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CASE REPORT

Dental management of a pediatric patient with angelman syndrome under general anesthesia

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Angelman syndrome (AS) is a genetic disorder characterized by cognitive impairment, locomotor difficulties, distinctive behavioural patterns, and speech impairment. The syndrome is associated with a partial deletion of chromosome 15, which affects the subunit of gamma-aminobutyric acid (GABA) receptor. Many central nervous system drugs used in anesthesia operate through these receptors. Consequently, patients with AS, who have impaired GABA receptors, often require general anesthesia even for minor procedures. The anesthetic management of these patients can be challenging due to potential complications, including seizures, vagal nerve hyperfunction, craniofacial malformations, and peripheral muscular atrophy. In this report, we describe the administration of general anesthesia with sevoflurane for a nine-year-old boy with AS who was undergoing treatment for tooth decay.

Keywords: anesthesia, Angelman syndrome, chromosome 15 abnormality, GABA receptor, ambulatory surgery

Introduction

In 1965, Dr Harry Angelman identified three children with developmental delays (1), initially referred to as "Happy Puppet Children." In 1987, this condition was renamed as Angelman syndrome (AS) (2, 3). AS is an autosomal dominant neurodevelopmental genetic disorder with maternal imprinting, linked to an abnormality in the ubiquitin–protein ligase E3A (UBE3A) gene located on chromosome 15 at q11–q13 region. Patients with AS exhibit intellectual debility, motor disorders, and difficulty maintaining balance and coordinating arm and shoulder movements (4). Behaviorally, individuals with AS may show hyperexcitability, inappropriate laughter, and difficulty with concentration and attention (5). There have been reports of malignant bradydysrhythmias triggered by laughing episodes and profound bradycardias that can occur during anesthesia.

Chromosomal studies have shown a deficiency in chromosome 15 at q11.2–q13 region, and a fluorescence in situ hybridization test has confirmed the diagnosis of AS. Despite normal findings in brain magnetic resonance imaging and electroencephalography (EEG), clinical features and medical evaluations provided essential diagnostic tools (6).

Differential diagnoses of AS.

Rett syndrome
Lennox–Gastaut syndrome
Non-evolutionary chronic encephalopathy
Childhood autism
Alpha-thalassemia associated with X-linked inheritance of intellectual disability

Individuals with AS often experience developmental delays, such as loss of speech, overexcitedness, and a short attention span, which make behavior management

FIGURE 1 | Patient with Angelman syndrome.

challenging. Additionally, they tend do display distinctive facial features, such as a wide-open mouth, mandibular protrusion, a thin upper lip, a small widely spaced teeth, midline diastema, and an anterior open bite. They may also exhibit a smaller head circumference (microcephaly/brachycephaly), a flat head, strabismus, and hypopigmentation of the skin and eyes (7).

Oral manifestations in AS include abnormal dysfunction of the tongue, lips, and cheeks, which can adversely affect the mouth's natural cleaning patterns and disrupt the proper alignment of teeth. Difficulties with sucking and swallowing can cause food to remain in the mouth longer, increasing the risk of caries. Excessive drooling, tongue thrusting, and hyperactivity, combined with limited cooperation during examinations, often make dental assessments challenging and may necessitate the use of general anesthesia (GA) (8).

This case report aims to share our experience with the anesthetic management of a patient with AS who underwent dental treatment under GA.

Case presentation

A nine-year-old boy visited the Dental Department, reporting pain in the lower right and left back tooth regions for the past 10 days. The pain was spontaneous, dull, and continuous. It aggravated on its own and was relieved after medication. Tooth conservation was planned under GA due to the patient's uncooperative behavior.

The child was hyperactive and exhibited distinctive behaviors associated with autism spectrum disorder, such as continuous smiling, heightened excitability, impaired speech, poor social interaction skills, and repetitive behaviors (see **Table 1**). Additionally, the child displayed independent walking and running, but with a distinctive posture marked by shrugged shoulders and slightly raised arms with flexed elbows.

The child was 149 cm tall and weighed 33 kg (**Figure 1**). He was the first child of non-consanguineous, healthy parents, without any documented history of allergies and seizures. The child exhibited a below-average intelligence quotient. Delivery was vaginal with a birth weight of 2.75 kg, and the infant achieved a normal appearance, pulse, grimace, and respiration (APGAR) score. The parents reported a squint in the child, along with developmental delays such as delayed sitting around the age of 1, although he child achieved independent walking around 24 months. Additionally, the child displayed an altered sleep–wake cycle, characterized by late bedtimes and early morning wakefulness.

On physical examination, the patient showed excessive drooling of saliva, impaired speech, frequent smiling, an easily excitable personality, peripheral spasticity, muscular atrophy, overactivity, and impaired attention.

Intraorally, the patient presented with multiple carious teeth with poor oral hygiene. Preoperatively, two intraoral periapical radiographs were taken using a film holder. The posterior periapical radiograph (#36, #46) revealed deep caries affecting the pulp. Laboratory findings, including EEG, electrocardiography (ECG), and a chest radiograph, appeared normal. We explained the treatment plan to the child's parents, who provided written consent and completed the necessary pre-anesthetic check-ups. After the pre-anesthetic evaluation confirmed the patient was fit for surgery, the patient was posted for treatment under GA.

TABLE 1 | Clinical features of Angelman syndrome.

Consistent	Frequent	Occasional
Functionally severe intellectual disability	Microcephaly with flat occiput/occipital groove	Scoliosis
Speech impairment*	Abnormal EEG	Increased sensitivity to heat
Behavioral phenotype (easily excited; happy, frequent laughter, hypermotric)*	Gastrointestinal difficulties (feeding problems, gastroesophageal reflux, constipation)	Growth disturbance depending on genotype
	Fascinated with water or cranky items Mouthing behavior*	Ocular problems (refractive and alignment errors)
	Ankle pronation	
	Sleep disturbance*	

*Clinical features seen in present case report.

The patient was given 10 mg midazolam oral syrup as premedication. Standard ASA monitor mask induction was carried out efficiently with O_2 (4 L/min), N_2O (6 L/min), and sevoflurane (8%). A 22-gauge angiocatheter was placed in the dorsum of the left hand. To reduce salivation and prevent bradycardia Glycopyrrolate 0.2 mg was administered. Phenylephrine (0.25%) nasal drops were applied to both nostrils in order to constrict nasal mucosa, hence minimizing nasal bleeding and easing nasal intubation. Intravenous rocuronium 0.6 mg/kg was administered to aid with intubation. 6-mm uncuffed, lubricated nasal RAE tube was efficiently passed through the left nostril and directed into the trachea through the vocal cords with the help of Magill forceps. To prevent aspiration, a throat pack was placed by the surgeon.

The patient was maintained on (50:50) N_2O:O_2 mixture. To achieve an end-tidal concentration of 1.5%, sevoflurane was delivered. Analgesia was administered via 2% lidocaine with 1:100,000 epinephrine by the surgeon. There were no findings of difficult intubation or difficult airway complications. Lung sounds were clear and bilateral, with no rales or rhonchi. Heart sounds were rhythmic, with no additional sounds or murmurs heard.

The following treatment plan was discussed with the child's parents:

(1) Oral hygiene instructions and diet counseling were provided to the caregiver.
(2) Oral prophylaxis was conducted, and periodontal health was monitored through assessments of gingival inflammation (bleeding on probing) and tooth mobility.
(3) Root canal treatment was performed on the mandibular right molar (#46), followed by crown preparation.
(4) Restorations were completed for the maxillary right and left molars (#16, #26).
(5) Extraction of the mandibular left molar (#36) was also carried out.

After a 7-day interval, a porcelain-fused-to-metal (PFM) crown, prepared in a dental laboratory, was placed on tooth #46.

An intravenous dose of ketorolac (20 mg) was administered prior to the end of the procedure to minimize postoperative pain. Similarly, dexamethasone (4 mg) and ondansetron (4 mg) injections were given 65 and 33 min, respectively, before the end of the procedure to prevent postoperative nausea and vomiting. The postoperative recovery was smooth, and the patient was discharged on the second day post-surgery.

Discussion

AS is a genetic neurological disease with an estimated prevalence ranging from 1:10,000 to 1:40,000. Accurately determining its prevalence is challenging due to underdiagnosis and the diverse phenotypic expressions of the syndrome. Additionally, there is no evidence to suggest a gender predominance in the occurrence of the syndrome (9, 10). In this case report, the patient was a boy. However, there is no evidence that AS is more common in males.

AS cannot be noticed at birth or during infancy; it is usually diagnosed after the age of four, when certain signs and behavior changes become noticeable. The life expectancy of individuals with AS is generally limited to around 15 years. These patients are commonly characterized as having "Happy Puppet Syndrome" due to their happy facial expressions, inappropriate laughing sessions, flapping of hands, and trembling gait (11).

Several clinical features of AS are important for dental surgeons. Abnormal function of the tongue, lips, and cheeks can disrupt their mouth's natural cleansing mechanism and impede proper alignment of teeth (5, 8). Children with AS are at high risk for dental caries due to difficulties in maintaining good oral hygiene because of motor coordination issues and cognitive impairments. Additionally, the frequent use of sugar-containing medications can lead to xerostomia, and an uncontrolled cariogenic diet can further exacerbate their routine dental care challenges (12).

Impaired communication in AS patients is primarily due to their language deficit. Other clinical features include hyperactive tendon reflexes, sleep problems, attention deficit disorder, sucking, and swallowing (7).

Patients with AS typically have a maternal deletion of chromosome 15q11-q13 involving the UBE3A gene, leading to frameshift mutation. Abnormal regulation of the β3 subunit of gamma-aminobutyric acid (GABA)-A receptors may affect receptor kinetics, making patients sensitive to these anesthetic agents (6). Many medications, such as anxiolytics, sedative—hypnotics, general anesthetics, and anticonvulsants, achieve their effects through interactions with these receptors. Agents such as midazolam, propofol, and other potent inhalants can activate these GABA receptors, increasing the likelihood of unexpected complications in anesthesia management of these patients (13–15). Typically, a child with AS exhibits striking high-voltage slow-wave activity, which is a distinctive finding on an EEG (16). However, in this case report, both EEG and ECG findings were unremarkable, and no such abnormality was observed. In the present case, midazolam injection was administered to reduce anxiety, followed by sevoflurane inhalation and mask anesthesia for the procedures (17).

Intensive education regarding oral hygiene is equally important for both the child and their caregiver, as the child's involuntary movements and lack of motor skills hinder their ability to brush their teeth independently. Special emphasis

should be placed on teaching correct brushing techniques to minimize distractions and overstimulation. Bright colors, especially red and yellow, should be avoided in the dental office environment. Constant and frequent compliments are beneficial for the child. However, if parents lack motivation to maintain good oral hygiene, it becomes challenging to prevent dental decay, but with regular dental check-ups and support of caregivers, a child can prevent the tooth decay (7).

Conclusion

Patients with this syndrome often need anesthesia even for minor dental treatment due to cognitive impairments and communication challenges, which limit their ability to cooperate. The oral manifestations of AS result not only from the syndrome itself but also from abnormalities such as ataxia and myoclonus, leading to difficulties in maintaining proper oral hygiene. Patients may exhibit unconventional responses to benzodiazepines. While airway management was not complicated by craniofacial abnormalities in our case, dental specialists must be alert, as patients with AS have experienced abnormal slowing of the heart rate (malignant Brady dysrhythmias) during anesthesia.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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