CLINICAL VIGNETTE

Anesthetic Considerations for a Patient with Bainbridge-Ropers Syndrome

Eric Zhang, MS4, Elizabeth Tsai, MD and Fei Zheng-Ward, MD

Background

Bainbridge-Ropers Syndrome (BRPS) is a developmental disorder characterized by an assortment of distinct features, including severe intellectual disability with speech delay, hypotonia, dysmorphic facial features with high arched palate and anteverted nares, marfanoid habitus, feeding difficulties, and delayed psychomotor development.[1,2] BRPS was first reported in 2013 by Bainbridge et al., who observed individuals sharing features with Bohring-Opitz syndrome. As of 2018, an estimated 200 cases of BRPS were diagnosed.[3] The cause of BRPS is due to a pathogenic truncation of ASXL3, a gene that provides instruction for a protein involved in chromatin remodeling.[4]

The exact physiologic mechanism in which the mutations cause disease is unclear. The clinical presentation of BRPS is also complex as patients found to have the same ASXL3 mutation have widely varying characteristics.[5] However, given the potential for dysmorphic facial features and hypotonia, patients with BRPS present unique anesthetic challenges. We present a patient with BRPS who underwent general anesthesia with oral endotracheal intubation for cystoscopy, bilateral ureteroscopy and laser lithotripsy.

Case Report

A 56-year-old male with BRPS presented for cystoscopy, bilateral ureteroscopy and laser lithotripsy for renal calculus. The patient's medical history includes: cerebral palsy, severe cognitive deficits with severe language impairment, and nephrolithiasis with hematuria. His surgical history includes multiple laparotomies for small bowel obstruction. He had no known drug allergies and he takes daily rivaroxaban 20mg.

On physical exam, the patient had a body mass index of 27.1 with normal vital signs. He was nonverbal but was able to walk with a walker and understand basic commands. Cardiac and respiratory systems were within normal limits. Airway exam revealed a Mallampati classification III view, adequate mouth opening and thyromental distance, but limited neck mobility. There were no abnormal lesions or ulcers seen in the oral pharynx, but his dentition was decayed with multiple missing teeth.

On the day of surgery, after informed consents were obtained and verified, the patient was brought to the operating room after premedication with midazolam as an anxiolytic. Standard monitors consisting of capnography, pulse oximetry, heart rate, EKG, temperature, and non-invasive blood pressure were used throughout the case. After pre-oxygenation with supplemental oxygen via face mask, the patient underwent induction with fentanyl, propofol, and rocuronium via peripheral intravenous access. There was no difficulty with mask induction and ventilation. A Macintosh size 3 blade was used to insert a 6.5cm cuffed endotracheal tube, which was successfully secured with continuous return of end tidal Co2 confirming the correct position of the endotracheal tube.

Intraoperatively, the patient was placed in the lithotomy position with head supported and in the neutral position. All his extremities were kept less than 90 degrees to prevent stretching of the nerves and possible neuropathy. Anesthesia was maintained with sevoflurane for the duration of the 3-hour case. His vital signs remained stable throughout the surgery. After extubation, the patient was transferred to the post-anesthesia care unit for further monitoring. The patient was fully awake and breathing comfortably with a patent airway and was discharged home with his caretaker later the same day.

Discussion

Anesthetic management for patients with BRPS present unique challenges due to a constellation of clinical manifestations. Here are some anesthetic considerations when delivering care to these patients.

<u>Craniofacial Abnormalities</u>

Patients with BRPS commonly have dysmorphic facial features, which can include high arched palate, microcephaly and micrognathia. Airway management for patients with craniofacial disorder poses many challenges. As such, preoperative management for patients with BRPS necessitate a thorough airway assessment. During the induction of general anesthesia, difficult airway adjuncts such as supraglottic airway, fiberoptic bronchoscope, bougie, and video laryngoscope should be readily available.

Hypotonia

Hypotonia can also affect anesthetic management, especially in children, due to excess sensitivity to nondepolarizing neuromuscular blockade or delay in return of neuromuscular function following administration of sugammadex.[6] Thus, the use of a nerve stimulator is recommended. Succinylcholine should be avoided due to increased risk of myotonia and electrolyte disturbances. Postoperative respiratory insufficiency is the greatest concern after anesthesia in patients with hypotonia, and opioids should be used sparingly to minimize respiratory depression that could lead to respiratory complications. Additionally, the possibility of postoperative intubation should be considered and discussed with the patient.

Poor Feeding and Growth

Patients with BRPS, especially during infancy, have a multifactorial cause of failure to thrive, including feeding difficulties and poor swallow reflex related to hypotonia. Patients with poor swallow reflexes can be at increased risk for aspiration and prophylactic H2-antagonists may be warranted. While feeding issues can improve with age, many patients may exhibit poor growth throughout childhood. Furthermore, these patients have low body fat and their thermoregulation may be impaired. As a result, care should be taken in maintaining normothermia intraoperatively through the use of warming blankets or other external warming devices, fluid warmer, and making sure the operating room temperature is appropriate.

Conclusion

Bainbridge Roper Syndrome is a recently discovered autosomal dominant genetic condition which can be difficult to characterize due to its wide range of phenotypes. However, with careful consideration of potential complications and pre-anesthesia evaluation of individual patients, the care team can minimize risks to these patients.

This middle-aged man with Bainbridge Roper syndrome underwent general anesthesia for cystoscopy, bilateral ureteroscopy and laser lithotripsy for treatment of renal calculus. His surgery, anesthetic course, and post-operative period were uneventful. We reviewed the special considerations for patients with Bainbridge Roper Syndrome undergoing anesthesia and the attention needed in areas of airway management, aspiration precautions, thermoregulation, and hypotonia.

REFERENCES

1. **Russell B, Graham JM Jr**. Expanding our knowledge of conditions associated with the ASXL gene family. *Genome Med*. 2013 Feb 21;5(2):16. doi: 10.1186/gm420. PMID: 23672984; PMCID: PMC3706972.
2. **Srivastava A, Ritesh KC, Tsan YC, Liao R, Su F, Cao X, Hannibal MC, Keegan CE, Chinnaiyan AM, Martin DM, Bielas SL**. De novo dominant ASXL3 mutations alter H2A deubiquitination and transcription in Bainbridge-Ropers syndrome. *Hum Mol Genet*. 2016 Feb 1;25(3):597-608. doi: 10.1093/hmg/ddv499. Epub 2015 Dec 8. PMID: 26647312; PMCID: PMC4731023.
3. **Bainbridge MN, Hu H, Muzny DM, Musante L, Lupski JR, Graham BH, Chen W, Gripp KW, Jenny K, Wienker TF, Yang Y, Sutton VR, Gibbs RA, Ropers HH**. De novo truncating mutations in ASXL3 are associated with a novel clinical phenotype with similarities to Bohring-Opitz syndrome. *Genome Med*. 2013 Feb 5;5(2):11. doi: 10.1186/gm415. PMID: 23383720; PMCID: PMC3707024.
4. **Ababneh F, Nashabat M, Alfadhel M**. A new case of Bainbridge-Ropers syndrome (BRPS): delineating the phenotype and review of literature. *JBCGenetics*. 2019; 2(1);65-9.
5. **Balasubramanian M, Willoughby J, Fry AE, Weber A, Firth HV, Deshpande C, Berg JN, Chandler K, Metcalfe KA, Lam W, Pilz DT, Tomkins S**. Delineating the phenotypic spectrum of Bainbridge-Ropers syndrome: 12 new patients with *de novo*, heterozygous, loss-of-function mutations in *ASXL3* and review of published literature. *J Med Genet*. 2017 Aug;54(8):537-543. doi: 10.1136/jmedgenet-2016-104360. Epub 2017 Jan 18. PMID: 28100473.
6. **Ragoonanan V, Russell W**. Anaesthesia for children with neuromuscular disease. *Continuing Education in Anaesthesia Critical Care & Pain*. 2010;10(5):143-7. https://doi.org/10.1093/bjaceaccp/mkq028.