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Anesthetic problems in a child with Waardenburg's syndrome and Hirschsprung's disease

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Introduction

Waardenburg's syndrome consists of characteristic facial deformities, pigmentation anomalies, and congenital deafness [1]. Recently, a pathogenetic association between Hirschsprung's disease and Waardenburg's syndrome has been hypothesized [2–4]. Although affected patients require surgical treatment, very little has been published about the anesthetic implications. We describe a patient who has these congenital entities, and problems in her anesthetic management are discussed.

Case history

A 2.1-kg female was born at a gestational age of 39 weeks after spontaneous vaginal delivery. The Apgar score at 1 min was 4, and the patient was observed in a neonatal intensive care unit for 2 days. On day 7, abdominal distention and bilious vomiting developed. Plain abdominal X-rays and a barium enema revealed findings that were clinically consistent with Hirschsprung's disease. On day 41, the infant was transferred to the Juntendo University Hospital for surgical treatment. The following findings were noted: white forelock, broad nasal root, depigmentation of the iris, and nystagmus.

The infant's operations and their anesthetic management are summarized in Table 1.

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On day 45, a rectal biopsy was performed. As peripheral venous cannulation was difficult, anesthesia was induced with halothane 1% maximum and nitrous oxide 50% in oxygen with spontaneous respiration. Tracheal intubation was accomplished easily with suxamethonium, and ventilation was controlled manually. Caudal anesthesia was then given with 0.8% lidocaine 2 ml. Ringer's lactate solution 6 ml·kg^{-1}·h^{-1} was infused during the operation. Recovery from anesthesia was smooth. On the first day after the operation, an unexpected convulsion occurred, most likely due to hyponatremia, as the serum sodium value was 126 mmol·l^{-1}. Phenobarbital was given for 2 days. The histological examination confirmed aganglionosis.

On day 52, an ileostomy and central venous cannulation for total parenteral nutrition were required. Anesthesia was induced with halothane and maintained without halothane because of a hypotensive tendency. Whole blood 39 ml was transfused due to preoperative anemia. Four days after ileostomy, an emergency reconstruction of the stoma was performed due to intestinal prolapse. Anesthesia was induced and maintained without nitrous oxide because of abdominal distention. While the trachea was intubated without a muscle relaxant, peripheral venous cannulation was extremely difficult. After anesthetic induction using only 0.5% halothane, the brachial systolic pressure decreased from a preinduction value of 90 mmHg to 40 mmHg. The recovery period was uneventful.

On day 63, an emergency laparotomy was needed because of postoperative intraabdominal hemorrhage, with the lowest hematocrit value reaching 18%. On arrival at the operating room, the patient was in a preshock state. Blood transfusion had already been initiated. After preoxygenation, tracheal intubation was performed while she was awake. Anesthesia was maintained with only 33% nitrous oxide in oxygen, and pancuronium. The bleeding point was found on the omentum, and hemostasis was performed uneventfully.

Table 1. Operations and anesthetic management

No.	Age	Weight	Operation	Duration of operation	Premedication	Induction[b]	Maintenance[b]	Muscle relaxant
1	45D	2.6kg	Rectal biopsy	18M	Nil	GOF	GOF Caudal lignocaine	Suxamethonium
2	52D	2.6	Ileostomy, rectal biopsy TPN catheter insertion	4H 05M	Nil	GOF	GO	Suxamethonium Pancuronium
3	56D	2.6	Stoma reconstruction[a]	45M	Nil	OF	OF	Nil
4	63D	2.6	Laparotomy and hemostasis[a]	1H 05M	Nil	Awake	GO	Pancuronium
5	4M	3.1	TPN catheter insertion	30M	Atropine	GO	GOE	Pancuronium
6	6M	4.2	Stoma reconstruction TPN catheter insertion	6H 15M	Atropine	GOF	GOF	Suxamethonium Pancuronium
7	8M	5.5	TPN catheter insertion	35M	Nil	GOF	GOF	Pancuronium
8	1Y1M	7.9	Pull-through procedure Stoma closure	5H 29M	Nil	Thiopentone	GOE	Pancuronium
9	1Y2M	7.8	Anal plasty	15M	Nil	GOE	GOE	Vecuronium
10	1Y3M	7.6	Stenotic intestine resection TPN catheter insertion	3H 50M	Atropine	Thiopentone	GOE Fentanyl	Vecuronium
11	1Y7M	7.8	Gastroesophageal endoscopy	14M	Atropine	Thiopentone	GOF	Vecuronium
12	1Y9M	7.9	TPN catheter insertion	1H 28M	Atropine	Thiopentone	GOE	Vecuronium
13	1Y9M	8.2	TPN catheter insertion	25M	Nil	Thiopentone	GOE	Vecuronium
14	2Y11M	10.4	Skin grafting	1H 25M	Atropine Hydroxyzine	GOI	GOI	Vecuronium

D, days; M, months; Y, years; TPN, total parenteral nutrition.
[a] Emergency operation.
[b] G, nitrous oxide; O, oxygen; F, fluothane; E, enflurane; I, isoflurane.

Hemoglobin and hematocrit values recovered to 11.9g·dl^{-1} and 32%, respectively, at the end of the operation.

At 3 months of age, when an auditory brainstem response confirmed profound bilateral hearing loss, the patient was finally diagnosed as having Waardenburg's syndrome. Congenital blindness was also confirmed due to depigmentation and degeneration of the retina and the macula lutea. An echoencephalogram disclosed diffuse brain atrophy, and an electroencephalogram revealed an absence of sleep spindles. Chromosomal analysis showed a normal 46 XX pattern. At 1 year of age, anesthesia was induced rapidly with thiopental when a venous line was inserted preoperatively. At 2 years of age, sedative premedication was given to ease anxiety and fear. After operation 14, a skin grafting of a nonhealing ulcer from a burn on the left foot, an unexpected convulsion again occurred. A clinical diagnosis of tetany was made with serum calcium of 3.6mmol·l^{-1}, and which remitted on calcium infusion. At 3 years of age, when discharged from our hospital, the patient's developmental age was estimated to be about 12 months.

Discussion

Waardenburg's syndrome is characterized by: (a) dystopia canthorum, (b) synophrys, (c) heterochromia iridis, (d) high broad nasal root, (e) pigmentary disturbances of the hair and skin (white forelock), and (f) congenital deafness [1]. An autosomal dominant inheritance has been suggested with a varying penetrance [5]. The diagnosis of sporadic Waardenburg's syndrome was made in this patient, who manifested four out of six signs [6].

Waardenburg's syndrome is thought to be a genetic disorder of the neural crest cells. Hirschsprung's disease is a congenital defect of the Meissner and Auerbach plexi, which are also derived from the neural crest cells. Therefore, these two entities are speculated to be associated disorders [7,8]. Congenital blindness, a sign of fundal disturbance, and nystagmus, a sign of vestibular disturbance, could have arisen from the identical pathogenetic process. Other anomalies, including cleft lip and palate, tracheoesophageal fistula, anal atresia, meningocele, and ventricular septal defect, have been reported to be associated with Waardenburg's syndrome [5,9].

The following problems were encountered in this patient:

Malnutrition. Because of total aganglionosis, intestinal activity is unpredictable. Parenteral nutrition was required for more than 20 months due to recurrent enterocolitis and poor oral intake. Conservative treatment failed to heal the skin ulcer. Arterial blood pressure dropped quickly, even with a low concentration of volatile anesthetics. Preoperative venous cannulation

was so difficult that a volatile agent was the only acceptable way to induce anesthesia, especially during infancy.

Convulsions and electrolyte imbalance. Convulsion and tetany occurred due to only moderate hyponatremia and hypocalcemia, respectively. No severe electrocardiographic change was noted. In addition to repeated operations on the intestine, enterocolitis made it difficult to keep serum electrolytes within the normal range. If a low seizure threshold is related to a neural crest cell disorder, it may be wise to avoid extreme hyperventilation or highly concentrated volatile anesthetics. From our experience, no particular anesthetic technique can be recommended. Changes in volatile anesthetics and muscle relaxants had no noticeable effect on this patient's condition.

Congenital deafness and blindness. Even the simplest communication was very difficult with this patient. Normal mental development is usually expected with appropriate visual stimuli, even in a deaf Waardenburg's syndrome patient. However, the association of blindness with deafness in this patient may have impeded her mental development. Early diagnosis of a sensory disturbance is important for proper psychological management. Adequate sedation is recommended perioperativly. It may be helpful to have the person who cares for the child present during both induction and the recovery period of anesthesia.

When anesthesiologists treat a child with Hirschsprung's disease and/or Waardenburg's syndrome other latent disturbances derived from disorders of the neural crest cells should be taken into consideration.

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