

Genetic heterogeneity of Angelman syndrome and its significance to the anesthesiologist

Sir,

A 4-year-old, 120 cm, 12 kg, male was scheduled for orchidopexy. He was mentally retarded, and his milestones were delayed. He was on treatment for focal complex partial and myoclonic seizures from the age of 3 years. Diffuse hypoplasia of the corpus callosum on magnetic resonance imaging, nonconvulsive status epilepticus on electroencephalography; patent foramen ovale on echocardiography and spina bifida at L4-5 on X-ray spine were reported.

The child had characteristic facies [Figure 1]. Molecular genetic studies of chromosome 15 were normal. No premedication was given. Vitals were stable; fentanyl 2 µg/kg and glycopyrrolate (0.06 mg) were administered. After inhalational induction with 2% sevoflurane and successful bag mask ventilation placement of classic laryngeal mask airway (size 2) was attempted which failed despite multiple attempts. Endotracheal intubation (5 mm cuffed) was easily accomplished. Laryngoscopy revealed a large floppy epiglottis. Muscle relaxants were avoided, and anesthesia was maintained with sevoflurane 1-1.5 vol%. The perioperative course was uneventful.

Angelman syndrome (AS) is a neurogenetic disease with prevalence of 1:10,000-40,000.^[1] It is characterized by developmental delay, microcephaly, seizures, movement disorders, absent speech, frequent laughter,



Figure 1: Angelman syndrome: Beaked nose, bat shaped ears, long thin facies and prognathism. High arched palate and Mallampati Grade 0 was noted on airway examination

easy excitability, and hand-flapping (“Happy Puppet Syndrome”).

Genetic basis for the disorder is complex, but limited to abnormalities of chromosome 15; interstitial deletion of 15q11-13 of maternal chromosome (Class I), uniparental disomy (UPD) and failure to inherit a maternal copy of ubiquitin-protein ligase E3A (Class II), “imprinting” defects (Class III) and patients with mutations in the gene encoding ubiquitin protein ligase (Class IV). Patients with chromosome 15 deletions are most severely affected; those with UPD and imprinting defects are the least. Patients in Class V (10-15%) have clinical features of AS, but no demonstrable cytogenetic abnormality. Our patient belonged to this group.

Genetic abnormalities of chromosome 15 result in concomitant deletions of region encoding for the B3 subunit of the GABA-A receptor.^[2,3] Anti-anxiety medications, sedative hypnotics, general anesthetics and anti-seizure drugs act through the GABA receptor, and thus response of patients with AS to these drugs is unpredictable. Patients may also have a dysregulation of NMDA or AMPA receptors. It is therefore reasonable to minimize the use of benzodiazepine and halogenated ethers (inhalational anesthetics).

Anatomical, facial and oropharyngeal abnormalities in patients with AS may have hampered the placement of the supraglottic device in our patient.

Generalized muscular hypertonia and temporary respiratory compromise has been reported postoperatively by Maguire^[3] in an adult with AS. Increased sensitivity to muscle relaxants may be the cause and use of neuromuscular monitoring is mandatory if muscle relaxants are administered.

Assessment of postoperative pain is difficult due to lack of communication skills. Developmental delay, agitated behavior and scoliosis make the placement and assessment of regional anesthesia difficult.^[4] They have predominant vagal tone and may have episodes of bradycardia and asystole from an increase in the intrathoracic pressure and valsalva effect.^[5] Laparoscopic surgeries and neuromuscular reversal agents like neostigmine should be avoided.

There is no conclusive evidence for or against the use of any anesthetic agent in patients with AS because of the genetic heterogeneity. Minimum doses should be used in patients belonging to Class I (most severely affected). Our patient belonged to Class V (no genetic abnormality), and we report a normal pharmacological response to anesthetic agents. Uneventful perioperative course has also been described in previous studies.^[2] Further research in the form of case series/prospective observational studies are needed to confirm or refute the same.

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