CASE REPORT

Anaesthesia and orphan disease: airway and anaesthetic management in Huntington's disease

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Accepted 5 October 2017

SUMMARY

We present a case that highlights the issues surrounding the delivery of a safe general anaesthetic to a patient with Huntington's disease (HD) and bulbar dysfunction. In the case of a 46-year-old patient undergoing laparoscopic percutaneous endoscopic gastrostomy tube insertion, we discuss the rationale behind our chosen method and anaesthetic agents as well as airway issues specific to HD. In a patient whose condition would not allow for an awake fiberoptic intubation, we opted for a modified rapid sequence induction. Special considerations were made with regard to muscle relaxation given the complications associated with inadequate paralysis and reversal in patients with HD. The technique we describe may also apply to other patient categories, such as patients with movement disorders, bulbar dysfunction and dementia.

BACKGROUND

Huntington's disease (HD) is a rare genetic neurodegenerative disorder characterised by the triad of motor, psychiatric and cognitive disturbance in adulthood.¹ HD is caused by autosomal-dominant transmission of a mutation of the Huntingtin (HTT) gene on chromosome 4p16.3. The HTT gene encodes for the production of a protein called huntingtin, which appears necessary for normal neurodevelopment. The HTT gene contains a polyQ region in which a series of cytosine-adenine-guanine (CAG) repeats code for the amino acid glutamine. There is considerable interindividual variability in the length of the trinucleotide expansion, with normal being between 6 and 35 CAG repeats. The pathogenesis of HD is due to the development of a mutant form of huntingtin (mHTT) as a result of the expansion of the CAG repeats exceeding the normal limit of 35 repeats.² The neurotoxicity of mHTT causes basal ganglia degeneration, neuronal death as well as widespread dysregulation of GABAergic, dopaminergic and glutamergic signalling systems.¹

Over 90% of patients with HD have an affected parent—the remaining cases are caused by a de novo mutation. The penetrance of the HD phenotype depends on the length of the trinucleotide repeat expansion. The inheritance of at least 40 CAG repeats results in full penetrance, whereas HTT alleles with 36–39 CAG repeats have reduced penetrance and variable clinical expression.²

HD presents with symptoms of chorea, dystonia, hypokinesia, ataxia, cognitive decline and

behavioural difficulties with typical onset between the third and fifth decade of life.¹ The age of onset is principally influenced by the length of the CAG repeat. Adult-onset HD usually occurs with a CAG length of 40–55 repeats, whereas a diagnosis of HD within the first two decades of life (juvenile onset) is associated with the inheritance of 50–60 CAG repeats.²

As the disease progresses, chorea spreads to all muscles, including the respiratory muscles, and dysphagia with dysfunction of pharyngeal muscles develops increasing the risk of aspiration. Aspiration pneumonia is the primary cause of death, followed by suicide.¹

The prevalence of HD in the UK is 12.3 per 100 000 population.³ Approximately 1 in 100 patients presenting with clinical characteristics suggestive of HD lacks the mutated HTT gene and is classified as having an HD phenocopy (table 1).⁴

Owing to the low prevalence of the disease, there is a paucity of data on the anaesthetic management of patients with HD. A search of the literature revealed limited selection of case reports. HD poses many anaesthetic challenges, especially to the anaesthetist who only occasionally anaesthetises patients with HD. Bulbar dysfunction puts patients with HD at risk of inhalation of gastric contents.¹ In addition, prolonged apnoea, prolonged recovery, exaggerated response to sodium thiopental and succinylcholine, increased sensitivity to midazolam, postoperative agitation and psychosis, intense shivering and generalised tonic spasm have all been reported as perioperative complications.⁵

The limited evidence available precludes the proposal of specific anaesthetic drugs and techniques. The ideal anaesthetic management for these patients is yet to be determined. However, the primary goal is to protect the airway and achieve a rapid and safe recovery.

We present the successful anaesthetic management of a patient with HD and bulbar dysfunction.

CASE PRESENTATION

A 46-year-old woman who had been diagnosed with HD at the age of 40 years presented for an elective laparoscopic-assisted percutaneous endoscopic gastrostomy tube insertion. Physical examination revealed both rigidity and severe choreic movements in all limbs. She had developed bulbar dysfunction and was being fed via a temporary nasogastric tube (NGT). She was also unable to articulate speech due to choreic tongue movements, and she was wheelchair bound. Apart from HD,

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To cite: Nguyen PT, Meeks D, Liotiri D. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-221354

Table 1 Spectrum of Huntington's disease mimicking disorders⁴

HD phenocopy	Affected gene	Mode of inheritance
HDL 1	<i>PRNP</i>	Autosomal dominant
HDL 2	<i>JPH3</i>	Autosomal dominant
HDL 3	Unknown	Autosomal recessive
HDL 4 (SCA17)	<i>TBP</i>	Autosomal dominant
Neuroferritinopathy	<i>FTL</i>	Autosomal dominant
Wilson's disease	<i>ATP7B</i>	Autosomal recessive
Benign hereditary chorea	<i>TITF1</i>	Autosomal dominant
Chorea-acanthocytosis	<i>VPS13A</i>	Autosomal recessive
McLeod syndrome	<i>XX</i>	X linked

FTL, ferritin light chain; HD, Huntington's disease; HDL, Huntington's disease-like syndrome; JPH3, junctophilin 3; PRNP, prion protein; SCA, spinocerebellar ataxia type 17; TBP, TATA box-binding protein; TITF1, thyroid transcription factor 1; VPS13A, vacuolar protein sorting-associated protein 13A; XK, xylulokinase.

the patient's medical history did not include any other comorbidities. Current medications included lorazepam, olanzapine, trazodone, tetrabenazine, desogestrel, ranitidine and buprenorphine. Her laboratory values and her ECG did not reveal any abnormality. Her anaesthetic history included an uncomplicated general anaesthetic for tonsillectomy in childhood. Airway assessment was difficult due to the choreoathetoid tongue movements, but she was predicted to be a potential difficult airway (Mallampati 3 score, chin receding into the soft tissue of the neck).

The patient was transferred to the anaesthetic room without being premedicated. Routine monitoring included pulse oximetry, non-invasive and invasive blood pressure, ECG, end-tidal carbon dioxide and gas monitoring, monitoring of the depth of anaesthesia and neuromuscular blockade. A modified rapid sequence induction (RSI) with cricoid pressure was planned. Following thorough suction of the NGT and adequate preoxygenation to 90% end-tidal oxygen concentration, induction of anaesthesia was achieved with intravenous administration of 50 µg of fentanyl and 170 mg of propofol. Train of four (TOF) stimulation was applied to check adductor pollicis response, 70 mg (1 mg/kg) of rocuronium was then administered and the patient was deemed ready for intubation when TOF was 0 (1 min after administration of rocuronium). Apnoeic oxygenation and cricoid pressure were applied during this period. The D-Blade of the C-MAC videolaryngoscope was used for the first intubation attempt which revealed a Cormack-Lehane grade 4 view. Manoeuvres to improve the view were abandoned owing to the drop in peripheral capillary oxygen saturation (SpO₂) to 92%. Gentle facemask ventilation was applied with maintenance of cricoid pressure. Cricoid pressure proved to impede ventilation at this point; therefore, it was released temporarily and reapplied after ability to ventilate was confirmed. SpO₂ improved to 100%, and a second intubation attempt revealed a grade 3 view. A cuffed endotracheal tube with an inner diameter of 7 mm was passed through the trachea with the aid of a bougie. After confirmation of tracheal intubation by capnography, tube fogging and chest auscultation, cricoid pressure was released, and a repeat laryngoscopy showed that a grade 1 view was now possible.

Anaesthesia was maintained with desflurane thereafter. The concentration of desflurane was regulated to maintain the Bispectral Index (BIS) between 40 and 60 and normal mean arterial pressure. The patient remained haemodynamically stable during the operation, which lasted a total of 50 min. The TOF ratio was 10% at the end of the operation. Sugammadex 200 mg was administered and the patient was placed in 45° head-up

position. She was extubated once fully awake and TOF ratio was above 90%.

OUTCOME AND FOLLOW-UP

Her postoperative course was uncomplicated. She was transferred to a general ward, and she was discharged from the hospital the following day.

DISCUSSION

Airway management is a real challenge in patients with HD. HD is characterised by involuntary choreatic movements, associated with respiratory compromise, oropharyngeal dysphagia, orobuccolingual dyskinesia and a loss of facial, truncal and limb motor control.⁵ Despite preoperative fasting, the abnormal oesophageal and gastric motility due to bulbar dysfunction and the presence of a small feeding NGT may not guarantee that the stomach will be completely empty following NGT suction.⁶ Bedside gastric ultrasonography is an emerging technique to assess residual gastric volume and guide anaesthetic management. Such a technique could help evaluate the risk of aspiration; however, lack of experience with this technique precluded its use.⁷ RSI was the preferred method of intubation because of the assumed increased aspiration risk associated with bulbar dysfunction. Awake fibre-optic intubation (AFOI) has been described as a suitable technique for patients at risk of aspiration⁸; however, it was not an option here as the patient's choreiform movements and difficulties with communication would have made AFOI challenging.

Rocuronium was chosen over suxamethonium as there have been cases reported of prolonged action of suxamethonium in patients with HD. The incidence of decreased pseudocholinesterase activity is higher in patients with HD than in normal patients, which could explain this correlation.⁹ Suxamethonium has been traditionally advantageous in RSI because of its quick onset time. When suxamethonium is contraindicated, rocuronium is the best available option for RSI. High dose (1 mg/kg) rocuronium has shown to achieve a rapid onset of 60 s. Other non-depolarising neuromuscular blocking drugs such as atracurium and *cis*-atracurium do not achieve rapid onset comparable to suxamethonium even when given in high doses and may produce adverse effects such as histamine release, laudanosine neurotoxicity, suboptimal intubation conditions and a prolonged block.¹⁰ However, deep neuromuscular blockade caused by rocuronium is not a problem nowadays with the availability of the specific reversal agent sugammadex. To the best of our knowledge, RSI using rocuronium and its specific reversal agent sugammadex in patients with HD has not been described in the literature so far.

There are also reports of prolonged apnoea with thiopentone but not with propofol; therefore, propofol was chosen as the induction agent.⁹ We chose to use desflurane for maintenance to allow for a more rapid recovery and faster return of airway reflexes.¹¹ We also monitored the anaesthetic depth (BIS Monitoring) to avoid excessively deep anaesthesia and to reduce emergence and recovery times. Of note, the starting BIS value (BIS awake) of 92 was lower than normal in accordance with a growing body of literature that recognises that BIS awake can be lower in patients with neurological disorders.¹² We used only a small amount of opiates (fentanyl 100 µg) to avoid prolonged apnoea. Increased salivation in HD may lead to inhalation of saliva both during induction and emergence from anaesthesia. Although drugs with antisialagogue effect may be of benefit, these drugs possess anticholinergic effects which may adversely affect chorea and also cause unnecessary sedation, blurred vision, decreased intestinal motility and lower oesophageal tone.¹¹ For

these reasons, we avoided using antisialagogues. We performed RSI with cricoid pressure on, suction immediately available and aimed for a rapid recovery to overcome problems related to increased salivation. Similarly, we chose to use ondansetron as an antiemetic because ondansetron lacks the anticholinergic effects of cyclizine. Dopamine antagonistic promotility agents such as metoclopramide and prochlorperazine were also avoided to prevent motor compromise.⁹

The rationale for using TOF ratio was to accurately measure muscle relaxation. Given that underlying motor function issues may impair the interpretation of TOF, we felt that it was important to adhere to gold standards. We decided to monitor TOF ratio because it is considered an objective method to assess neuromuscular blockade.¹³ Inadequate muscle relaxation before laryngoscopy may provoke the gag reflex, whereas residual paralysis in a patient with bulbar dysfunction may impair post-operative recovery and may predispose to aspiration or airway and breathing problems.¹¹ We attempted the first laryngoscopy only after TOF was 0, and we reversed residual paralysis to achieve TOF ratio above 90% before we extubated our patient. The risk of aspiration during emergence is equally as high for patient with HD; therefore, extubation was delayed until the patient was awake, and there was return of the airway reflexes.¹¹

Whether cricoid pressure should be regularly applied or not as part of classic RSI remains a matter of current debate. In our case, cricoid pressure may have contributed to poor laryngoscopy views by distorting the anatomy of the airway. Initially, the epiglottis and laryngeal structures were difficult to identify. The subsequent difficulty to ventilate the patient mandated the release

and repositioning of the cricoid pressure. However, despite this, only a grade 3 view was obtained. Cricoid pressure is applied to protect the airway during the period of loss of consciousness and placement of the cuffed tracheal tube and is a standard for RSI in the UK. It has been shown to prevent gastric distension in gentle mask ventilation and can also help improve the view on laryngoscopy. However, this advantage may be lost if poorly applied as found in this case. If cricoid pressure is hindering further intubation attempts, then the Difficult Airway Society guidelines do recommend taking off cricoid pressure and reapply if regurgitation is seen.¹⁴ However, there is an emerging trend to move away from the standard RSI due to the risks associated with cricoid pressure and apnoea. The concept of 'controlled' RSI and intubation, where gentle facemask ventilation is allowed and cricoid pressure is avoided, is gradually becoming a more popular and evidence-based technique.¹⁵

Contributors All authors meet the authorship criteria and certify that they have made substantial contribution to the conception, design, acquisition, analysis and interpretation of data related to this case report; drafting the work and revising it critically for important intellectual content and final approval of the version to be published. Conception and design of case report: PTN, DM and DL. Acquisition of data: PTN and DL. Analysis and interpretation of data: PTN, DM and DL. Drafting the manuscript: PTN, DM and DL. Revising the manuscript critically for important intellectual content: PTN, DM and DL. Approval of the version of the manuscript to be published: PTN, DM and DL. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors will take public responsibility for the contents.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ Patients with Huntington's disease (HD) may present a real challenge for the anaesthetist. It is important to realise that preoperative airway assessment may prove to be difficult in these patients. Therefore, preparations for difficult airway management should be made in advance.
- ▶ These patients are at high risk of pulmonary aspiration of gastric contents due to bulbar dysfunction. When awake fibreoptic intubation is not an option, then the alternative is rapid sequence induction (RSI) to protect the airway against aspiration.
- ▶ As succinylcholine has been associated with prolonged apnoea due to reduced pseudocholinesterase levels, rocuronium is probably a safe alternative.
- ▶ Objective muscle relaxation monitoring and reversal with sugammadex seem to be a beneficial technique to manage neuromuscular blockade in patients suffering from HD. Patients suffering from movement disorders, bulbar palsy and dementia may also benefit from this technique.
- ▶ Facemask ventilation should be considered in the context of RSI with maintenance of cricoid pressure. However, when cricoid pressure is poorly applied, it may distort laryngoscopy view and hinder further intubation attempts and facemask ventilation, and thus, it may compromise oxygenation. On this occasion, its release may be well justified. It is our reflection on this case that made us believe that routine identification of the cricoid cartilage in advance, when the patient is still awake, may overcome issues related to poorly applied cricoid pressure.

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