Holt–Oram Syndrome: Anesthetic Challenges and Safe Outcome

Abstract

Holt–Oram syndrome (HOS) is an autosomal dominant disease with skeletal and cardiac manifestations. We here are presenting a 31-year-old man and a diagnosed case of HOS, with an ulceroproliferative lesion on lateral border of the tongue, was posted for wide excision of lesion with primary closure and left side radical neck dissection.

Keywords: *Anesthesia, autosomal, Holt–Oram syndrome, mutations*

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Introduction

Holt–Oram syndrome (HOS) is a rare genetic disease with an autosomal dominant fashion of inheritance. The gene involved in the phenotypic manifestation of this disease is the *T-box* transcription factor product (TbX5 protein) located on long arm of chromosome 12q24[1] also called as hand–heart syndrome; skeletal defects are universal affecting the preaxial side of the upper limbs and range from absent thumb to phocomelia. Cardiac system is affected structurally with secundum type of atrial septal defect (ASD) and ventricular septal defect being the most common abnormality. Ion channels, particularly potassium and calcium, are affected which manifest in the form of rhythm disturbances which are rather common in HOS.[1,2]

History

A 31-year-old gentleman, presented with a 3-month history of an ulceroproliferative lesion (4 cm × 2 cm) on lateral border of the tongue, diagnosed to be a case of squamous cell carcinoma on biopsy. He was posted for wide excision of lesion with primary closure and left side radical neck dissection. He was 145 cm in height, 45 kg in weight, and had a bilateral hand deformity, consisting of finger such as thumbs. He denied similar history in family. The radial artery could not be palpated on left side and patient had an irregularly irregular pulse of 87/min with pulse deficit of 33. He had undergone patch closure for a large ASD 4 years back uneventfully. His electrocardiogram revealed atrial fibrillation. Echocardiography showed global hypokinesia with left ventricular ejection fraction of 30%–35%, mild mitral regurgitation, ASD patch intact with no residual shunt, and mild pulmonary hypertension (pulmonary artery systolic pressure of 38 mm of Hg). Airway examination revealed Mallampati Class II. His mouth opening was 3 cm with slight protrusion of tongue. He was diagnosed to be a case of HOS on the basis of his limb and heart defects. Genetic testing was offered to the patient to consolidate the diagnosis, but this could not be done because of financial constraints. He was on oral metoprolol 50 mg, furosemide 20 mg, and spironolactone 20 mg for atrial arrhythmias.

In operating room, left femoral artery was cannulated under local anesthesia for invasive blood pressure (IBP) monitoring. The anesthesia workstation was flushed overnight with pure oxygen at a flow rate of 10 L/min, after the vaporizers were removed. New circuit and soda lime canister were attached. Anesthesia was induced with 1.5 mg midazolam, 150 mcg fentanyl, and 70 mg propofol under beat to beat invasive IBP monitoring by femoral artery cannulation. Neuromuscular blockade was facilitated with 50 mg rocuronium and size 7 mm ID nasotracheal tube was placed. Anesthesia was maintained on total intravenous anesthesia (TIVA) with propofol and fentanyl infusion and intermittent rocuronium boluses and

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oxygen with air (40:60). No inhalational agent was used. Bispectral index (BIS) monitoring was instituted for assessing the depth of anesthesia. A pacemaker sheath was inserted in the left subclavian vein, for institution of transvenous pacemaker intraoperatively if required in view of perioperative arrhythmia and reports of sinus arrest and sudden death in patient with HOS.[3]

Despite the severe arrhythmias intraoperatively, he remained hemodynamically stable hence no treatment was actively instituted for the arrhythmia. BIS was kept around 50. Postoperatively, his heart rhythm continued to be unstable with intermittent episodes of atrial flutter and fibrillation. Aspirin 150 mg once a day was added to his medication. His femoral arterial line and subclavian introducer sheath were removed on 3rd postoperative day (POD) and he was discharged from surgical Intensive Care Unit on 6th POD.

Discussion

HOS, with an incidence as low as 1 in 100,000, is an autosomal dominant syndrome.[3,4] There is marked phenotypic heterogenicity among patients of this syndrome, some have more severe cardiac manifestations other have more pronounced skeletal defects. Skeletal defects are universal,[1] but range from subclinical radiological features to short thumb, syndactyly, clinodactyly, complete agenesis of preaxial bones, phocomelia with hypoplastic bones, muscles, and vasculature. Cardiac defects range from structural heart defects, of which ostium secundum type of ASD is the most common. Almost every type of arrhythmia has been reported in these patients ranging from sinus node dysfunction, sinus arrest, atrioventricular node block, atrial fibrillation, wandering pacemaker, and Wolff–Parkinson–white syndrome. In one study done in 55 patients to study the various cardiac defects in HOS, at least 3 had reported complete heart block which required permanent pacemaker and 1 patient had sinus arrest.[5,6] Cardiomyopathy, end-stage renal disease, stroke, difficult intubation, and ventilation have also been reported. The various anesthetic implications for this rare syndrome have been mostly gathered from sporadic case reports published. The plan of instituting TIVA for this patient was based on a previous single case report of malignant hyperthermia (MH)-like symptoms in a 2-year-old child posted for repair of cardiac defect.[7] There is no proven correlation between HOS and MH, but a recent paper from animal studies provides evidence that TbX5 induces the expression of a specific member of the CaMK-II (the Type II multifunctional Ca2+/calmodulin-dependent protein kinase) family.[8] Furthermore, it is understood that the various types of cardiac rhythm disturbances that affect these patients could be related to abnormal potassium channel regulation. Given these facts, it may be assumed that there can be a link between the two conditions, and hence, it may be wise to avoid inhalational agents. Among the previous case reports of patients with HOS undergone surgery, two patients have received general anesthesia uneventfully[6,9] while one patient underwent surgery under neuraxial blockade.[10]

Conclusion

The pleiotropic nature of this disease warrants careful preanesthetic checkup of these patients presenting for surgery. The preoperative workup of these patients should include a careful history and clinical evaluation to rule out major cardiac and other visceral abnormality. Intraoperative early detection of heart block and severe arrhythmias with hemodynamic instability may require pacing of the heart.

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Conflicts of interest

There are no conflicts of interest.

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