

Case Report

General anesthesia in fibrodysplasia ossificans progressive: a case report and clinical review

Jin-Xing Liu, Rong Hu, Yu Sun, Hong Jiang

Department of Anesthesiology, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University, Shanghai, China

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Abstract: Fibrodysplasia ossificans progressiva (FOP) is a rare and devastating genetic disorder of connective tissue characterized by heterotopic bone formation and progressive musculoskeletal disability. Soft-tissue trauma may exacerbate this condition and lead to further ossification. We described the anesthetic and perioperative management of a 23-year-old male with FOP scheduled for dental extraction requiring general anesthesia. Preoperative examination revealed multisystem involvement including cranial and cervical ankylosis and severe restrictive lung disease. Nasal fiber-optic endotracheal intubation was chosen in our patient. Anesthesia was maintained with total intravenous anesthesia and ventilation was controlled throughout the surgery. Endotracheal tube was remained for mechanical ventilation until the second postoperative day and aggressive respiratory physiotherapy was performed after extubation. Additionally, extreme caution was taken to a femoral vascular access and an arterial catheter. Positioning of the patient was meticulous and air warming blanket was used to minimize soft tissue trauma. No significant documented intraoperative and postoperative adverse events appeared attributable to the anesthesia.

Keywords: Fibrodysplasia ossificans progressiva, anesthesia

Introduction

Fibrodysplasia ossificans progressiva (FOP) is considered the most catastrophic congenital disease of progressive heterotopic ossification (HO) in humans. It is extremely rare with a worldwide prevalence of approximately one in two million [1]. HO usually appears in childhood after spontaneity or trauma, presenting as swellings in soft tissues, which then progressively transform into ectopic bone leading to serious limitations of joints movement. Eventually complete ankylosis of the widespread joints and muscles turn the patient into a 'stone man' [2]. Death often results from cardiopulmonary failure secondary to involvement of the thoracic muscles [3].

Anesthetic management for patients with FOP is challenging facing a lot of complex situations, such as cervical spine fusion, thoracic insufficiency, and sensitivity to any trauma which would further exacerbate ectopic bone formation.

We described a case with FOP who underwent dental and oral-maxillofacial treatment requir-

ing general anesthesia and reviewed the previous case reports and anesthetic managements.

Case report

A 23-year-old male (60 kg, 170 cm) diagnosed with FOP complained of oral pain resulting from multiple carious two months ago and was scheduled for dental extraction. Firstly, the patient presented tender swellings in his face. At the age of 4, further similar swellings appeared on his neck and shoulder. At age of 10, he had fusion of thoracolumbar spine with upper thoracic scoliosis, and severely limited temporomandibular joint (TMJ) movements.

Physical examination revealed complete ankylosis of the TMJ, and the maximal mouth opening was 1 mm. His head remained in a fixed neutral position because of rigid neck and shoulders. An osseous bridge with the length of 6 cm was palpable in the muscles of the posterior neck, connecting the occipital bone and back (**Figure 1**). The patient had thoracic and lumbar scoliosis. His right arm was ankylosed in a flexed position and the left arm in an extend-



Figure 1. Lateral neck CT 3-dimensional generated image showing ossification of the adjacent neck muscles formed an osseous bridge.

ed position. His both lower extremities had minimal motion. All biochemical and hematological investigations were within normal limits. Electrocardiography was unremarkable except a sinus tachycardia and right axis deviation. Echocardiography revealed mild mitral valve regurgitation. Pulmonary function showed a serious restrictive lung disease with a forced vital capacity (FVC) of 1.6 L, a forced expiratory volume in one second (FEV1) of 1.3 L, and a FEV1/FVC ratio of 81.25%.

On the day of surgery, the patient was taken to the operating room and a 20-gauge peripheral intravenous (IV) line was established. The operating table was adjusted to conform to his position and the joints were padded to avoid pressure sores. Routine monitoring devices (pulse oximeter, electrocardiogram and noninvasive blood pressure cuff) were initiated. Because the jaw, neck and shoulders were locked in position, any airway-opening maneuvers were impossible. We therefore decided to proceed with a nasal fiberoptic intubation under light sedation with tracheotomy tray standby. Glycopyrrolate was given IV to reduce oral secretions. Oxygen was given at 5 L/min via facemask and the patient was sedated with midazolam 1 mg IV and fentanyl 0.15 mg IV. Both nostrils were administered with neo-syn-

ephrine and 4% viscous lidocaine. Five minutes later, a fiberoptic scope was inserted through the right naris slowly and 4% lidocaine was delivered to anesthetize the nasopharyngeal and oropharyngeal area by spray-as-you-go method through the fiberoptic scope suction port. On a good view of the vocal cords, 3.0 ml of 4% lidocaine was applied. A lubricated 6.5 mm endotracheal tube (ETT) was then advanced gently into the trachea. After confirmation of end-tidal carbon dioxide (ETCO₂), anesthesia was induced with 100 mg propofol and 50 mg rocuronium. Mechanical ventilation via a volume-controlled mode was adjusted to maintain ETCO₂ and inspiratory pressures in normal ranges. A left radial arterial catheter and a femoral catheter were placed, taking particular care to avoid

tissue trauma. In addition, the air warming blanket provided a constant temperature of 37°C with the rectal temperature monitored. Anesthesia was maintained with propofol and remifentanyl infusions. Rocuronium was used for muscle relaxation (**Figure 2**).

The operation lasted eight hours, which consisted of bilateral osteotomies to gain access to the oral cavity and extraction of involved teeth. The hemodynamics, body temperature and arterial blood gas analysis remained within normal limits throughout the procedure. The estimated blood loss was 1000 ml. Two units of packed red blood cells (PRBC), 1000 ml colloidal solution and 2000 ml of Ringer's lactate were given. Total urine volume was 2100 ml.

After the surgical procedure, the patient was transferred to ICU and remained on mechanical ventilation with sedation. On the second postoperative day, nasotracheal tube was withdrawn when the patient was fully awake and adequately ventilated. He was discharged from hospital one week later and his mouth opening was 2 cm. One year after extraction, we learned that his postoperative healing of the extraction tooth was good, and no progression of symptoms in other sites associated with anesthesia was observed.



Figure 2. Intraoperative patient position with careful padding and nasal intubation performed for anesthesia.

Discussion

The multisystem abnormalities put anesthesia of patients with FOP in a quite challenging situation, in which intubation, positioning, vascular access and regional anesthesia may be technically difficult to perform. Additionally, minor tissue trauma during anesthesia manipulations may become precipitating factors [1, 4]. Inadequate perioperative management can exacerbate the disease or even cause death [5]. We conducted a Medline search for 'Fibrodysplasia ossificans progressiva and anesthesia' and found a total of 9 specifically described case reports with general anesthesia from English publications (**Table 1**) [2, 4-11]. One patient underwent two surgical procedures within a 10-year period to relieve his oral pain [5].

Preoperative evaluation of the consequences of ossification is crucial to make the anesthetic plan and foresee possible complications. The craniofacial and cervical status need to be investigated since the degree of difficulty of airway management corresponds to the degree of limitation caused by HO [12]. Atlanto-axial subluxation had been reported [4] and a potential risk of spinal cord damage existed. Although

our patient had no evidence of overt cervical spine instability, ossification of the adjacent neck muscles formed an osseous bridge. Meticulous care should be taken during airway and neck manipulations. Kyphoscoliosis and fixation of the chest wall made the patient suffer from severe restrictive pulmonary disease, which leads to potential risks of high airway pressure during mechanical ventilation [7] and postoperative pulmonary complications [13]. Right ventricular dysfunction had been reported in older patients with longer disease duration [14] and echocardiography was useful to assess cardiac function. Ossification of the cardiac connective tissue may cause conduction defects [4], which can be detected as right bundle branch block, ST segment changes, left axis deviation and supraventricular tachycardia [15]. The movement range of other joints was noted in order to optimize patient position during surgery.

General anesthesia was chosen, although it was dangerous for our patient. Shipton et al [2] used ketamine without intubation for a 10-minute procedure. We considered it was safer to secure the airway with a tracheal tube during dental extractions as the other two authors [5,

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Table 1. Summary of nine previous case reports with general anesthesia

Authors (Year)	Surgery	Patient's age (sex)	Induction agents	Intubation route/technique	Maintenance agents	Complications
Shipton et al (1985) [2]	Eye surgery	18 YO (M)	Ketamine, droperidol, pethidine	Unintubated	Ketamine	Uneventful
Lininger et al (1989) [6]	Gynecological surgery	32 YO (F)	Ketamine, midazolam, fentanyl	Nasal/blind	Vecuroium, isoflurane	Uneventful
Stark et al (1990) [7]	Gynecological surgery	37 YO (F)	Thiopental sodium, atracurium	Oral/direct vision	Fentanyl, isoflurane, morphine sulfate, nitrous oxide	Uneventful
Newton et al (1990) [4]	Oral-maxillofacial surgery	14 YO (M)	Droperidol, fentanyl, midazolam	Nasal/FOB	Enflurane, nitrous oxide	Uneventful
Singh et al (2003) [8]	Gynecological surgery	21 YO (F)	Diazepam, propofol	Oral/FOB	Sevoflurane, fentanyl	Uneventful
Vashisht et al (2006) [9]	Oral-maxillofacial surgery	12 YO (F)	Sevoflurane	Nasal/FOB	Sevoflurane	Uneventful
Tumolo et al (2006) [10]	Brain surgery	18 MO (M)	Fentanyl, midazolam, propofol	Nasal/FOB	Sevoflurane, remifentanyl, rocuronium	Uneventful
Wadenya et al (2010) [5]	Oral-maxillofacial surgery	20 YO (M)	Not reported	Nasal/FOB	Not reported	Emergency tracheotomy during extubation
	Dental extraction	30 YO	Midazolam, fentanyl, propofol	Nasal/FOB	Desflurane	Uneventful
Gorji et al (2011) [11]	Orthopedic spine procedures	39 YO (F)	Dexmedetomidine, midazolam	Nasal/FOB	Propofol, fentanyl	Tracheostomy for respiratory support

YO: years old; MO: months old; F: female; M: male; FOB: fiberoptic bronchoscope.

9]. Overstretching the jaw for intubation may cause additional trauma to the TMJ [16, 17]. Even if mouth opening was normal, oral intubation by direct laryngoscopy was not chosen by Singh et al [8] and Tumolo et al [10]. Most patients [4, 5, 9-11] presenting with fusion of the cervical spine, limited mouth opening or ankylosis of the TMJ received fiberoptic nasal intubation. Although preoperative tracheotomy should be avoided in case of possible ossification at the site of incision [6], it should always be available as a backup measure. One unsuccessful fiberoptic intubation was reported and blind intubation with a smaller tube was used successfully [6].

Awake or light-sedated fiberoptic intubations for the patients with FOP were proposed [1, 16]. In the series, only one case utilized muscle relaxants after feasible ventilation was proved [7]. Vashisht et al [9] chose inhalational induction to preserve child's spontaneous respiration in order to tolerate the procedure. However, most adult patients received intravenous induction agents [4-6, 8, 10]. The use of dexmedetomidine for sedation [11] was reported in a newer publication, but it was not favorable for our patient because of his sinus bradycardia. We gave smaller dose analgesia and sedation in order to secure the airway in a more controlled situation. Meanwhile, a significant amount of time was spent on anaesthetizing the airway carefully. Airway nerve blocks were intentionally avoided and spray local anesthetics were preferred instead [8].

Lininger et al [6] used vecuronium to maintain adequate muscle relaxation without any adverse reaction. Stark et al [7] had similar results with atracurium. He considered HO involves primarily the connective tissue of muscles instead of the muscle fibers themselves and the ultimate state of disuse atrophy contraindicating the use of succinylcholine. In our case, short-acting drugs including propofol/remifentanyl/rocuronium without inhalational agent were used for the operation. We selected total intravenous anesthesia (TIVA) concerning the association of some skeletal muscle diseases with the occurrence of malignant hyperthermia (MH) [18]. Although inhaled agents have been used safely in some patients [4-10], we still take precautions for MH. Temperature monitoring was used throughout the procedure and rectal temperature signals were in the nor-

mal range. Excessive blood loss was also encountered as another case [11]. Gross ossification of the operation site and the surrounding tissues were considered to hold responsible. No significant adverse clinical events occurred after blood transfusions.

We kept the tracheal tube until the next day because of the following considerations: 1) possible surgery-related tissue swelling or bleeding progression, 2) respiratory support to ameliorate oxygenation, increase functional residual capacity, and improve respiratory performance [11]. Wadenya et al reported the patient experienced an immediate life-threatening airway obstruction during the extubation process, requiring an emergency tracheotomy [5]. After extubation, respiratory physiotherapy had been recommended by the majority of authors, which was an important step in preventing postoperative complications such as pneumonia, hypoxemia and atelectasis [6-8, 10, 11]. Early pneumonia was aggressively treated using antibiotics and breathing exercises were encouraged. However, Gorji et al reported the patient had a tracheotomy on respiratory support after two weeks of postoperative ventilation [11].

During operation, we tried to avoid factors precipitating new ossification, which was one of the most important aspects of treatment [4]. Repeated tissue trauma should be avoided during any form of injection [8]. Femoral IV access and arterial catheter to our patient were accomplished without ossification at the insertion sites later. Positioning of the patient was meticulous and air warming blanket was used to minimize soft tissue trauma. Although the operation lasted for 8 hours, no positioning injury occurred. Furthermore, surgical and anesthesia manipulations were achieved by an experienced team with utmost care to prevent additional application of force.

In conclusion, we encountered a patient with the very rare disorder called FOP. Although the anesthetic challenges are numerous, careful preparation and appropriate intraoperative management are important to minimize complications from the disease.

Disclosure of conflict of interest

None.

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Address correspondence to: Dr. Hong Jiang, Department of Anesthesiology, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, 639 Zhizaoju Road, Shanghai 200011, China. E-mail: jiaotongliujinxiang@163.com

References

- [1] Kaplan FS, Le Merrer M, Glaser DL, Pignolo RJ, Goldsby RE, Kitterman JA, Groppe J, Shore EM. Fibrodysplasia ossificans progressiva. *Best Pract Res Clin Rheumatol* 2008; 22: 191-205.
- [2] Shipton EA, Retief LW, Theron HD, de Bruin FA. Anesthesia in myositis ossificans progressiva. *S Afr Med J* 1985; 67: 26-28.
- [3] Kaplan FS, Zasloff MA, Kitterman JA, Shore EM, Hong CC, Rocke DM. Early mortality and cardiorespiratory failure in patients with fibrodysplasia ossificans progressiva. *J Bone Joint Surg Am* 2010; 92: 686-91.
- [4] Newton MC, Allen PW, Ryan DC. Fibrodysplasia ossificans progressiva. *Br J Anesth* 1990; 64: 246-50.
- [5] Wadenya R, Fulcher M, Grunwald T, Nussbaum B, Grunwald Z. A description of two surgical and anesthetic management techniques used for a patient with fibrodysplasia ossificans progressiva. *Spec Care Dentist* 2010; 30: 106-9.
- [6] Lininger TE, Brown EM, Brown M. General anesthesia and fibrodysplasia ossificans progressiva. *Anesth Analg* 1989; 68: 175-6.
- [7] Stark WH, Krechel SW, Eggers GW Jr. Anesthesia in 'stone man': myositis ossificans progressiva. *J Clin Anesth* 1990; 2: 332-5.
- [8] Singh A, Ayyalapu A, Keochekian A. Anesthetic management in fibrodysplasia ossificans progressiva (FOP): a case report. *J Clin Anesth* 2003; 15: 211-3.
- [9] Vashisht R, Prosser D. Anesthesia in a child with fibrodysplasia ossificans progressiva. *Pediatr Anesth* 2006; 16: 684-8.
- [10] Tumolo M, Moscatelli A, Silvestri G. Anesthetic management of a child with fibrodysplasia ossificans progressiva. *Br J Anesth* 2006; 97: 701-3.
- [11] Gorji R, Li F, Nastasi R, Stuart S. Fibrodysplasia ossificans progressiva: anesthetic management in complex orthopedic spine procedures. *J Clin Anesth* 2011; 23: 558-61.
- [12] Narqozian C. The airway in patients with craniofacial abnormalities. *Pediatr Anaesth* 2004; 14: 53-9.
- [13] Meier R, Bolliger KP. Anesthesiologic problems in patients with fibrodysplasia ossificans progressiva. *Anaesthesist* 1996; 45: 631-4.
- [14] Kussmaul WG, Esmail AN, Sagar Y, Ross J, Gregory S, Kaplan FS. Pulmonary and cardiac function in advanced fibrodysplasia ossificans progressiva. *Clin Orthop Relat Res* 1998; 346: 104-9.
- [15] Connor JM, Evans CC, Evans DA. Cardiopulmonary function in fibrodysplasia ossificans progressiva. *Thorax* 1981; 36: 419-23.
- [16] Nussbaum BL, Grunwald Z, Kaplan FS. Oral and dental healthcare and anesthesia for persons with fibrodysplasia ossificans progressiva. *Clin Rev Bone Miner Metab* 2005; 3: 239-42.
- [17] Mori Y, Susami T, Haga N, Tamura K, Kanno Y, Saijo H, Takato T. Extraction of 6 molars under general anesthesia in patient with fibrodysplasia ossificans progressiva. *J Oral Maxillofac Surg* 2011; 69: 1905-10.
- [18] Bandschapp O, Girard T. Malignant hyperthermia. *Swiss Med Wkly* 2012 Jul 31; 142: w13652. doi: 10.4414/smw.2012.13652.