J Anesth (2012) 26:445–448
DOI 10.1007/s00540-012-1342-5

CLINICAL REPORT

Anesthetic management of three pediatric cases with Pena–Shokeir syndrome

Shogo Tsujikawa · Ryu Okutani · Kenji Tsujii · Yutaka Oda

Received: 22 March 2011 / Accepted: 23 January 2012 / Published online: 15 February 2012

Abstract Pena–Shokeir syndrome is a rare, early lethal disease. It is characterized by fetal growth restriction; craniofacial deformities, for example micrognathia and microcephaly; multiple ankyloses; and pulmonary hypoplasia. For patients with this syndrome, maintenance of airway and control of perioperative respiratory complications are important for anesthetic management. We report 3 pediatric cases of Pena–Shokeir syndrome undergoing tracheostomy and arthrolysis under general anesthesia using sevoflurane, nitrous oxide, fentanyl, and vecuronium bromide. Anesthetic procedures including mask ventilation, tracheal intubation, and extubation were successfully performed without complications during and after surgery. In patients with Pena–Shokeir syndrome, inhalational anesthetics can be safely used for induction and maintenance of anesthesia, although it is important to assume that difficult airway management might be encountered.

Keywords Pena–Shokeir syndrome · Cerebro-oculo-facio-skeletal syndrome · Anesthetic management · Pediatric · Airway

Introduction

Pena–Shokeir syndrome is an inherited disorder characterized by intrauterine growth restriction, craniofacial deformities, multiple ankyloses, and pulmonary hypoplasia [1–3]. Another phenotype referred to as cerebro-oculo-facio-skeletal syndrome [4], has similar features but without pulmonary hypoplasia, and has been regarded as Pena–Shokeir II syndrome [3, 5]. Although most patients with these syndromes are stillborn or die soon after birth, as a result of developmental delay, and respiratory and neurological problems [1–4], some require surgical procedures, for example tracheostomy and vocal cordotomy soon after birth to enable survival [6, 7]. For anesthesia in patients with this syndrome, maintenance of airway, adequate ventilation, and control of perioperative respiratory complications are of crucial importance; however, there are only a few reports describing anesthesia for these patients [7]. Herein, we report anesthetic management for 2 cases of Pena–Shokeir I syndrome and 1 case of Pena–Shokeir II syndrome.

S. Tsujikawa (✉) · R. Okutani · K. Tsujii · Y. Oda
Department of Anesthesiology, Osaka City General Hospital and Children's Hospital, 2-13-22 Miyakojima-hondori, Miyakojima-ku, Osaka 534-0021, Japan
e-mail: seashogo@shirt.ocn.ne.jp

R. Okutani
e-mail: ryu0909@kcat.zaq.ne.jp

Case presentation

Patients' characteristics, complications and surgical procedures are summarized in Table 1. No patients had remarkable family history or abnormal laboratory data before anesthesia. Examination on the day before surgery revealed good facial mask fitting despite the presence of micrognathia in all patients. There were no limitations in opening mouth or neck extension. For possible difficult airway, fiberscope, oral, nasal, and laryngeal mask airways were prepared before anesthesia for all patients.

Case 1

Continuous positive airway pressure ventilation via the nose was required after birth for respiratory distress owing

Table 1 Patients' characteristics

	Case 1	Case 2	Case 3
Age (months)/gender	7/male	27/male	34/male
Weight (kg)/height (cm)	3.6/63	11.8/80	11.0/84
Pena–Shokeir syndrome type	Type I	Type I	Type II
Gestation weeks at birth/birth weight (g)	37/2,123	38/2,489	39/2,894
Apgar score 1/5 min	6/8	4/9	Unknown
Antenatal diagnosis	Pulmonary hypoplasia Polyhydramnios	Pulmonary hypoplasia	Polyhydramnios
Complications	Micrognathia West syndrome[a] Cryptorchidism	Micrognathia Vertical talus	Micrognathia Hypertelorism Depressed nose tip Joint contractures
Surgery	Tracheostomy	Arthrolysis	Arthrolysis
Surgery/anesthesia time (min)	20/80	169/282	150/230

All patients were delivered via cesarean section with an antenatal diagnosis of intrauterine growth restriction

[a] West syndrome was characterized by spastic movement of the upper and lower extremities

to pulmonary hypoplasia and upper airway stenosis resulting from low pharyngeal muscle tone. A tracheotomy was scheduled. Peripheral oxygen saturation (SpO_2) was 100% and end-tidal carbon dioxide tension ($EtCO_2$) was 50 mmHg under spontaneous respiration with O_2 inhalation of 1 l/min before anesthesia. Without premedication, anesthesia was induced with sevoflurane and 66% nitrous oxide in oxygen, with monitoring of non-invasive blood pressure, 3-leads ECG, and pulse oximetry. Concentration of inhalational sevoflurane was initially 1%, gradually increased to 8%. Mask-to-face ventilation was easy and direct laryngoscopy revealed Cormack grade II. An endotracheal tube (internal diameter 3.5 mm) was inserted without difficulty after administration of fentanyl 10 μg and vecuronium 1 mg. Maintenance of anesthesia was achieved with intermittent IV fentanyl (1 μg/kg) and sevoflurane (1–2%). During surgery, circulatory conditions remained stable under mechanical ventilation with pressure control mode; $PaCO_2$ was maintained between 35 and 45 mmHg and SpO_2 was 100% under $FiO_2 = 0.4$. After surgery, neuromuscular blockade was reversed by atropine 0.02 mg/kg and neostigmine 0.05 mg/kg. The patient was transferred to the general ward under oxygen administration. SpO_2 was above 95% and $EtCO_2$ was between 50 and 60 mmHg under O_2 inhalation of 1 l/min. Two days after surgery, lung atelectasis was detected by chest X-ray; this was improved by endotracheal suctioning and postural changes. Ten days after surgery the patient was discharged without further complications.

Case 2

He had severe respiratory distress owing to pulmonary hypoplasia and required continuous positive airway pressure ventilation under tracheal intubation for the first week after birth. He was discharged from the hospital at the age of 6 months and did not require oxygen therapy at home and SpO_2 was above 95% on room air.

Arthrolysis for congenital vertical talus under general anesthesia was scheduled. Before anesthesia, chest X-ray was normal and SpO_2 was 98% on room air. Without premedication, anesthesia was induced and maintained as described in Case 1, tracheal intubation was easily performed with stylet after confirming Cormack grade II. During surgery, $EtCO_2$ was maintained between 35 and 45 mmHg, SpO_2 was 100% under $FiO_2 = 0.4$. The tracheal tube was removed postoperatively after reversal of vecuronium in the operating theater, and SpO_2 was above 95% on room air. He was transferred to the general ward under oxygen administration.

Case 3

He did not require ventilatory support after birth. However he was not able to walk because of multiple joint contractures. Although he had hypertelorism and depressed tip of the nose, there were no respiratory problems and chest X-ray was normal. Arthrolysis was scheduled for congenital left hand camptodactylia. Midazolam 8.5 mg was administered orally 30 min before induction of anesthesia for premedication, and SpO_2 was 98% on room air before anesthesia. Anesthesia was performed by the method described for Cases 1 and 2. There was no difficulty in mask ventilation or tracheal intubation. During anesthesia SpO_2 was 100% and $PaCO_2$ was 30–35 mmHg under $FiO_2 = 0.4$. During and after surgery, respiratory and circulatory conditions remained stable and the tracheal tube

was removed in the operating theater after reversal of vecuronium. Ten days after surgery, the patient was discharged from the hospital without any complications.

Discussion

Pena–Shokeir I syndrome was first reported as an early lethal disorder in 1974 [1]. It is a rare, autosomal recessive disorder and approximately one hundred cases have been reported [2]. Prediction of recurrence risk is imprecise, because of multi factorial etiology, and varies from 5 to 25% [3]. Clinical presentation is characterized by intrauterine growth restriction, craniofacial anomalies, limb anomalies, pulmonary hypoplasia, short umbilical cord, and polyhydramnios [2, 3]; fetal akinesia/hypokinesia have been regarded as the predominant cause of these deformities [8]. Another autosomal recessive disorder, initially reported by Lowry [9] and named cerebro-oculo-facio-skeletal syndrome by Pena and Shokeir [4], has findings similar to those of Pena–Shokeir I syndrome, and has been regarded as Pena–Shokeir II syndrome [3, 5]. It is distinguished from Pena–Shokeir I syndrome by the presence of microcephaly, microphthalmia, and/or cataracts, and the absence of pulmonary hypoplasia [4, 5].

As a result of delayed development, problems with anesthesia, for example difficulties in airway management and vulnerability to respiratory complications, may be encountered for patients with either Pena–Shokeir I or II syndrome [2, 3]. Repeated bronchospasm during anesthesia and abrupt onset of acute respiratory distress are also reported [7, 10]. As observed in case 1, seizures resulting from inherited cerebral dysgenesis may also be complicated [2]. In these 3 cases, all had micrognathia and 2 cases of Pena–Shokeir I syndrome had pulmonary hypoplasia and required ventilatory support after birth.

We performed mask-to-face ventilation using inhalational agents and confirmed adequate ventilation during induction; tracheal intubation was then performed without difficulties after administration of vecuronium. From the perspective of airway maintenance, our procedure was preferred to that using intravenous agents, for example propofol and thiopental, because depth of anesthesia is easily controlled, with the presence of spontaneous respiration, and the anesthetic effect can be promptly withdrawn in the event of impending airway obstruction. Previously, we have safely performed anesthesia in patients with arthrogryposis multiplex congenita, a symptom complex of non-progressive, multiple congenital joint contractures, muscle wasting which is often associated with Pena–Shokeir syndrome [11], by using inhalational agents [12]. Despite safe anesthetic procedure in our 3 cases, it should be remembered that affected patients may require further respiratory management after surgery because of intrauterine maldevelopment and pulmonary hypoplasia.

Besides Pena–Shokeir I and II syndromes, fetal akinesia/hypokinesia is a predominant cause of several diseases, because of Potter syndrome, trisomy 18, the lethal multiple pterygium syndrome, and Neu–Laxova syndrome, and patients with these diseases are characterized by features commonly observed in those with Pena–Shokeir I syndrome [3]. Although differential diagnoses of these diseases from Pena–Shokeir syndrome can be made on the basis of renal aplasia and oligohydramnios [2], karyotyping of amniotic fluid cells [13], remarkable fetal edema in the head and trunk resulting from obstruction of the jugular lymphatic channels [14], skin restriction and ichthyosis [15], and histological examination of muscle fibers [16], anesthetic management for patients affected with these diseases would be similar to that for Pena–Shokeir syndrome.

Pena–Shokeir I syndrome is usually lethal in utero or during the first few days of life, and only a few patients had been reported to have survived beyond 12 months [10]. Patients with Pena–Shokeir II syndrome, even differentiated by lack of pulmonary hypoplasia from Pena–Shokeir I syndrome, usually die within the first 3 years of life [4]. In sharp contrast, all of our cases are surviving longer than expected in those reports, and without ventilator support. This is probably attributable to the development of infection control and respiratory support shortly after birth. As far as we are aware, there are no reports describing repeated anesthetic management for patients with Pena–Shokeir syndrome. Multiple operations may be required for the plasty of treating craniofacial and skeletal deformities, as in patients with arthrogryposis multiplex congenita, and airway management including endotracheal intubation and tracheostomy might become more difficult with advancing age.

Onset of malignant hyperthermia has been reported both in patients with Pena–Shokeir syndrome [10] and with arthrogryposis multiplex congenita [17]. In our 3 cases we used inhalational anesthetics because there were no family histories of malignant hyperthermia, and diagnosis of arthrogryposis multiplex congenita was not made in any of the patients. Increase of body temperature was not detected during anesthesia, either. Detailed inquiry of family history concerning malignant hyperthermia is required before performing anesthesia in patients with Pena–Shokeir syndrome.

In conclusion, we provided anesthetic management for 3 patients with Pena–Shokeir syndrome. Ventilation and tracheal intubation were successfully performed using inhalational agents. It is important to assume that difficult airway management might be encountered.

References

1. Pena SD, Shokeir MH. Syndrome of camptodactyly, multiple ankyloses, facial anomalies, and pulmonary hypoplasia: a lethal condition. J Pediatr. 1974;85:373–5.
2. Hall JG. Pena–Shokeir phenotype (fetal akinesia deformation sequence) revisited. Birth Defects Res A Clin Mol Teratol. 2009;85:677–94.
3. Hall JG. Analysis of Pena Shokeir phenotype. Am J Med Genet. 1986;25:99–117.
4. Pena SD, Shokeir MH. Autosomal recessive cerebro-oculo-facio-skeletal (COFS) syndrome. Clin Genet. 1974;5:285–93.
5. Kho N, Czarnecki L, Kerrigan JF, Coons S. Pena–Shokier phenotype: case presentation and review. J Child Neurol. 2002;17:397–9.
6. Kutschera J, Friedrich G, Urlesberger B, Eber E, Mueller W. Endoscopic laser posterior cordectomy in a newborn with bilateral vocal fold paralysis and cerebro-oculo-facio-skeletal (Pena–Shokeir II) syndrome. Eur J Pediatr. 2004;163:120–1.
7. Nakamura A, Kawahito S, Katayama T, Kawano T, Nitta K, Inui D, Kitahata H, Oshita S. Bronchospasm during anesthesia in a patient with Pena–Shokeir syndrome. Masui. 2005;54:1146–8.
8. Moessinger AC. Fetal akinesia deformation sequence: an animal model. Pediatrics. 1983;72:857–63.
9. Lowry RB, MacLean R, McLean DM, Tischler B. Cataracts, microcephaly, kyphosis, and limited joint movement in two siblings: a new syndrome. J Pediatr. 1971;79:282–4.
10. Boesen PV, French CE. Acute respiratory distress in Pena–Shokeir syndrome. Ear Nose Throat J. 2004;83:772–3.
11. Mease AD, Yeatman GW, Pettett G, Merenstein GB. A syndrome of ankylosis, facial anomalies and pulmonary hypoplasia secondary to fetal neuromuscular dysfunction. Birth Defects Orig Artic Ser. 1976;12:193–200.
12. Oda Y, Yukioka H, Fujimori M. Anesthesia for arthrogryposis multiplex congenita—report of 12 cases. J Anesth. 1990;4:275–8.
13. Shenker L, Reed K, Anderson C, Hauck L, Spark R. Syndrome of camptodactyly, ankyloses, facial anomalies, and pulmonary hypoplasia (Pena–Shokeir syndrome): obstetric and ultrasound aspects. Am J Obstet Gynecol. 1985;152:303–7.
14. Moerman P, Fryns JP, Cornelis A, Bergmans G, Vandenberghe K, Lauweryns JM. Pathogenesis of the lethal multiple pterygium syndrome. Am J Med Genet. 1990;35:415–21.
15. Coto-Puckett WL, Gilbert-Barness E, Steelman CK, Stuart T, Robinson HB, Shehata BM. A spectrum of phenotypical expression OF Neu–Laxova syndrome: three case reports and a review of the literature. Fetal Pediatr Pathol. 2010;29:108–19.
16. Torii I, Morikawa S, Tanaka J, Takahashi J. An autopsy case of Pena–Shokeir syndrome: severe retardation of skeletal muscle development compared with neuronal abnormalities. Pediatr Pathol Mol Med. 2002;21:467–76.
17. Kunimoto K, Abe M, Ota M, Yogosawa T, Nishiguchi M. Cases of myotonic syndromes due to succinylcholine. Masui. 1968;17:885–9.