J Anesth (2006) 20:26–29
DOI 10.1007/s00540-005-0353-x

Journal of
Anesthesia

Clinical reports

Perioperative respiratory complications caused by cystic lung malformation in Proteus syndrome

Masaki Nakane, Mikako Sato, Hisashi Hattori, Yukio Matsumoto, Manabu Otsuki, and Masahiro Murakawa

Department of Anesthesiology, Fukushima Medical University School of Medicine, 1 Hikarigaoka, Fukushima 960-1295, Japan

Abstract
A 7-year-old girl with Proteus syndrome, complicated with severe kyphoscoliosis and cystic lung malformation, developed respiratory complications during and after posterior spinal fusion under general anesthesia. We speculated that low oxygenation while in the prone position contributed to ventilation perfusion mismatch owing to the cystic lung malformation that existed predominantly in the right lung, and that postoperative respiratory failure was caused by initially increased bronchial mucous secretions and secondary persistent bacterial pneumonia. Cystic lung malformation rather than reduced respiratory function, although both can be a cause of mucous clearance impairment, should be considered as one of the predictive factors for perioperative respiratory failure in Proteus syndrome.

Key words Proteus syndrome · Respiratory failure · Kyphoscoliosis · Cystic lung malformation · Intubation difficulty

Introduction

Proteus syndrome, named after the ancient Greek demigod in 1983, is a rare condition characterized by overgrowth of multiple tissues, connective tissue nevi, epidermal nevi, and hyperostosis [1]. At present, approximately 70 cases of the syndrome have been reported. It has been suggested that the cause of this syndrome is a mosaic somatic mutation leading to abnormal growth of the affected areas. Only one report mentioning perioperative management of the syndrome has focused on airway problems [2] such as intubation difficulty caused by overgrowth and deformity of the cervical vertebrae, fixed torticollis, anomalous teeth, and enlarged epiglottis. Pulmonary cystic malformation occurs in approximately 13% of patients with this syndrome, regardless of their scoliosis status [3]. In this report, we present a Proteus syndrome patient who underwent posterior spinal fusion for severe kyphoscoliosis under general anesthesia and developed respiratory failure during and after the operation, possibly related to cystic lung malformation.

Address correspondence to: M. Nakane
Received: September 17, 2004 / Accepted: August 2, 2005

Case report

The patient, a 7-year-old girl, appeared to be normal at birth, but gradually developed the polymorphous characteristics of Proteus syndrome, including hemihypertrophy, scoliosis, partial gigantism of her hand and foot, subcutaneous tumors, exostosis, epidermal nevi, and thickened skin on the palm. She underwent three surgical treatments under general anesthesia for epidermal nevus and deformities of the extremities. Tracheal intubation during the third surgery, at 3 years of age, was reported to be difficult. Right scoliosis and elongation of the neck had gradually developed since then, and posterior spinal fusion with rod instrumentation and thoracoplasty were scheduled at 7 years of age. The patient's height was 124 cm and her weight was 21 kg. Physical examination revealed severe spinal curvature, a 75-mm rib hump, and a marked deformity of the thoracic cage. Her neck was elongated because of the overgrowth of the cervical vertebrae, and its flexion and leftward rotation were limited. A chest X-ray showed right kyphoscoliosis from T6 to L3 and a Cobb's angle of 115° (Fig. 1). The results of pulmonary function testing indicated a pattern of severe restrictive defects, as evidenced by a vital capacity (VC) of 0.661 (40% of predicted VC) and a forced expiratory volume at 1 s ($FEV_{1.0}$) of 0.571 (87% of forced VC). Maximum expiratory flow-volume loops, however, suggested a pattern of lower airway obstruction, to some degree. Arterial blood gas (ABG) data showed a Pa_{O_2} of 73 mmHg (93% Sa_{O_2}), a Pa_{CO_2} of 40 mmHg, and a pH of 7.39 on room air

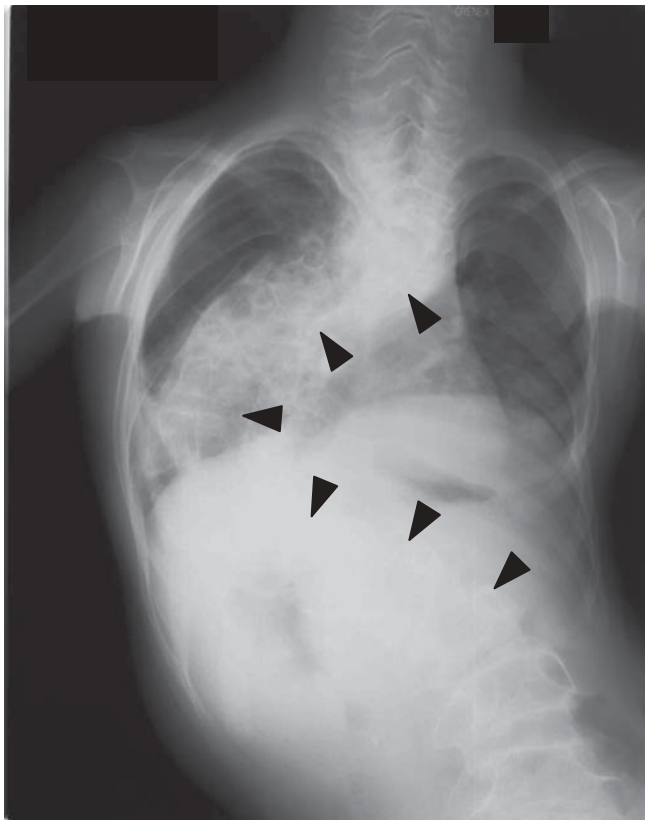
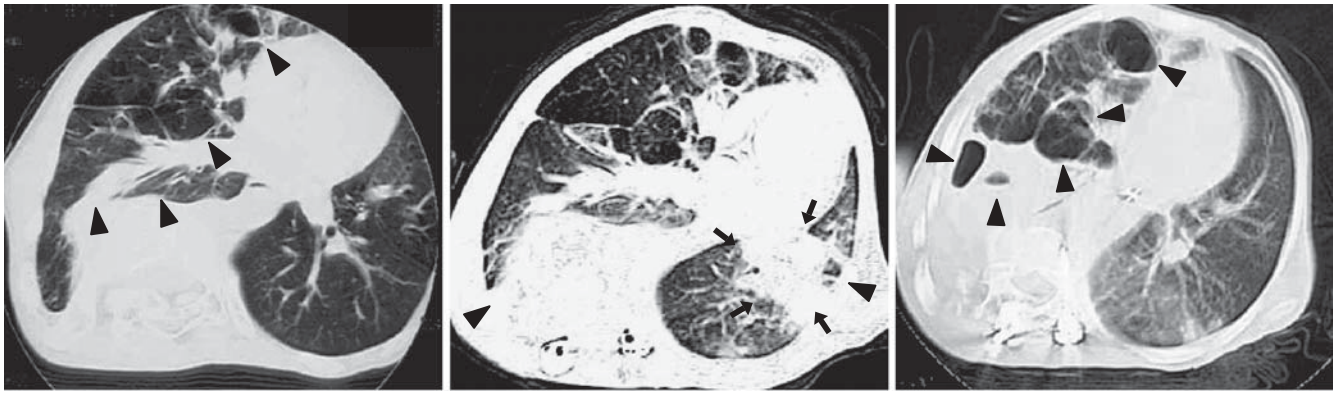


Fig. 1. Posteroanterior projection of chest X-ray shows severe curvature of the spine (*arrowheads*) and right kyphoscoliosis from T6 to L3 (Cobb's angle of 115°). Severe deformity of the thoracic cavity is also shown. However, the patient had no deviation or stenosis of the trachea. Overinflation could be pointed out in the left lung but is undetectable in the right lung because of overlap with the curved spine

in the supine position (with a spontaneous respiratory rate of 24 breaths/min). Although she had some limitations of daily activities related to her leg deformities, she had never complained of dyspnea. Other results of blood and urine testing were within the normal range, and her electrocardiogram was normal. She had no neurologic abnormalities and no mental retardation. Severe deformity of the thoracic cavity was also noted on the CT scan (Fig. 2a). Moreover, we were able to confirm cystic lung alterations such as multiple bulla formation and collapsed lesions, possibly related to previous lung inflammation (Fig. 2a).

A mixture of 5% sevoflurane and 67% nitrous oxide was used for induction of general anesthesia through a mask. Observation of the larynx by direct laryngoscopy was unsuccessful because of her neck elongation, as had been anticipated preoperatively, despite complete muscle relaxation induced by vecuronium administered after confirming mask ventilation was not difficult. A 5.0-mm-internal-diameter reinforced endotracheal tube was smoothly inserted orally into her trachea using bronchofiberscopic technique and fixed at the 20-cm mark over the right side of her lips after adequate positioning of the tube was confirmed by bronchofiberscope. Anesthesia was maintained with continuous intravenous (IV) administration of propofol, intermittent IV administration of fentanyl, and inhalation of nitrous oxide in oxygen. The $S_{P_{O_2}}$ was 98% after intubation; ventilation consisted of $F_{I_{O_2}}$ of 0.33, tidal volume of $10\,ml \cdot kg^{-1}$, respiratory rate of 10 breaths/min, and positive end-expiratory pressure (PEEP) of $3\,cmH_2O$. However, $S_{P_{O_2}}$ decreased to 90% immediately after the



a,b c

Fig. 2. a Preoperative chest computed tomography (CT) scan shows cystic lung alteration (*arrowhead*) including emphysematous changes with multiple bulla formation and collapsed lesions (possibly caused by previous pleural inflammation), predominantly in the right lung. In the prone position, the right lung is on the lower side of the thoracic cavity because of its severe deformity caused by right scoliosis. **b** Postoperative chest CT scan (postoperative day 2) shows bilateral bronchial obstruction caused by massive mucous secretions, multiple partial atelectasis (*arrows*), and consolidation at subpleural regions of both lungs (*arrowheads*). **c** Chest CT scan 2 months after surgery shows formation of multiple cysts (*arrowheads*), some with fluid collection, in the right lung. Compared to the right lung, the left lung seemed to have remained relatively normal

patient was rotated from the supine to the prone position. Respiratory sound was bilaterally normal, and pulmonary resistance did not change. Bronchofiberscopy found no airway problems, adequate tracheal tube positioning, and no sputa within the visible limits of the bronchus. The $S_{P_{O_2}}$ was still 94%–95%, and the $Pa_{O_2}/F_{I_{O_2}}$ (P/F) ratio was 144, after 1 h. The $S_{P_{O_2}}$ recovered gradually to 99%–100% after 5 h, and ABG data revealed a P/F ratio of 342. Intraoperative blood loss was more than 670 ml, and 1 unit of homologous concentrated red blood cells was transfused. Duration of anesthesia was 552 min.

Following the operation, mechanical ventilation using synchronized intermittent mandatory ventilation (SIMV) + pressure support (PS) mode with a Puritan Bennett 7200 was started under sedation in the ICU. The initial ventilation settings were $F_{I_{O_2}}$ of 0.6, tidal volume of 10 ml·kg^{-1}, SIMV respiratory rate of 10 breaths/min, PS of 5 cmH_2O, and PEEP of 5 cmH_2O. ABG data after restoring the body position to supine revealed a P/F ratio of 460. The chest X-ray taken immediately after the operation showed no abnormal changes compared with preoperative films, and the tracheal tube was located in an adequate position. Although extubation was attempted on the next morning under continuous positive airway pressure (CPAP) with PEEP of 3 cmH_2O and $F_{I_{O_2}}$ of 0.4, bronchial obstruction as a result of increased massive secretions required reintubation within several hours.

Sputum cultures during the first 3 days after surgery did not detect any bacteria. Bronchial obstruction and multiple partial atelectasis of the bilateral lungs were detected in the CT scan films on the second postoperative day (Fig. 2b). The extraction of an inadequately positioned screw, which had been found at the time of computed tomography (CT), was performed under general anesthesia with continuous propofol and IV morphine. Hypoxia again occurred after changing her position from supine to prone, despite using no nitrous oxide, but gradually decreased, as experienced during the preceding surgery. A similar incidence occurred again during the third operation for wound infection. Following this operation, a high fever caused by bacterial pneumonia persisted for several days, and the patient required ventilatory support for 1 month. She eventually recovered and was transferred to a general ward. A CT scan taken after 2 months showed formation of multiple cysts in the right lung with some fluid (Fig. 2c).

Discussion

The exact cause of cystic lung malformation in Proteus syndrome is unknown. It has been speculated that abnormal muscular, elastic, or fibrous connective tissues of small airways may be related to the development of pulmonary emphysematous changes [3]. Respiratory failure by progressive cystic lung alteration can be a cause of death even in young patients. Because approximately 13% of patients with Proteus syndrome have cystic lung alterations, evaluation of the lung, especially screening for pulmonary insufficiency, as described by Biesecker et al. [4] is of tremendous importance. Only one case has been reported with cystic lung malformation, and it had no associated scoliosis or previous history of pleuritis [3]. Although our patient had no such previous history, the chest CT scan diagnosed pulmonary emphysematous changes with multiple bulla formation and overinflation of the lung, which is called cystic lung malformation, and collapsed, scar like lesions of the pleura. The pulmonary function test showed a severely restrictive pattern to which scoliosis found in more than 50% of patients with Proteus syndrome [5] could have contributed. Some reports of surgical indications for scoliosis suggested that a VC of more than 15 ml/kg is necessary for posterior spine surgery to be safely performed. However, some investigators were unable to predict postoperative respiratory complications by means of preoperative VC [6].

Although our patient had emphysematous changes in the lung, this had not been identified as an obstructive pattern in the respiratory function test because of the severely restrictive case. Maximum expiratory flow-volume loops, however, could show a lower-airway obstructive pattern to some degree. Body plethysmography would be useful for evaluation of the preoperative respiratory condition, if available. Because the cystic lung malformation itself further exaggerated the respiratory condition in our case, the CT scan findings might provide a predictive factor for perioperative respiratory failure. In addition, the relatively long operation time and use of mechanical ventilation would have contributed to the respiratory complications.

Although it has been reported that patients in the prone position were better oxygenated than those in the supine position, during general anesthesia [7], our patient experienced low oxygenation in the prone position on three occasions under general anesthesia. The chest CT in our patient showed cystic and collapsed lesions, predominantly in the right lung. In the prone position, her right lung was on the lower side of the thoracic cavity because of the clockwise rotation of her severe scoliosis (see Fig. 2a). The low oxygenation during the prone position, therefore, could have been caused by ventilation perfusion mismatch, particularly in the right lung. This hypothesis is supported by the observed recovery of oxygenation shortly after returning to the supine position. The only thing we regret was the use of nitrous oxide during the first surgery because no other

anesthesia machine that could use an air–oxygen mixture was available at that time. Although one might point to nitrous oxide as a cause of the intraoperative respiratory failure in our case, we found a similar incidence of the low oxygenation in prone positioning during the second and the third operations despite not using this gas, which appears to indicate the trivial contribution of nitrous oxide to the phenomenon observed.

The patient developed multiple partial atelectasis and gravitational consolidation of both lungs following massive bronchial secretions on the second postoperative day (see Fig. 2b). The initial increase in bronchial mucous secretions and persistent bacterial pneumonia resulted in prolonged respiratory insufficiency. The fact that mucous clearance was impaired after the operation may suggest not only the influence of reduced respiratory function but also the existence of small airway abnormalities, which are considered to be a cause of cystic lung alteration in Proteus syndrome [3]. Therefore, cystic lung malformation should be considered as one of the predictive factors for perioperative respiratory failure in Proteus syndrome.

References

1. Wiedemann HR, Burgio GR, Aldenhoff P, Kunze J, Kaufmann HJ, Schirg E (1983) The Proteus syndrome. Eur J Pediatr 140:5–12
2. Pennant JH, Harris MF (1991) Anesthesia for Proteus syndrome. Anaesthesia 46:126–128
3. Samlaska CP, Levin SW, James WD, James WD, Benson PM, Walker JC, Perlik PC (1989) Proteus syndrome. Arch Dermatol 125:1109–1114
4. Biesecker LG, Happle R, Mulliken JB, Weksberg R, Graham JM, Viljoen DL, Cohen MM (1999) Proteus syndrome. Diagnostic criteria, differential diagnosis, and patient evaluation. Am J Med Genet 84:389–395
5. Newman B, Urbach AH, Orenstein D, Dickman PS (1994) Proteus syndrome: emphasis on the pulmonary manifestations. Pediatr Radiol 24:189–193
6. Kinear WJM, Kinear GC, Watson L, Webb JK, Johnston IDA (1992) Pulmonary function after spinal surgery for idiopathic scoliosis. Spine 17:708–713
7. Pelosi P, Croci M, Calappi E, Cerisara M, Mulazzi D, Vicardi P, Gattinoni L (1995) The prone positioning during general anesthesia minimally affects respiratory mechanics while improving functional residual capacity and increasing oxygen tension. Anesth Analg 80:955–960