Case Report

Anesthetic nuances in Segawa's syndrome: A case report and review of the literature

ABSTRACT

Segawa's syndrome, dopamine-responsive dystonia, is a rare genetic disorder that typically begins in childhood by around 4–6 years of age. It is characterized by abnormal gait and dystonia. A 33-year-old man presented for autologous skin grafting of a nonhealing wound under general anesthesia. Successful anesthetic management of patients with this rare disease, though analogous in many ways to that of patients with Parkinson's disease, still pose significant challenges. We present anesthetic nuances to be considered in the management of a patient with Segawa's disease along with a pertinent review of the literature.

Key words: Dopamine responsive dystonia; general anesthesia; Parkinson's disease; regional anesthesia; Segawa's syndrome

Introduction

Segawa's syndrome (dopamine-responsive dystonia [DRD]) is a rare genetic disorder, first described by Masaya Segawa,[1] that typically begins in childhood by around 4–6 years of age. Occasionally, it may present first time in second or early third decades. It is characterized by abnormal gait (uncoordinated or clumsy manner of walking) and dystonia (usually affecting legs).[2] Its estimated prevalence is 0.5 per million population and female to male ratio is 2.5:1.[3] The disorder responds well to treatment with levodopa.[4]

Being a rare case and limited literature available regarding anesthetic concerns previously, herein, we report successful management of this case. Anesthetic concerns include, but are not limited to, proper selection of anesthetic drugs and management of autonomic instability due to levodopa therapy. We describe the nuances involved in giving anesthesia to patients suffering from this rare disease and review the literature providing many learning points.

Case Description

A 33-year-old male patient of 65 kg diagnosed with Segawa's syndrome 1 year back, presented with a nonhealing wound over the left upper shoulder and back. The patient was bedridden for more than a year, had a dystonic posture of limbs, generalized wasting of muscles, and equinovarus deformity of both feet. Cognition was intact and slurring of speech was present. His mother also was suffering from Segawa's disease. On examination, his vitals were within

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normal limits. Airway examination was normal. The chest was clear on auscultation. However, the breath-holding time was 12 s (due to prolonged immobilization). The cardiovascular system was normal on examination. Routine blood investigations including kidney and liver function, chest X-ray, and electrocardiogram (ECG) were within normal limits. Magnetic resonance imaging (MRI) of the brain was normal. He was taking tablet levodopa 100 mg + carbidopa 10 mg combination three times a day and tablet trihexyphenidyl 2 mg twice daily. He was planned for autologous skin grafting of the nonhealing wound. Written and informed consent was obtained from the patient and his family members. He was kept nil per oral for 6 h for solid food and 2 h for clear fluid before surgery and was advised to continue all the medications till the morning of surgery.

In the operating room, baseline vitals were recorded (HR-96/min, BP-106/74 mmHg, SpO2-98%). Arterial cannula placed in the right radial artery. He was premedicated with inj. midazolam 0.03 mg/kg IV, inj. glycopyrrolate 0.004 mg/kg, and inj. fentanyl 2 mcg/kg IV. Inj. dexamethasone 0.12 mg/kg as an antiemetic was given. He was induced with injection propofol 2 mg/kg in slow incremental doses, and muscle relaxation obtained by injection atracurium 0.5 mg/kg. Orotracheal intubation was done. Anesthesia was maintained with sevoflurane (0.8–1%) in the oxygen-nitrous oxide mixture (2:1 ratio) and injection atracurium (given as intermittent boluses). Intraoperative analgesia was maintained with inj. paracetamol 15 mg/kg and inj. diclofenac sodium 75 mg. Intraoperative monitoring of invasive BP, HR, ECG, SpO_2, end-tidal CO_2 was done. The procedure lasted for 1 h. The patient remained hemodynamically stable throughout the procedure except for two episodes of hypotension with BP 69/50 mmHg and 83/55 mmHg, which responded well to intravenous fluids (1 L crystalloid and 500 mL colloid) and inj. phenylephrine 150 mcg. At the end of the surgery, neuromuscular blockade was reversed with inj. glycopyrrolate 0.008 mg/kg and inj. neostigmine 0.05 mg/kg. The patient was extubated after ensuring adequate tidal volume and regular respiration. Regular monitoring of vitals was done in the postoperative period. Tablet levodopa was continued postoperatively.

Discussion

Segawa's syndrome is a rare hereditary progressive disease characterized by marked diurnal fluctuation of symptoms with the worsening of symptoms in evening and improvement in the morning. It is inherited as an autosomal dominant trait in 80% of cases and is due to a mutation in GTP-cyclohydrolase-1 (*GCH-1*) gene on 14q22.1-q22.2. This gene encodes GTP-cyclohydrolase1 which is involved in the synthesis of tetrahydrobiopterin (BH_4), an essential cofactor for tyrosine hydroxylase (the rate-limiting enzyme in dopamine synthesis).[5,6] Consequently, these patients have a deficiency of dopamine in the dopaminergic neurons of basal ganglia leading to characteristic dystonia. Deficiency of dopamine neurotransmitter in the central nervous system (CNS) explains the resemblance of symptoms of this disease to Parkinson's disease. Improvement in dystonia with the replacement of dopamine with levodopa therapy further corroborates with the pathogenesis of the disease. An autosomal recessive trait is due to a mutation on 11p15, which encodes the tyrosine hydroxylase.

This disease poses significant challenges from an anesthesia point of view due to the disease *per se* and the chronic levodopa therapy which these patients are on. First of all, abnormal body habitus and flexed posture (because of dystonia) make these patients prone to restrictive lung disease leading to increased risk of respiratory and cardiovascular complications. Prolonged immobilization in some of these patients due to inadequate/delayed treatment may lead to chest infections, which increases the requirement for postoperative ventilatory support. Furthermore, dystonia may involve neck (spasmodic torticollis) or face and jaw (oromandibular dystonia) leading to difficulty in mask ventilation and intubation. So an adequate preoperative assessment keeping this fact in mind is to be done. In addition, these patients are on prolonged levodopa treatment, so are more prone to dehydration (due to nausea and vomiting caused by levodopa as its side effect) and hypovolemia. Hypovolemia is due to decreased norepinephrine stores in the heart and decreased renin release caused by prolonged levodopa therapy. Thus, adequate fluid management should be done in the perioperative period. Counterintuitively, dopamine excess from levodopa may increase myocardial contractility and heart rate causing increased blood pressure. Therefore, autonomic instability in these patients leading to abrupt fall and/or rise in blood pressure is another issue during anesthesia. Hence, anesthetic drugs should be given slowly and carefully.

For premedication, glycopyrrolate, in general, is the preferred anticholinergic as it does not cross the blood-brain barrier. However, anticholinergics like atropine which cross the blood-brain barrier can also be used safely especially in children with Segawa's disease since we know that cholinergic antagonism is equivalent to dopamine agonist activity in CNS and indeed, anticholinergics like trihexyphenidyl are also used in the treatment of this disease. Ondansetron (a serotonin antagonist) is safe for the prevention and treatment of emesis.

However, dopamine antagonists (such as metoclopramide) should be avoided at all costs as they worsen dystonia.[7] Opioids such as fentanyl must be administered cautiously as they are known to cause muscle rigidity[8] especially when given in large doses. Acute dystonia after alfentanil has also been described.[9] Dystonia after fentanyl was not seen in our patient (maybe because of the smaller doses and administration of muscle relaxant).

Among intravenous anesthetic agents, we used propofol in our patient. Since propofol administration has rarely been associated with excitatory phenomenon including opisthotonos, dystonia, and myoclonic seizures;[10] therefore, it should be used cautiously in these patients. This dystonia is also seen with ondansetron primarily when used along with propofol.[11] Thus, we preferred to use dexamethasone instead of ondansetron in our case. Ketamine produces exaggerated sympathetic nervous system response though it has been successfully used in patients receiving levodopa in some case reports.[12] Thiopentone has also been successfully used in one case report.[13] It can be inferred from the available literature that thiopentone is probably the drug of choice for induction in Segawa's syndrome followed by propofol which should be used cautiously.

Since inhalational agents inhibit synaptic reuptake of dopamine, they increase the dopamine concentration extracellularly. Hence, they are of value when used as a maintenance agent during anesthesia. However, halothane is better avoided as it sensitizes the heart to catecholamines leading to arrhythmias. Isoflurane and sevoflurane, being less arrhythmogenic, are comparatively safer but hypotension is still a concern.

Though, there is a single report of succinylcholine induced hyperkalemia in a patient on levodopa,[14] Priscu *et al*.[13] have

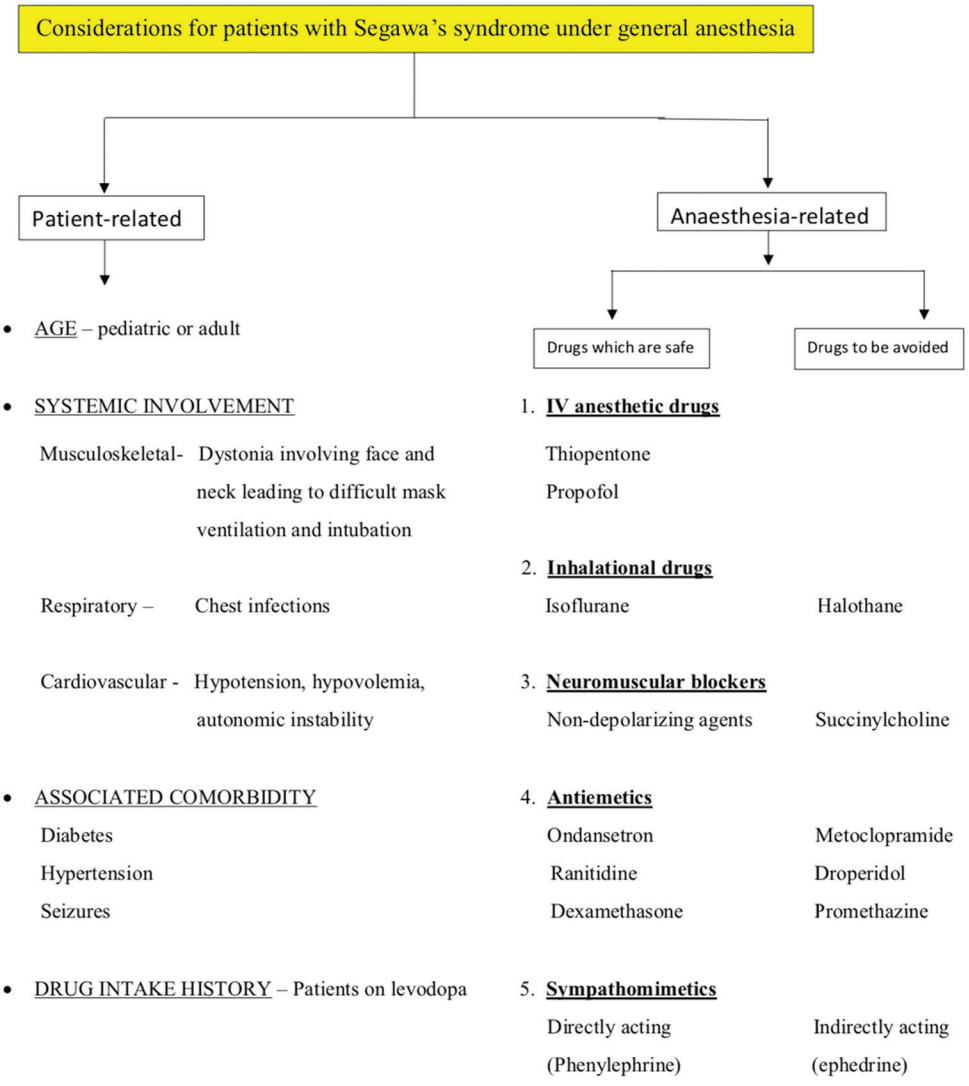

Figure 1: Anesthetic considerations in Segawa's syndrome patients under general anesthesia

used succinylcholine successfully without any side effect in a patient of Segawa's syndrome. However, nondepolarizing muscle relaxants are safer as they are not associated with adverse effects. Rocuronium, vecuronium, and atracurium can be used safely. Rocuronium (instead of succinylcholine) may be the right choice in emergency surgeries in such patients. When required, sympathomimetic drugs are to be used very cautiously as they can cause an acute rise in blood pressure. Directly acting sympathomimetics (phenylephrine) should be preferred over indirectly acting sympathomimetics (ephedrine) Figure 1.

Regional anesthesia would be better for patients with this disease as compared to general anesthesia due to potential risks of the latter, there are caveats in using regional anesthesia. Since these patients frequently have hemodynamic instability, regional anesthesia can cause/aggravate the hypotension. Moreover, there is no available literature to our knowledge showing that one of them is superior to the other.

Conclusion

Anesthetic management of patients with Segawa's syndrome is analogous in many ways to a patient of Parkinson's disease due to the similar pathophysiological processes and treatment by levodopa involved in both the diseases. General anesthesia can be given safely in these patients. Thiopentone followed by propofol are the drugs of choice for intravenous induction. Among the inhalational agents, all are safe except the halothane. Rocuronium, instead of succinylcholine, may be the right choice in emergency surgeries.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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