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CASE REPORT

Anaesthetic considerations in a child with fibrodysplasia ossificans progressiva

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Fibrodysplasia ossificans progressiva (FOP) is an extremely rare genetic disorder characterised by extraskeletal ossification of connective tissue. Affected individuals often become completely immobilised by their third decade of life. Amongst numerous anaesthetic concerns, the airway management of patients with FOP may prove to be the greatest challenge. This case report describes the anaesthetic management of a three-year-old girl with FOP and highlights the difficulties encountered during airway management.

Keywords: airway management, fibreoptic intubation, fibrodysplasia ossificans progressiva, paediatric anaesthesia

Introduction

Fibrodysplasia ossificans progressiva (FOP) is a rare genetic disorder characterised by extraskeletal ossification of connective tissue such as tendons, ligaments and the connective tissue in skeletal muscle.[1–3] Affected individuals are often completely immobilised by their third decade of life.[3] As the disease progresses, complications may arise secondary to thoracic insufficiency syndrome.[4] However, in young children, the main anaesthetic challenge may prove to be the airway management.[3,5,6] Only a few reports on the anaesthetic management of young children with FOP exist.[6] This case report describes the anaesthetic management of a three-year-old girl with FOP.

Case report

Two days after a fall, a three-year-old girl developed a painful swelling of her right knee and was unable to walk. She was seen by a general practitioner who referred her to the orthopaedic outpatient department at our hospital. Following a clinical and radiological examination the orthopaedic surgeon made the diagnosis of fibrodysplasia ossificans progressiva with an acute flare-up. The patient was scheduled for a semi-urgent manipulation under anaesthesia and splinting of her right knee the following day.

At birth, the mother had noted shortening of her daughter's first toes bilaterally but was not concerned about this. At the age of two years the patient had developed a painful soft tissue swelling over her back. A general practitioner was consulted but no diagnosis was made, and no treatment was offered. By the time she presented to our institution, about 15 months later, the patient had developed significant kyphosis and mild scoliosis of her thoracic spine. Her neck was completely fixed in mild flexion and her sternocleidomastoid muscles were ossified. She had reduced mouth opening with an inter-incisor gap of 5 mm. Despite this, she did not appear malnourished and she weighed 15.5 kg. She had significantly reduced range of motion in all large joints with fixed flexion deformities in elbow, hip and knee joints. Limited chest excursion was noted, and her breathing was predominantly diaphragmatic. There was no history of recurrent chest infections and no evidence of cardiac

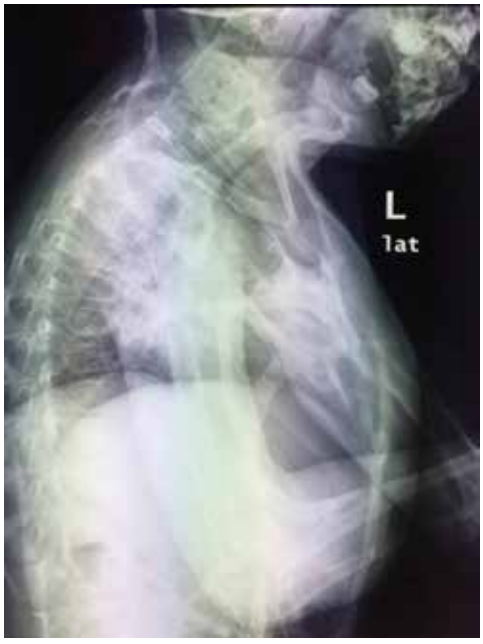

Figure 1: Lateral chest radiograph showing soft tissue ossification and ankylosis of cervical spine and upper limb joints. Ossified sternocleidomastoid muscles can also be seen.

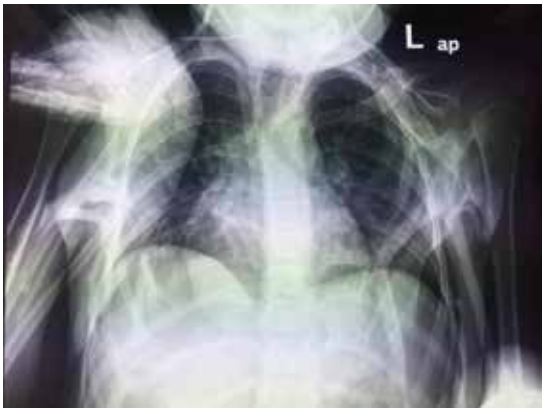

Figure 2: Chest radiograph showing heterotopic ossification of soft tissues and joints.

dysfunction. She was not on any chronic medication and had no previous surgical history. Radiographs (Figures 1–3) revealed extensive ectopic bone formation.

Preoperative premedication was withheld. After careful positioning of the patient on the theatre bed, routine monitoring (electrocardiogram, non-invasive blood pressure and pulse oximetry) was placed and all pressure points were padded. A 22G intravenous cannula was inserted without difficulty in a superficial vein on the dorsum of her right hand. Anaesthesia was induced with sevoflurane and oxygen. Oxymetazoline 0.025% drops were then instilled in both nostrils. With the patient breathing spontaneously, an attempt was made at introducing a 2.8 mm bronchofibrevideoscope (Olympus Medical Systems Corp, Tokyo, Japan) nasally. However, the anatomy of the mid-nasal vault was significantly distorted, so that the bronchoscope could not be advanced. Fortunately, the presence of dental decay provided enough space for the bronchoscope and the subsequent insertion of the endotracheal tube orally over the bronchoscope, without aggressive manipulation of the temporomandibular joints. Once the vocal cords were adequately visualised, 30 mg of propofol was administered intravenously and the trachea was intubated with a size 4.5 uncuffed endotracheal tube introduced over the bronchoscope. Pressure-controlled ventilation was uneventful, and anaesthesia was maintained with sevoflurane in an oxygen and air mixture.

Our patient's vitals remained within normal limits throughout the 45-minute procedure and she was extubated once fully awake. Her stay in the recovery room and later in the ward was uneventful. Six weeks after her surgery she sustained another fall and injured her left arm. The radiographs revealed a fracture of one of the heterotopic ossifications at the elbow joint and no further surgery was required. Our patient is now receiving care from a multidisciplinary team.

Discussion

FOP is an extremely rare autosomal dominant disorder[7,8] with an estimated prevalence of one affected individual per two million population.[9,10] Most new cases of FOP arise from sporadic mutations in the activin A type I receptor (ACVRI) gene. ACVRI is a bone morphogenic protein (BMP) type 1 receptor gene.[2] The mutation causes activation of ACVRI, even in the absence of its ligand. This uninhibited BMP signalling then initiates new bone formation by promoting osteoclast formation.[2,3,11]

The heterotopic ossification that is characteristic of FOP may be initiated by trauma or may occur sporadically.[2] At birth, affected individuals appear normal except for characteristic shortening and congenital hallux valgus of their first toes bilaterally.[3,12,13] During early childhood, painful soft tissue nodules appear, which then progressively ossify. The initial lesions are confined to the neck and back region but later spread distally.[3,14] The heterotopic bone is morphologically identical to skeletal bone[1] and often severely restricts the mobility of affected individuals by their third decade of life.[3] Certain skeletal muscles including the tongue, diaphragm and extraocular muscles are not affected by FOP. Cardiac muscle and smooth muscle are also not involved.[3,8]

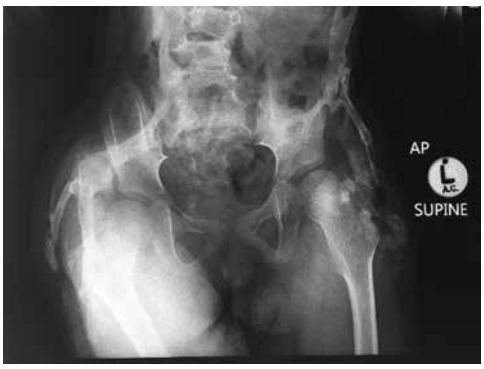

Figure 3: Radiograph showing extensive ectopic soft tissue ossification and ankylosis of the hip joints and lower lumbar spine.

The median age of survival of patients with FOP is 45 years and the two leading causes of death are pulmonary infections and right-sided heart failure secondary to thoracic insufficiency syndrome.[4] Campbell *et al.*[15] define thoracic insufficiency syndrome as 'the inability of the thorax to support normal respiration or lung growth'.

Currently, there is no cure for FOP and the management of FOP is predominantly supportive. Surgical removal of heterotopic bone, osteotomies and surgical contracture releases are not recommended, as they may further induce the formation of heterotopic bone.[3] Anecdotal evidence supports the early use of glucocorticoids for the management of new flare-ups and the use of anti-inflammatory agents for the management of chronic discomfort.[16] Prophylactic measures include the avoidance of intramuscular injections,[17] prevention of falls and the administration of influenza vaccines.[3] The influenza vaccines should be administered subcutaneously and not during periods of flare-up.[3] Cardiac and respiratory function should be evaluated periodically, and a multidisciplinary team should be involved in the functional optimisation of patients with FOP.[3]

Anaesthetic considerations

Airway management

Most of the difficulty with the airway management of patients with FOP arises from the effects of the disease on the temporomandibular joints (TMJs) and the cervical spine.[3,18,19] Ankylosis of the TMJs is common in FOP[3,5,14] and overstretching of the jaw may cause enough trauma to the TMJs to result in localised flare-up and further ossification.[5] Neck stiffness may already be present at an early age in children with FOP and usually precedes heterotopic bone formation.[3,14,20] Numerous anatomical abnormalities of the cervical spine have been identified in patients with FOP and include tall, narrow vertebral processes as well as large pedicles and spinous processes. Fusion of facet joints and spinous processes between the second and the seventh cervical vertebrae starts during early childhood. This is a separate pathological process from the formation of heterotopic bone.[20] Flare-ups in the soft tissue of the neck, particularly in the submandibular area, may further compromise the integrity of the upper airway.[3,21]

Anatomical deformity caused by joint ankylosis and ossification[3] may interfere with optimal patient positioning during airway management.[22] Furthermore, the effects of the disease on the thoracic spine and the chest wall may cause respiratory dysfunction[4] and patients may therefore desaturate more rapidly than anticipated.

In patients with FOP, there should generally not be any difficulty in achieving an adequate seal during facemask ventilation. Difficult facemask ventilation may, however, still occur due to

ankylosis of the TMJs. The reduced mouth opening may prevent atraumatic oral airway insertion and reduced jaw protrusion may interfere with the jaw thrust manoeuvre.[22,23]

Ankylosis of the TMJs and the cervical spine may make the insertion of supraglottic airway devices as well as video-assisted and direct laryngoscopy impossible.[3,18,22] Forceful manipulation of the upper airway should always be avoided, as this may induce further flare-ups.[5] Tumolo *et al*.[6] therefore recommend that direct laryngoscopy should not be performed during non-emergency airway management in patients with FOP, even if mouth opening is adequate.

Tracheostomy and transtracheal injections should be avoided in patients with FOP to prevent ectopic ossification of the airway.[6] An otolaryngologist should, however, be present in theatre in case a surgical airway rescue procedure needs to be performed.[24]

Several reports recommend nasotracheal fibreoptic intubation in an awake or lightly sedated patient as the safest airway management technique in patients with FOP.[5,24–26] This technique is often not feasible in paediatric patients.[6,24,27] Kilmartin *et al*.[24] reviewed 42 cases in which general anaesthesia was administered to patients with FOP presenting for dental treatment. An awake fibreoptic intubation was performed in almost all adult cases. In 14 of their 19 paediatric cases, fibreoptic intubation was performed under sedation. Four paediatric cases, however, required induction of anaesthesia, with maintenance of spontaneous ventilation, prior to nasotracheal fibreoptic intubation. The ages of these four patients ranged from 5 to 10 years.

In our three-year old patient, we elected to perform a volatile induction to allow fibreoptic intubation during spontaneous ventilation. However, nasal intubation was not possible due to distorted anatomy of the mid-nasal vault. Inability to perform nasal intubation due to distorted nasal anatomy in a patient with FOP has previously been reported by Shipton *et al*.[28] Fortunately, the presence of dental decay in our patient provided enough space to allow orotracheal fibreoptic intubation. Caries, gingivitis and periodontitis are common in FOP patients as ankylosis of the TMJs makes dental care more difficult.[5] Once the vocal cords had been adequately visualised, we administered 30 mg of intravenous propofol, prior to intubating the trachea. This provided ideal conditions for an atraumatic intubation.

Thoracic insufficiency syndrome and cardiopulmonary complications

In patients with FOP, thoracic insufficiency syndrome develops due to a combination of costovertebral malformations and early fixation of the chest wall.[4,29] Ossification of paravertebral soft tissue also impairs normal thoracic spine growth, which may then result in the development of kyphoscoliosis. This may further contribute to the thoracic deformity and dysfunction.[4] Chest wall excursion is reduced early in the disease process. Fortunately, the diaphragm is not affected by the disease and diaphragmatic function alone is usually sufficient for basal ventilatory requirements in patients with FOP, who usually have reduced mobility.[29] Lung function testing usually reveals significantly reduced lung volumes with relatively normal flow rates and normal capillary oxygen saturation.[29,30] Pneumonia is the commonest cause of death in patients with FOP.[4]

Physical examination of patients with FOP does not usually reveal signs of cardiac failure, but evidence of right ventricular dysfunction is often present on electrocardiogram (ECG). Kussmaul *et al*. identified a higher prevalence of right ventricular dysfunction on ECG in patients with FOP who were older, had prolonged disease duration, had severe restrictive lung disease and had higher haemoglobin concentrations.[30] Cardiac muscle is not affected directly by FOP, but cardiac connective tissue may be affected. This may explain some of the cardiac conduction abnormalities that have been reported in the literature.[29]

Despite having some clinical evidence of thoracic insufficiency, our patient had no history of recurrent chest infections and her ECG showed no evidence of right ventricular dysfunction. Mechanical ventilation was uncomplicated and there was no need for postoperative ventilatory support.

Vascular access and regional anaesthesia

Subcutaneous injections and the careful insertion of superficial intravenous catheters are not contraindicated in FOP. Traumatic insertion of intravenous and arterial lines may, however, precipitate heterotopic bone formation. Any form of intramuscular injection may cause an acute flare-up of FOP at the injection site and should be avoided.[3,5,8,17,31] Regional anaesthesia is therefore not advised,[26] but the use of ultrasound guidance may allow the safe placement of needles close to superficial nerves without penetrating muscle and connective tissue.[32] The musculoskeletal deformities present in patients with FOP may also make it technically more difficult to insert needles with precision.[18,26] Furthermore, patients who have severe deformities should be positioned carefully on the operating table and pressure points should be padded to avoid soft tissue trauma.[6,24]

Nutritional status

Ankylosis of the TMJs may prevent mastication[3,6,8] and affected individuals may be restricted to soft or liquid diets.[33] Patients are therefore often underweight and their general nutritional status should be evaluated carefully.[6]

In conclusion, FOP is an extremely rare and devastating disease. Even in young children, the disease may be severe enough to present the attending anaesthetist with significant challenges. A thorough preoperative assessment and meticulous anaesthesia plan are essential. All patients with FOP should be managed by a multidisciplinary team.

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