in patients with GSS. Nevertheless, a standardised approach for airway examination and management is recommended.

Myoclonus or muscle spasm represent a feature of GSS and may impair mouth opening.

Pre-existing dysphagia may lead to desaturation in sedation besides regional anaesthesia or after extubation in general anaesthesia due to aspiration risk. The demand for coughing to mobilise secretion may fail because of a lack in cognitive abilities. Furthermore, there is a report of an unexpected upper airway obstruction after tracheal extubation due to pseudobulbar palsy in a patient with GSS. The patient was supported via chin-lift and head extension procedure in addition to a close monitoring of vital signs [15].

Particular preparation for transfusion or administration of blood products

No specific recommendations are given. There are no reports of typical bleeding disorders in patients with GSS.

Particular preparation for anticoagulation

If anticoagulation is needed due to vascular or cardiac comorbidities, it should be continued as usual with respect to kind and degree of the surgery as well as the chosen anaesthetic procedure.

Particular precautions for positioning, transportation and mobilisation

Due to existing contractures in many patients with GSS, careful patient positioning should be performed for surgery. Ataxia, tremor or myoclonus may aggravate positioning, transport and mobilisation. The same applies to dementia and cognitive impairment with a consequent lack of cooperation. These facts may require sedation or even general anaesthesia.

Interactions of chronic disease and anaesthesia medications

There are nor a disease specific long-term medications neither reports on particular interactions in patients with GSS.

Anaesthetic procedure

Preoperative Evaluation: see details above

Premedication: might be performed weighing the benefits and risks in individual patients, especially the risk of silent aspiration due to a present dysphagia.

Patient positioning and placement of monitoring and catheters: very careful with respect to myoclonus, muscle spasm, contracture and a lack of cooperation due to dementia or cognitive impairment. For vessel puncture, regional anaesthesia as well as catheter placement ultrasound may be helpful.

Anaesthesia: Induction of anaesthesia should be performed with consideration of patient-specific risk factors unrelated to GSS. Airway management may be challenging (see above). In one published case report on general anaesthesia in a patient with GSS, propofol and vecuronium (under neuromuscular monitoring) was used for induction uneventfully. Ephedrine was used in case of hypotony after induction. The same team used sevoflurane and nitrous oxygen for maintenance. Reversal of muscle relaxation was performed with a mixture of neostigmine and atropine [15].

There are no reports about (neuroaxial) regional anaesthesia in patients with GSS, but with respect to the facts mentioned above, there also doesn't exist any general refusal for this procedure.

Particular or additional monitoring

Using particular monitoring depends on the patient's individual risk and comorbidities.

Possible complications

Aspiration because of present dysphagia as well as recurring pneumonia may cause complications in the perioperative setting [15]. Airway management may be challenging due to muscle spasm or contractures (see above).

An important objective is the prevention of infection, transmission or contagion in treating patients with GSS. A transmission from human to humans as iatrogenic transmission, from humans to animals under experimental conditions and from animals to humans (like in BSE) is known. The World Health Organization (WHO) guideline recommends that persons with confirmed or suspected Transmitted Spongiforme Encephalopathy (TSE) are the highest risk patients and must be managed using specific precautions. There is neither indication for transmission by the respiratory route, nor are there specific recommendations for anaesthetists in accordance with GSS as one of the TSE.

Basically, the patient should be scheduled for the end of the routine. The entire team should wear disposable hydrophobic material including apron, double gloves, masks and glasses or face shield during the full procedure. Subsequently, the items should be discarded and incinerated or cleaned and decontaminated according to WHO guidelines. Furthermore, the number of team members should be reduced to an absolute minimum and all unnecessary materials should be removed.

Beside proper barrier protection, the use of only disposable equipment is strongly recommended. This applies for every tool and instrument the anaesthetic team works with. Any instruments in direct contact with mouth, pharynx, tonsils, and respiratory tract (i.e., face masks, breathing circuits, cannulas or laryngoscopes) should be destroyed or incinerated, if there doesn't exist single-use material for them. Alternatively, reusable instruments should be cleaned and decontaminated according to WHO guidelines [16]. Infectivity of blood is still controversial. Needles contacting cerebrospinal fluid for neuroaxial regional anaesthesia should be destroyed as well [15, 16]. The operating room must be cleaned thoroughly (using vinyl chloride monomers).

Post-operative care

Postoperative care should be based upon the patient's pre-existing conditions as well as the surgical or interventional procedure. Intensive Care Unit may be required for monitoring vital signs, and in presence of dysphagia one should be aware of aspiration [15].

Disease-related acute problems and effect on anaesthesia and recovery

Emergency-like situation: sudden desaturation may appear due to aspiration as consequence of dysphagia, airway obstruction or pseudobulbar palsy [15].

Differential diagnosis: olivopontocerebellar atrophy, spinocerebellar degeneration, Wilson's disease, multiple sclerosis, Alzheimer's disease, metachromatic leukodystrophy, abetalipoproteinemia (Bassen-Kornzweig syndrome), Refsum disease, intermittent porphyria, thyroid disease, Huntington's chorea, and essentially nearly every neurodegenerative disorder and various dementing disorders [7].

Ambulatory anaesthesia

Specific recommendations for or against ambulatory anaesthesia cannot be given as no published literature exists regarding this topic. Progress of the disease, degree of surgery and kind of anaesthesia, present comorbidities as well as potential necessary postoperative monitoring should be considered.

Obstetrical anaesthesia

Patients with GSS are fertile, thus obstetrical anaesthetist might face women with GSS for labour analgesia. There are neither reports of neuroaxial regional anaesthesia nor of confinement in patients with GSS. However, the lack of reports should result in well concerned interdisciplinary decision regarding the selection of anaesthesia techniques for women with GSS. Especially the recommendations regarding the risk of infection should be observed too (see above).

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