

Case Report

Osteogenesis Imperfecta: Genetic Overview and the Role of Anesthesiologists

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Abstract

Osteogenesis Imperfecta (OI) is a rare disorder of type 1 collagen with 13 currently identified types attributable to inherited abnormalities in type 1 collagen amount, structure, or processing. OI is a genetic disorder with skeletal, vascular, and soft tissue involvement with different clinical presentations. Since these patients need different surgical procedure in their lifetime, anesthesiologists are involved with their preoperative care and should be familiar with pathogenesis and anesthetic considerations of osteogenesis imperfecta. Here we represent a case of osteogenesis imperfecta, which was candidate for Video Assisted Thoracic Surgery (VATS) and review the literature.

Keywords: Osteogenesis Imperfecta, Video Assisted Thoracic Surgery

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Introduction

Osteogenesis Imperfecta (OI) is a rare disorder of type 1 collagen with 13 currently identified types attributable to inherited abnormalities in type 1 collagen amount, structure, or processing (1). OI comprises a heterogeneous group of disorders characterized by susceptibility to bone fractures ranging in severity from perinatal death to a subtle increase in fracture frequency (2). In addition to the skeletal phenotype, common additional extraskeletal manifestations include blue sclera, dentinogenesis imperfecta, vascular fragility, and hearing loss (1). Despite the low prevalence, the wide range of heterogeneity in features and advances in treatment makes OI a disease with special requirements and considerations. OI is a differential diagnosis for child abuse and different specialists, including orthopedist, pediatricist, dentists and even psychiatrists, are

involved in treatment procedures to give the affected people a qualified life. Evidently, the role of anesthesiologists in this multidisciplinary approach may not be disregarded. Therefore, anesthesiologists should have proper knowledge about the variable genetic abnormalities and the consequent apparent and invisible features of OI, may affect the perioperative management.

Case presentation

A 44 years old man was brought to the emergency department after falling trauma. He was a known case of osteogenesis imperfecta diagnosed at the age of 18 years, made him disqualified for military service. He had a history of some long bone fractures in the past with minor trauma. His daily performance was acceptable without any respiratory or cardiac symptoms. He was homeless without any

relatives so there were limited data about family history.

He weighed 70 kg, was conscious and his hemodynamic parameters were in normal range. He had blue sclera (Fig. 1) without vision impairments. The neck and jaw movements were normal with mallampati score of 2. Apart from poor dentition, the mouth and pharynx were normal. In lung auscultation there was decreased sound in the left hemithorax, congruent with pleural effusion on chest X-ray, besides a prominent aortic arch. Further X-ray studies demonstrated right scapula, humerus, tibia and knee fractures. Lab tests findings showed leukocytosis. The spirometry showed normal pattern. In echocardiography the ejection fraction was 60% and the pulmonary artery pressure was 28 mmHg with mild tricuspid regurgitation. Bone densitometry proved low bone marrow density in spine and hip.

Chest tube insertion was planned in emergency department while the operation team prepared for unexpected hemorrhage and emergent thoracotomy and isogroup cross matched packed RBC was requested for probable event. After proper splinting and padding, the patient was transferred cautiously to operating room for visual assisted thoracoscopic surgery (VATS) to evaluate the source of hemothorax. The difficult airway equipments were prepared as well. The routine OR monitoring alongside temperature monitoring with nasopharyngeal probe attached and two large bore intravenous (IV) access number 18 and 16 were inserted under local anesthesia. He did not receive anything per os (NPO) during the last several hours. For surgical procedure all the intraoperative requirements for difficult intubation, malignant hyperthermia (MH), proper positioning and blood products were prepared beforehand. Total intravenous anesthesia (TIVA) was our choice for general anesthesia with full monitoring. The premedication included midazolam 2 mg, lidocaine 80 mg and fentanyl 150 µg via intravenous rout. The intubation was done with left side double lumen tracheal tube (DLT) number 39 after the induction of anesthesia with 140 mg propofol and 40 mg atracurium. Maintenance of anesthesia provided using propofol infusion to keep the depth of anesthesia in the range of 40 to 60 on cerebral state monitoring. Then the



Figure 1. Blue Sclera.

patient changed to right lateral decubitus position (LDP). During procedure there was about 150cc drainage of blood which caused no hemodynamic instability with no rising in temperature and end tidal CO₂. At the end of VATS, DLT changed to 7.5 mm armored tracheal tube and orthopedic surgery began. Orthopedic procedure lasted about 3 hours with minor hemorrhage and at the end patient was awakened and extubated uneventfully.

Discussion

Osteogenesis imperfecta (OI), commonly called "brittle bone disease", is a genetic disorder characterized by increased bone fragility and decreased bone density due to quantitative and/or qualitative abnormalities of type I collagen (3). It is a variable condition with a range of clinical severities (4). Most of the cases of OI are inherited in autosomal dominant fashion with mutations in COL1A1 or COL1A2 genes. Over last few years, twelve genes for autosomal recessive OI have been identified (5). After 2006, mutations were identified in the CRTAP, FKBP10, LEPRE1, PLOD2, PPIB, SERPINF1, SERPINH1, SP7, WNT1, BMP1, and TMEM38B genes, associated with recessive OI and mutation in the IFITM5 gene associated with dominant OI. Mutations in PLS3 were recently identified in families with osteoporosis and fractures, with X-linked inheritance pattern. In addition to the genetic complexity of the molecular basis of OI, extensive phenotypic variability resulting from individual loci has also been documented (6).

Osteogenesis imperfecta is classified into 11 types to date, on the basis of their clinical symptoms and genetic components (7). For simplicity, the objectives of treatment can be reduced to three typical

situations: the lethal perinatal form (type II), in which the problem is survival at birth; the severe and moderate forms (types III-IX), in which the objective is 'autonomy' and the mild form (type I), in which the aim is to reach 'normal life' (8). The hallmark feature of OI is bone fragility, with susceptibility to fracture from minimal trauma, as well as bone deformity and growth deficiency. OI has multiple secondary features, including macrocephaly, blue sclera, dentinogenesis imperfecta, hearing loss, neurological defects (macrocephaly and basilar invagination) and cardiopulmonary complications (the major cause of mortality directly related to OI) (9).

Thanks to the genetic discoveries, bisphosphonates therapy and new surgical and rehabilitation method, a new era is developed for life span with rising quality in the population affected by this rare disease. As long as all surgical procedures need anesthesia, anesthesiologist should be aware of all aspects of OI which may interfere with anesthesia in perioperative period. Commonly encountered complications include a difficult airway, intraoperative bleeding due to platelet dysfunction, respiratory compromise due to skeletal deformity, and congenital cardiac anomalies (10). Cardiovascular effects are identifiable in childhood even in mild forms of OI. Aortic dilation is the predominant finding, while valvular abnormalities are infrequent (11). Cautious moving and positioning to avoid further fractures and meticulous monitoring of temperature due to the risk of malignant hyperthermia should not be underestimated. Proper preparation and preoperative assessment is important, as is the choice of anesthetic technique (10). Even though a direct relationship between OI and MH has not been proven (12), TIVA is the choice in OI to reduce the risk of MH during intraoperative period. Succinylcholine and volatile anesthetics are avoided in anesthesia management in OI. Cardiopulmonary assessment can reveal hidden problems especially in mild forms of OI and prevent further complications.

Our patient, regarding to clinical manifestation, was in mild category. Since the airway was not compromised and the team was ready for difficult airway management including surgical tracheostomy, induction with IV anesthetic and nondepolarizing muscle relaxant was performed. The position and

movements were carefully supervised by attendants. Certainly, close and full monitoring was the priority of our intraoperative care.

Conclusion

As a result of novel achievements in genetic and cellular studies and uprising hope to treat the patients with rare genetic disorders, anesthesiologists find themselves in new era of required skillful adaptable individuals who can work in dynamic situations (13-16). In addition to the fragile bones and probable difficult intubation, the risk of MH or probable hypermetabolic state, the risk of bleeding and cardiopulmonary complication should never be neglected in the shadow of urgent and emergent procedures.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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