Anesthesia for Pediatric Patients with Prader-Willi Syndrome: Report of Two Cases

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Prader-Willi syndrome (PWS) is a sporadic disorder of chromosome abnormalities with an estimated prevalence of 1 in 15,000. It mainly affects the central nervous system, and often involves the hypothalamus. Both general and regional anesthesia for these patients is difficult mainly due to morbid obesity. Other common problems include hypotonia, disturbance in thermoregulation, arrhythmia, cor pulmonale, diabetes mellitus, behavior problems, and convulsions. We report on 2 pediatric patients with PWS receiving general anesthesia. The first patient experienced life-threatening episodes of severe hypoxemia in the postanesthesia care unit (PACU) as well as in the pediatric intensive care unit (PICU). Nasal continuous positive airway pressure (CPAP) was suggested by the pediatric pulmonary medicine specialist, and thereafter the patient's condition improved. The clinical course of the second patient was uneventful except for transient intermittent episodes of bronchospasms during emergence. In addition, we discuss differences between these 2 cases and our strategy for the prevention of perioperative complications for PWS patients in the future. *(Chang Gung Med J 2003;26:453-7)*

Key words: Prader-Willi syndrome, obesity, obstructive sleep apnea syndrome, polysomnogram, continuous positive airway pressure.

Prader-Willi syndrome (PWS) is a genetic disorder classically characterized by hypotonia, hypomentia, and hypogonadism that is associated with obesity.[1,2] It is described as a 2-stage disorder with an infantile hypotonic phase followed by a childhood obese phase.[3] Children with PWS in the infantile phase may have the following clinical features: failure to thrive, developmental delay, delayed speech, typical faces, fair hair, blue eyes, etc. When the children grow up into the childhood phase, they usually have a voracious appetite resulting in obesity. Other common clinical features in this phase include short stature, small hands and feet, scoliosis, easy bruising, skin picking or other self-abuse, caries, excessive daytime sleepiness, temper tantrums, and squinting. We present our anesthetic experience with 2 pediatric patients with genetically proven PWS by chromosomal examination in the childhood obese phase.[4]

CASE REPORTS

Case 1

A 5-year-old male PWS patient, with a body weight of 50 kg, who presented with obstructive sleep apnea (OSA) syndrome, was scheduled for a bilateral tonsillectomy and uvulopalatopharyngoplasty. He had been admitted to our hospital several times previously due to pneumonia and asthmatic attacks. General anesthesia was induced with 100

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mg propofol intravenously and sevoflurane via a facemask. Then an endotracheal tube was smoothly inserted without the help of a muscle relaxant.

Anesthesia was maintained with sevoflurane in oxygen only. Dexamethasone 10 mg was given intravenously about 1 hour before the end of the operation for prevention of laryngeal edema and asthmatic attack. The endotracheal tube was removed once the patient was fully awake. However, his O_2 saturation (SpO_2) decreased to 70%, and his respiratory rate increased to 70/min just a few minutes after he arrived in the postanesthesia care unit (PACU). When the patient was stimulated, he cried and his SpO_2 became > 80%. The breathing sound was coarse, and moist rales were noted. The patient was reintubated in the PACU after being given 200 mg sodium thiopental and 5 mg vecuronium intravenously. A follow-up portable chest X-ray showed increased bilateral infiltration. Then the patient was sent to the pediatric intensive care unit (PICU) for further care. He was extubated in the PICU 2 days later, but several episodes of severe hypoxemia (SpO_2 of 50%~70%) occurred when he was sleeping. After consultation with a pediatric pulmonary medicine specialist, a polysomnogram was performed, and nasal continuous positive airway pressure (CPAP) was suggested. The patient's condition gradually improved, and he was finally discharged 9 days later.

Case 2

A 4-year-old male PWS patient, with a body weight of 35 kg, manifested severe skin-picking behavior resulting in rectal bleeding and a prolapsed rectum. Emergent surgery was arranged to check the bleeding and perform injection sclerotherapy with hypertonic glucose water. This patient is mentally retarded: he attacked nurses in the emergency unit and the ward when they attempted to set up an intravenous line for him; thus no venepuncture could be performed before he was sent to the operating room.

General anesthesia was induced with sevoflurane via a facemask. Then an intravenous line was set up after the patient was sedated, with 150 mg sodium thiopental given intravenously to deepen the anesthetic level and 50 mg succinylcholine given intravenously to facilitate endotracheal intubation. The endotracheal tube was smoothly inserted, and neither stridor nor wheezing was audible after intubation. Anesthesia was maintained with sevoflurane, and the operation was uneventful. However, intermittent episodes of bronchospasms were noted with severe CO_2 retention detected by capnography during emergence from the anesthesia. These bronchospasms were relieved by intravenous Xylocaine (1.5 mg/kg) and fenoterol (Berotec) inhalation. The endotracheal tube was successfully removed 30 min after cessation of the volatile anesthetic. The patient was then sent to the PACU for close observation. He was discharged to ward 1 hour later with no adverse respiratory events. His subsequent hospital course was uneventful.

DISCUSSION

PWS was first described by Prader, Labhart, and Willi in 1956. It is now known that PWS is caused by abnormalities of the imprinted region of proximal 15q and results from the absence of normally active paternal genes in this region. This absence results from a paternal interstitial deletion, a maternal uniparental disomy, or a mutation or other abnormality in the imprinting process.[5] The classic concept of PWS is of a biphasic disorder with an infantile hypotonic phase followed by a childhood obese phase; both of our patients were in the childhood obese phase.

According to limited information from the previous literature concerning anesthesia for patients with PWS, both general and regional anesthesia are challenging. Using general anesthesia may result in difficult airway management (mask ventilation and/or endotracheal intubation). Nevertheless, landmarks for regional anesthesia may be obscured due to morbid obesity. Other common problems include difficult venepuncture, food-seeking behavior, disturbance in thermoregulation, diabetes mellitus, arrhythmia, and cor pulmonale.

There are few case reports about anesthesia for patients with PWS. Mackenzie reported 2 cases: a 2-year-old boy receiving general tube anesthesia and an 18-year-old patient receiving general mask anesthesia; both courses were uneventful.[6] Dearlove et al. reviewed a case series and pointed out that children with PWS whose body weights were normal posed no problems for anesthesia.[7] On the other hand, patients with a body weight larger than the 97th percentile would probably have problems with

difficult venepuncture and obstructive sleep apnea. Both our patients had a body weight far above the 97th percentile, thus complicating the anesthetic management. Kawahito et al. reported on a 9-year-old boy who weighed 17 kg, was 111 cm tall, and was associated with delayed psychomotor development who received general anesthesia.[8] The patient had no upper airway infection before anesthesia, but remarkable stridor was noted immediately after endotracheal tube intubation, and hypercapnia was shown by capnography. Under the impression of bronchospasms, intravenous aminophylline and steroids were given, and the inhalation agent was changed from sevoflurane to halothane, which effectively relieved the spasms. This management is controversial considering that the co-administration of aminophylline and halothane might induce arrhythmia,[9] especially premature ventricular contractions.

The second patient in our report experienced no episode of bronchospasms after endotracheal intubation or throughout the operation. However, intermittent stridor was detected by auscultation during emergence from the anesthesia, and hypercapnia was detected by capnography. Prompt diagnosis of bronchospasms was made, and thus intravenous Xylocaine (1.5 mg/kg)[10] and fenoterol inhalation (β2-selective agonist)[10,11] were given with a satisfactory response. We hesitated to administer steroids due to the accompanying systemic side effects and the fact that the patient had no history of bronchial asthma.

Finally we would like to briefly discuss the 2 cases in this report. Both patients had a body weight far above the 97th percentile, and hence we expected that a difficult airway and difficult venepuncture might be encountered. We chose general anesthesia because we believed that this was the safest approach in securing a patent airway for these patients during the operation. The induction technique was similar in both cases, neither narcotics nor intermediate or long-acting neuromuscular agents were given, and endotracheal intubation was performed smoothly in both cases. However, different outcomes occurred in the PACU, although both patients were extubated after fully awakening (eyes opening and crying).

We believe that the main difference between the 2 cases was the severity of the obstructive sleep apnea (OSA). The first patient was a victim of PWS complicated with OSA and also had had previous episodes of pneumonia and asthmatic attacks, and hence was at a higher risk for developing postoperative respiratory complications. Moreover, obstructive sleep apnea events on the first postoperative night might be more severe than preoperatively due to mechanical swelling from the surgery, disruption of laryngeal receptors from surgical manipulation, or effects of the anesthesia.[12] Actually this patient experienced several episodes of severe hypoxemia after extubation when he was sleeping in the PICU postoperatively; at that time no residual anesthetics should be considered as the cause of respiratory inhibition. Therefore we suggest that postoperative intensive care is necessary for PWS patients with severe OSA.

In addition, the preoperative evaluation of PWS patients with OSA must be individualized.[12] If these patients have associated cardiomegaly, cor pulmonale, and/or arrhythmia, they are at a higher risk for intraoperative shunting, desaturation, and heart failure. A recent upper respiratory infection (URI) predisposes children to intraoperative desaturation and wheezing; thus elective surgery should be postponed until complete recovery from a URI.[13] Moreover, a preoperative polysomnogram should be performed for PWS patients with severe OSA as a baseline so that comparison with the postoperative polysomnogram can be made. Appropriate medical therapy may also optimize the condition of patients, e.g. administration of steroids to asthmatics, preoperative oxygen, and/or CPAP.

The pathogenesis of sleep apnea syndrome in PWS patients is multifactorial in origin, including peripheral and central mechanisms.[14,15] The first patient in our report was diagnosed as a victim of OSA, and nasal CPAP was suggested after performing the polysomnogram. The improvement in the patient's condition after CPAP use also suggests that sleep-related disturbances in this case were mainly caused by the upper airway obstruction that was worsened by his morbid obesity.[16]

In summary, preoperative evaluation of patients with PWS should be individualized, and special attention must be paid to those patients complicated with severe OSA. Postoperative intensive care is strongly recommended for PWS patients with severe OSA to prevent sleep-related respiratory complications, even when neither narcotics nor intermediate or long-acting muscle relaxants are given.

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Prader-Willi 症候群之兒科患者的麻醉：二例報告

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Prader-Willi症候群 (PWS) 是一種罕見之遺傳疾病，此症候群爲染色體異常所引起，估計流行率約爲一萬五千分之一。PWS主要影響中樞神經系統，尤其是下視丘部位。由於此症候群常導致病態性肥胖的關係，無論採用全身或區域麻醉都相當困難。除此之外，尚有肌肉無力，體溫調節障礙，心律不整，肺心症，糖尿病，異常行爲問題，痙攣等。我們報告兩例患有PWS的兒科患者的麻醉，兩者均採用全身麻醉。第一例患者於手術後，分別在麻醉恢復室及兒科加護病房內，歷經數次相當危險的嚴重血氧過低狀態，經會診小兒胸腔科醫師，建議採用經鼻管作正壓換氣後，病人狀況才逐漸改善。第二例患者的手術與麻醉過程相當平順，只有在麻醉慢慢消退時，發生短暫的氣管痙攣現象。我們希望透過檢討以上兩病例的經驗，將來在處理這一類病患時，能夠避免或減少術後呼吸併發症的發生。(長庚醫誌 2003;26:453-7)

關鍵字：Prader-Willi症候群，肥胖，阻塞性睡眠窒息症候群，多項睡眠生理檢查，連續性正壓換氣。

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