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JCICM JOURNAL OF CLINICAL INTENSIVE CARE AND MEDICINE
ISSN 2639-6653

Case Report

Case report: Perioperative management of a patient with familial dysautonomia

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Abstract

Familial dysautonomia is a rare autosomal recessive neurodegenerative disease affecting cells of the autonomic nervous system. Patients with this disease are insensitive to pain but their autonomic nervous system is still activated with noxious stimuli. This report details a case of a patient with familial dysautonomia who underwent right ankle open reduction and internal fixation for a bimalleolar right ankle fracture. The patients preoperative and intraoperative course were uneventful but shortly after handoff to the intensive care unit, the patient experienced an autonomic crisis. Management of these patients is complex, requiring maintenance of physiologic homeostasis as well as preventing hemodynamic instability caused by noxious stimuli. Any deviations from baseline may cause an autonomic crisis, as happened in our patient. Herein, we detail the perioperative management of a patient with familial dysautonomia in further detail.

More Information

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Submitted: August 25, 2021
Approved: September 07, 2021
Published: September 08, 2021

How to cite this article: Sarebanha M, Valente L, Kalra M, Layon AJ, Crimi E. Case report: Perioperative management of a patient with familial dysautonomia. J Clin Intensive Care Med. 2021; 6: 029-032.

DOI: 10.29328/journal.jcicm.1001038

Glossary of Terms: IKAP: IκB Kinase complex–Associated Protein; ELP1: Elongator Complex Protein 1; ICU: Intensive Care Unit

Introduction

Familial dysautonomia also known as Riley-Day syndrome and hereditary sensory autonomic neuropathy (HSAN) type 3, is a rare autosomal recessive neurodegenerative genetic disorder, primarily affecting the Ashkenazi Jewish population. Cells from the autonomic and sensory nervous system are impacted by this disease [1]. The disorder results from two mutations involving the IκB kinase complex–associated protein (IKAP) gene which codes for the elongator complex protein 1 (ELP1). The mutations are a thymine to cytosine transition in intron 20 of the ELP1 gene, resulting in a frameshift mutation and truncated messenger ribonucleic acid protein. The second mutation occurs with a guanine to cytosine replacement in exon 19, resulting in substitution of arginine to proline, reducing phosphorylation [2]. The disease is associated with multiple cardiovascular, respiratory, gastrointestinal, and vision problems summarized in Table 1. Due to the symptoms of the disease, patients with familial dysautonomia require focused attention throughout their perioperative period in order to prevent an autonomic crisis from occurring.

Written Health Insurance Portability and Accountability Act authorization has been obtained from the patient's guardian.

Case description

A 38-year-old with a medical history significant for familial dysautonomia presented with a bimalleolar right ankle fracture after experiencing a fall. The patient did not report any pain but his family noted swelling and bruising around his ankle and after outpatient workup he was scheduled for a right

Table 1: Systems affected in familial dysautonomia and their symptoms.

System	Symptoms
Cardiovascular	Supine hypertension
	Autonomic crisis
	Orthostatic hypotension
Hematologic	Anemia of chronic disease
Pulmonary	Chronic lung disease
	Hypoxia
	Restrictive lung disease
	Bronchiectasis
	Hypercapnia
Ophthalmologic	Alacrima
	Optic nerve atrophy
	Corneal ulcerations
Gastrointestinal	Constipation
	Gastric dysmotility
Nephrology	Chronic kidney disease
	Hyponatremia
	Urinary retention

ankle open reduction internal fixation. The patient's familial dysautonomia was complicated by orthostatic hypotension, bronchiectasis, bilateral lower extremity neuropathy, ataxia, dysarthria, dysphagia, gastroesophageal reflux disease, chronic constipation, chronic kidney disease, blindness, and developmental delay. The patient's home medications included diazepam, clonidine, acetaminophen, midodrine, and pantoprazole. Past surgical history was significant for a spinal fusion, gastric fundoplication, and jejunostomy tube placement. His airway examination was Mallampati Class II and there was limited neck mobility. Vital signs were normal preoperatively.

Given the patient's pre-existing neuropathy, and in agreement with the family, we opted not to perform a regional block but to proceed with general anesthesia with an endotracheal tube. The patient was premedicated with intravenous midazolam. General anesthesia was induced with intravenous propofol, no paralytic and a 7.5 endotracheal tube. Anesthesia was maintained with a continuous infusion of propofol and dexmedetomidine. During the case blood pressure ranged between 110-180/55-100 mmHg and temperature 97.8-98° Fahrenheit. Emergence was uneventful, propofol and dexmedetomidine infusions were stopped and the patient was safely extubated. Total anesthetic time was 66 minutes.

Postoperatively, the patient was transferred to the intensive care unit (ICU) for close hemodynamic monitoring due to his familial dysautonomia. Shortly after arrival to the ICU, he experienced an autonomic crisis, characterized by loss of consciousness, hypertension with blood pressure 150/100, skin flushing and drooling. The patient received intravenous diazepam 5 mg and clonidine 0.2 mg via jejunostomy tube with no resolution of symptoms. Subsequently, a continuous intravenous infusion of dexmedetomidine at 0.7 micrograms/kilogram/hour was started with resolution of the crisis within 30 minutes. The patient's physiologic response to noxious stimuli from undergoing a surgical procedure was not adequately addressed during handoff from the operative room to the ICU team, but subsequently he was placed on a scheduled opioid regimen with oxycodone 5mg every 6 hours in order to prevent the occurrence of another autonomic crisis. Because the patient was unable to report actual sensations of pain, these medications were scheduled to be administered regularly. Two additional autonomic crises occurred secondary to constipation and need for manual disimpaction. Though the patient had a history of chronic constipation his symptoms worsened while in the hospital and required him to have more frequent manual disimpactions than he did prior to his admission. This occurred despite being on a bowel regimen with docusate. Once the patient was determined to be crisis free, with no episodes of hypertension, tachycardia or altered mental status for a full 24 hours, he went to the regular inpatient floor.

Discussion

Familial dysautonomia is a congenital disease whose rarity creates unique anesthetic considerations. The disease is caused by complete dysregulation of the autonomic nervous system, making patients susceptible to multiple complications. The altered ELP1 subunit of the elongator complex that interacts with ribonucleic acid polymerase, plays a role in gene transcription, cell migration, intracellular trafficking, transfer ribonucleic acid modification, cytoplasmic kinase signaling, and p53 activation [2]. Initial signs of familial dysautonomia begin at birth and include hypotonia, difficulty swallowing, and failure to respond to painful stimuli. As the disease progresses, manifestations are feeding difficulty, gastroesophageal reflux, nausea, vomiting, aspiration, recurrent pneumonia, developmental delay, labile blood pressures, variable body temperatures, absence of tears, scoliosis, ataxia and autonomic crisis. Autonomic crises are life threatening and can be classified by hemodynamic instability, vomiting, nausea, profuse sweating, skin blotching, and altered mental status.

Familial dysautonomia impacts multiple organ systems. Dysfunctions of the cardiovascular system include orthostatic hypotension, supine hypertension, bradycardia, complete atrioventricular block, and prolonged QT interval [3]. Respiratory system alterations include restrictive lung disease, central sleep apnea, breath holding, inadequate chemoreceptor response to hypoxia and hypercarbia, a lower oxygen saturation at baseline, and increased risk of pneumonia [3]. Gastrointestinal complications manifest as poor coordination of swallowing, decreased oral intake, and gastrostomy placement for appropriate feeding. Patients typically have gastroesophageal reflux disease and dysphagia, increasing their risk for aspiration. The systems affected by familial dysautonomia are summarized in Table 1.

Common triggers for an autonomic crisis are physiological stressors such as infection, noxious stimuli, surgery, dehydration, bowel impaction, bladder distention, and electrolyte abnormalities. It is imperative to provide adequate control of nociceptive pain, avoiding constipation, bladder distention, and maintaining normothermia throughout the perioperative course.

The complexity of this disease makes anesthetic management difficult. Patients require a complete metabolic panel, a complete blood count, and preoperative electrocardiograms. If patients have a pacemaker, device interrogation is required to determine battery function and the patient's reliance on the device. Chest radiography and arterial blood gas analysis are important as well. Patients commonly have gastroesophageal reflux and preoperative histamine H2 receptor antagonists should be considered. Ample fluid administration must be given 8-12 hours before surgery. Oftentimes, preoperative anxiolysis is crucial as emotional stressors may trigger a crisis.

The need for a preoperative arterial line is often dependent on the type and duration of the case as well as the patient's hemodynamics prior to surgery. After a thorough discussion with the surgeon we opted not to place an arterial line for this patient because the duration of the surgery was expected to be short and blood loss was expected to be minimal.

No anesthetic technique has been proven to be superior for patients with familial dysautonomia. The decision to provide general anesthesia or regional anesthesia was heavily debated for this case, and ultimately the risks and benefits of each technique were discussed with the family and the surgeon, and the decision was made to proceed with general anesthesia due to the patient's existing neuropathy. Rapid sequence induction with cricoid pressure is preferred due to the increased risk of aspiration. Invasive hemodynamic monitoring is recommended for longer cases. Intraoperative eye protection is essential because patients are prone to corneal ulceration, perforation and dry conjunctiva due to absent tears and corneal reflexes [3]. Maintaining normocapnia decreases blood pressure lability. Urine output and temperature should be continuously monitored in the operating room as deviations from baseline can result in crises. First line treatment for intraoperative hypotension is with a fluid bolus. This is because patients with familial dysautonomia exhibit an exaggerated response to exogenous cholinergic and adrenergic medications [3].

Anesthetic emergence in patients with familial dysautonomia often takes time due to delayed return of spontaneous breathing secondary to chemoreceptor dysfunction. Patients often have a diminished response to hypoxia, causing longer periods of apnea compared to patients without familial dysautonomia, and have greater oxygen desaturation. People with familial dysautonomia are unable to feel pain, but they have peritoneal and visceral sympathetic responses. Because of this, postoperative pain control needs to be immediately addressed to prevent the patient from going into a crisis, a point missed in the care of our patient. In retrospect, transitioning the patient to the intensive care unit while on dexmedetomidine or providing narcotics prior to emergence may have prevented a crisis from occurring.

Postoperative pulmonary care with incentive spirometry is beneficial because the restrictive lung disease associated with familial dysautonomia increases atelectasis. Encouraging patients to sit as soon as possible and elevating the head of the bed to 30° helps prevent positional hypertension. Nausea and vomiting can be controlled with diazepam, as it works on the gamma-aminobutyric acid A receptor as an anxiolytic, anticonvulsant, and antiemetic [4]. Clonidine is used for hypertension, with dosing recommended when diastolic blood pressures are greater than 85 mmHg [3]. Clonidine is beneficial because it increases cardiovagal outflow and baroreceptor sensitivity, while reducing blood pressure and heart rate [3]. If patients remain refractory to treatment with clonidine, a dexmedetomidine infusion should be initiated. Dexmedetomidine is more selective for the alpha 2 receptor than clonidine and thus it inhibits sympathetic outflow [5].

As mentioned in our case description, the patient experienced an autonomic crisis once transferred to the ICU. This highlights the necessity to prevent patients from experiencing physiologic responses to noxious stimuli in the postoperative period [6-13].

In summary, familial dysautonomia is a rare disease causing autonomic dysfunction. This requires that clinicians maintain the patient's hemodynamics and treat noxious stimuli in order to prevent them from developing a life threatening autonomic crisis. Special attention needs to be paid on handoff of patients from the intraoperative to postoperative period, as failure to provide adequate control of noxious stimuli can lead the patient to go into an autonomic crisis.

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