



Anesthetic Considerations of Patients with Angelman Syndrome: A Case Report

Sejal Menghani, DMD

Dental Anesthesia Program, NYU Langone - Brooklyn



Introduction

Angelman syndrome (AS) is a rare neurodevelopmental disorder with an estimated prevalence of 1:15,000 live births, characterized by severe intellectual disability, seizure disorders, ataxia, distinctive craniofacial features, and behavioral abnormalities, including frequent laughing and a happy demeanor.¹ Most commonly, AS is caused by a maternal deletion of the ubiquitin-protein ligase (UBE3A) gene at the Prader-Willi Angelman syndrome critical region 15q11-q13.¹ This deletion also affects the gamma-aminobutyric acid (GABA-A) beta-3 receptor subunit gene, which contributes to the high rate of epilepsy encountered in these patients.¹ Patients with AS typically require general anesthesia for otherwise routine procedures such as dental care due to their profound intellectual disability, nonverbal communication, and uncooperative behavior during medical evaluations.^{1,2}

Reports in the published literature suggest that most patients with AS tolerate anesthesia well when appropriate precautions are undertaken.¹ Nonetheless, due to the rarity of the syndrome, large-scale studies are lacking, and anesthetic management recommendations are primarily based on case reports and limited case series.

Anesthetic Considerations

I. Cardiovascular Effects and Vagal Hypertonia

- Vagal hypertonia in patients with AS creates a predisposition for bradycardia and asystole, triggered by laparoscopic procedures and administration of anesthetic drugs directly or indirectly affecting the vagus nerve.^{2,3}

II. Pharmacodynamic Unpredictability

- UBE3A and GABA-A receptor $\beta 3$ abnormalities cause variable responses to anesthetics.
- Benzodiazepines may cause prolonged sedation or complete lack of effect.^{1,4}

III. Airway Management Challenges

- Craniofacial features (microcephaly, prognathia, protruding tongue) may complicate intubation.^{1,2}

IV. Seizure Management

- 80% of patients with AS have seizure disorders.^{1,2}
- Continue antiepileptic medications perioperatively.
- Avoid ketamine in patients with frequent seizures due to proconvulsant properties.²

Case Report

Patient: 10-year-old, 35.4kg female PMHx presents to NYU Langone Hospital – Brooklyn with her mother for restorative dental treatment under general anesthesia.

Past Medical History: AS, developmental delay, autism, epilepsy (absence seizures), anxiety, nonverbal communication

Medications: Keppra, Epidiolex, Levocarnitine, Trazodone

Past Surgical History: none; **Allergies:** none

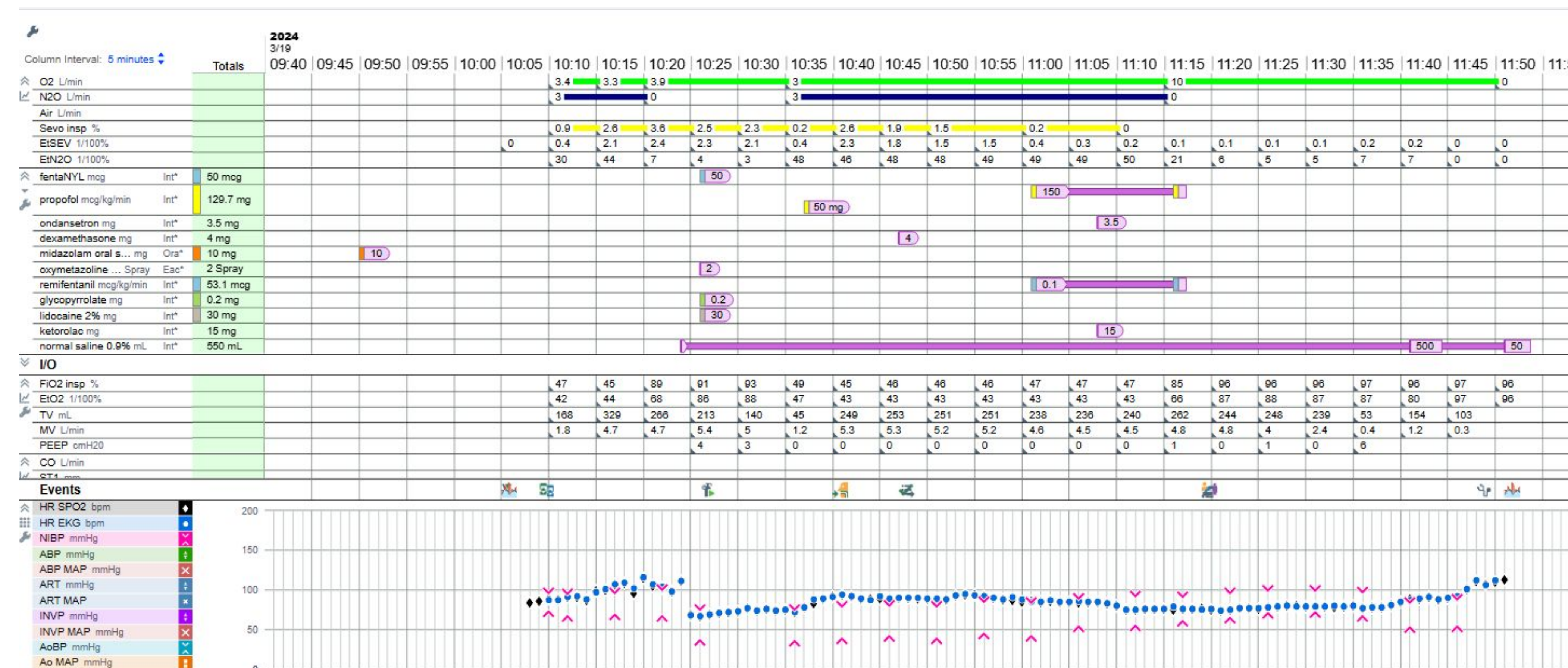
Physical Examination: Patient was uncooperative for Mallampati score assessment and was noted to have several features characteristic of AS, including brachycephaly (short and broad skull), wide mouth, prominent jaw with widely spaced teeth, protruding tongue, and a happy demeanor. CV and respiratory exam unremarkable (RRR, S1S2 without M/R/G, CTAB)

Induction: 10mg oral midazolam syrup was administered in the preoperative unit. In the operating room, mask induction was performed with nitrous oxide, oxygen, and sevoflurane. Standard ASA monitoring was applied, including non-invasive blood pressure, electrocardiography, pulse oximetry, and temperature monitoring. Intravenous access was obtained in the right great saphenous vein with a 22-gauge catheter. As shown in the intraoperative chart below, the heart rate (HR) notably dropped from 115bpm to 67bpm after administering 50mcg fentanyl. Given the significant drop, sevoflurane was turned off and we quickly administered 0.2mg glycopyrrolate and 30mg lidocaine IV. Once the HR came back up to 90bpm, we felt comfortable proceeding with the induction and administered 50mg propofol IV. We assessed mask ventilation and confirmed that there was no difficulty in ventilation.

Intubation: After preparing both nares with oxymetazoline spray, a size 5.5 cuffed nasal endotracheal tube (NETT) was introduced through the right nare. Video laryngoscopy was performed. A grade I Cormack-Lehane view was obtained with a McGrath and size 3 blade. Correct placement of the NETT was verified with auscultation and capnography.

Maintenance: The patient was transitioned from inhalational anesthesia with sevoflurane and nitrous oxide to TIVA with propofol 150mcg/kg/min and remifentanyl 0.1mcg/kg/min. The rest of the anesthetic was uncomplicated.

Emergence: The patient was safely extubated and transported to PACU on room air maintaining O2 saturation >95%.



Conclusions

- This case demonstrates that patients with AS can undergo general anesthesia safely when anesthesiologists anticipate syndrome-specific complications, maintain vigilant monitoring, and prepare appropriate interventions for cardiovascular instability and other potential challenges.
- The most significant anesthetic risk in patients with AS is the pronounced vagal hypertonia, in our case clearly illustrated by the dramatic heart rate reduction from 115 to 67 bpm following fentanyl administration.
- Prophylactic anticholinergic premedication should be strongly considered for cardiovascular protection, accompanied by continuous cardiac monitoring with immediate resuscitation capability including epinephrine availability.
- Continuation of antiepileptic medications and appropriate seizure precautions remain essential components of perioperative care.
- Anesthesiologists should prepare for potential airway difficulties by having videolaryngoscopy and alternative airway devices readily available, while exercising careful anesthetic titration with heightened awareness of pharmacodynamic variability, particularly with benzodiazepines and GABA-acting agents.

References

- Warner ME, Martin DP, Warner MA, Gavrilova RH, Sprung J, Weingarten TN. Anesthetic Considerations for Angelman Syndrome: Case Series and Review of the Literature. Anesth Pain Med. 2017;7(5):e57826.
- Bevinetto CM, Kaye AD. Perioperative considerations in the patient with Angelman syndrome. J Clin Anesth. 2014;26(1):75-79.
- Gardner JC, Turner CS, Ririe DG. Vagal hypertonia and anesthesia in Angelman syndrome. Paediatr Anaesth. 2008;18(4):348-349.
- Kim BS, Yeo JS, Kim SO. Anesthesia of a dental patient with Angelman syndrome -A case report-. Korean J Anesthesiol. 2010;58(2):207-210.
- Agarwal J, Datta R, Jaideep CN, Sharma A. Angelman syndrome and anaesthetic considerations. Indian J Anaesth. 2017;61(1):78-80.