Holt–Oram syndrome

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Summary
Holt–Oram syndrome (HOS) is a rare disorder characterized by congenital anomalies of the upper limbs and heart. Cardiac arrhythmias are common in patients with HOS. We successfully managed a 24-yr-old woman with HOS who underwent laparoscopic ovarian cystectomy. Potential problems in the anaesthetic management of patients with HOS are discussed. (Br. J. Anaesth. 1998; 80: 856–857)

Keywords: anaesthetic techniques extradural; complications arrhythmia; complications Holt–Oram syndrome

Holt–Oram syndrome (HOS) is a rare disorder characterized by congenital anomalies of the upper limbs and heart.1–4 Cardiac arrhythmias, irrespective of the presence or absence and severity of cardiac anomalies, often accompany HOS.1–3 Moreover, sudden death can occur in these patients.4

We managed a woman with HOS who underwent laparoscopic ovarian cystectomy after extradural anaesthesia supplemented with light general anaesthesia. There were no untoward events. Potential problems in the anaesthetic management of patients with HOS are discussed.

Case report
A 24-yr-old Japanese woman was to undergo laparoscopic ovarian cystectomy. Her parents, two brothers, and close relatives had no abnormalities of the upper limbs or heart.

She underwent a cardiac catheterization when 5 yr old after the detection of heart murmurs.1–4 Cardiac arrhythmias, irrespective of the presence or absence and severity of cardiac anomalies, often accompany HOS.1–3 Moreover, sudden death can occur in these patients.4

Physical examination before operation revealed anomalies of the upper extremities — hypoplastic clavicles and pectoralis major muscles and abducens palsy — and ocular refractive error. Chest x-ray showed a cardiothoracic ratio of 0.54, without increase in pulmonary vascular markings. Routine ECG showed strain-type ST–T changes in leads V4–V6. There were no delta waves. Continuous ambulatory Holter monitoring recorded five supraventricular and 20 monofocal ventricular premature contractions each day; however, there were no conduction abnormalities or tachycardia.

The patient was premedicated 2 h before surgery with pentobarbital 100 mg and diazepam 10 mg orally and 30 min before surgery with atropine 0.4 mg s.c. On arrival in the operating theatre arterial pressure was 142/76 mm Hg and heart rate 88 beat min−1. ECG monitoring was established, together with monitoring of arterial pressure (noninvasive) and central venous pressure, pulse oximetry and capnography. An extradural catheter was inserted in the Th12/L1 intervertebral space. Two percent mepivacaine 3 ml was given via the catheter. There was no discernible hypoaesthesia in the lower limbs after 2 min. The central venous pressure was 9 cm H2O. Injection of 2% mepivacaine 7 ml produced an area of hypoaesthesia to cold from Th6 to S3 after 5 min. The arterial pressure, heart rate and central venous pressure were 148/70 mm Hg, 82 beat min−1, and 8 cm H2O, respectively.

Anaesthesia was induced with thiopental 150 mg i.v. supplemented with butorphanol 1 mg and midazolam 3 mg. The trachea was intubated after vecuronium 4 mg i.v. Anaesthesia was maintained with nitrous oxide (67%) in oxygen, and ventilation was mechanically controlled. Laparoscopic ovarian cystectomy was begun after intraperitoneal insufflation of carbon dioxide with a pressure of 8 mm Hg. There were no haemodynamic changes of note during the surgery, which lasted 2 h 25 min. The trachea was extubated after neostigmine 2.5 mg and atropine 1.0 mg i.v. There was no conduction disturbance or supraventricular tachycardia during or after anaesthesia and surgery. The patient was discharged well 6 days after surgery.

Discussion
Holt–Oram syndrome is either familial or, in 30–85% of patients,5 occurs in isolated cases. Familial HOS is

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transmitted as an autosomal dominant trait and related, in most subjects, to mutations in a gene on chromosome 12q. The severity of upper-limb anomalies and anomalies of the heart shows a positive correlation that increases with successive generations. Subjects in HOS families with anomalies of the upper limbs but no heart anomalies are diagnosed as having HOS, because they can transmit both anomalies to their offspring, but the presence of both anomalies is a prerequisite for the diagnosis of HOS in isolated cases. Subjects with isolated HOS tend to have more severe anomalies of the upper limbs than do familial cases. As our patient’s family and close relatives had no anomalies of the upper limbs or heart, she was apparently an isolated case. Hypoplastic thumbs are suggestive of HOS. Of 98 subjects with hypoplastic thumbs, 16 (16%) proved to be cases of HOS. The anomalies of the upper limb in HOS vary in severity. They range from only hypoplasia of the thumb, clindactyly, brachydactyly, syndactyly or hypoplasia to agenesis of the radius or humerus or both, and ectromelia. Other associated anomalies often observed are hypoplasia of the clavicle and pectoralis major, and, less frequently, abducens palsy and ocular refractive error. As preoperative examination for non-cardiac surgery in adults with HOS sometimes discloses cardiac anomalies, it is important precisely to evaluate the cardiovascular system before any surgery in patients with hypoplastic thumbs.

We have found no reports on the management of patients with HOS in the English anaesthetic literature from 1966 to 1997. Potential problems in the management of such patients are associated with their cardiac anomalies, cardiac arrhythmias, and the hypoplastic vasculature.

Atrial and ventricular septal defects are common cardiac anomalies in individuals with HOS. Of 189 patients with HOS having cardiac anomalies, the most frequent single anomaly was atrial septal defect (41.8%), followed by ventricular septal defect (13.8%). Both of these defects are often associated with other heart anomalies. More complicated anomalies, such as tetralogy of Fallot, endocardial cushion defect and total anomalous pulmonary venous return, were observed in 33 (17.5%) of 189 subjects with HOS. In those who have moderate to severe cardiac anomalies, heart surgery is performed between the postnatal period and early childhood. The survival of individuals with HOS depends on the severity of their cardiac anomalies. Of the 189 subjects with HOS and heart anomalies, 12 (6.3%) died (the causes of death were not stated) all had moderate or severe heart anomalies. They constituted 36% of the 33 patients in this series with moderate or severe cardiac anomalies. Various types of arrhythmia occur in subjects with HOS. Most subjects with HOS who had arrhythmias had anatomical heart anomalies. However, 39% of those with familial HOS showed only ECG abnormalities and no anatomical heart anomalies. Spontaneous closure of atrial and ventricular septal defects with ageing cannot be ruled out in such subjects. Arrhythmias observed in subjects with HOS include sinus arrest, sinus node dysfunction, wandering pacemaker, bradycardia, atrio-ventricular block and right bundle branch block. Some patients needed a permanent cardiac pacemaker. Sudden death occurred in some HOS patients with no documented cardiac anomalies. Our patient had had transient supraventricular tachycardia and a transient WPW syndrome after operation for patch closure of the ventricular septal defect when 9 yr old. We found no reports of WPW syndrome in subjects with HOS.

Hypoplastic vasculatures are present in subjects with HOS. There are reports of patients in whom cardiac catheterization through femoral or arm veins was difficult. When our patient underwent cardiac catheterization when 5 yr old, to evaluate the anomalies of the heart, multiple femoral vein punctures were required. Some individuals with HOS have hypoplastic clavicles and pectoralis majors, and radial arteries that are difficult to palpate. It may be more reliable and safer in patients with HOS to cannulate blood vessels under ultrasound guidance, because their anatomical landmarks are different from those of normal subjects.

References