Fibrodysplasia ossificans progressiva (FOP) is a rare inherited disease in which progressive ossification of striated muscles leads to severe disability and respiratory impairment early in life and there are associated characteristic congenital skeletal malformations. Although this condition may prove demanding for the anaesthetist, few reports are available regarding anaesthesia in paediatric patients. We review the clinical features of the disease relevant to anaesthesia and describe the perioperative care of an 18-month-old boy with FOP who underwent endoscopic third-ventriculostomy for hydrocephalus associated with a brainstem mass. We emphasise the importance of an appropriate anaesthetic management of these patients, as inadequate care may lead to exacerbation of the disease with permanent sequelae.

Fibrodysplasia ossificans progressiva (FOP) is a severe disabling inherited disorder of connective tissue characterized by congenital malformation of the great toes, thumbs and vertebrae associated to progressive ossification of striated muscles.

Heterotopic ossification usually appears in childhood (2–6 yr) after spontaneous or trauma induced flare-ups, presenting as large, painful swellings in soft tissues including tendons, ligaments and skeletal muscle. These often progress and form mature bone tissue with resulting ankylosis of the major joints. Most patients are confined to a wheelchair by their 20s and they usually die before their 40s because of cardiopulmonary failure secondary to thoracic muscle involvement.

Trauma, including surgical biopsy or resection of heterotopic bone, may cause new flare-ups.

As these patients can have concurrent problems requiring surgery, the anaesthetist may be called to face a difficult situation. Furthermore, few reports are available in literature, especially regarding paediatric patients. FOP is a progressive disorder, so in the early phases of the disease the patient may present in quite good condition. Nevertheless, those involved in care of a patient with FOP should be aware that inadequate management can induce progression of the disease with permanent sequelae. One of the most common is the ankylosis of the temporo-mandibular joint.

We report the case of a child with FOP and describe the anaesthetic management.

Case report

An 18-month-old boy with a recent diagnosis of FOP presented with compensated hydrocephalus and expansive brainstem lesion. Past medical history revealed congenital bilateral hallucus valgo deformation, neck stiffness and several post-traumatic ossified lesions on the head (temporal and occipital region) and dorsum. A CT scan and an MRI showed a brainstem mass and concomitant progressive tetraventricular hydrocephalus. As no previous reports of intra-axial FOP localizations were found, the intracranial mass was considered as a separate, non-FOP issue. A ‘wait and see’ strategy was decided on, but the patient was scheduled for endoscopic third-ventriculostomy for the treatment of hydrocephalus.

Physical examination revealed good clinical condition, he was well-nourished and weighed 13.6 kg. He had heterotopic ossification of the dorsal and lumbar paravertebral muscles and of the left sternocleidomastoid. His neck was
The following day, an equivalent dose of dexamethasone 8 mg was administered. End tidal CO₂ and neuromuscular package under the air warming blanket. Rocuronium tube which had been previously softened by keeping the trachea was then intubated with a 4.5 uncuffed tracheal tube which had been previously softened by keeping the trachea. Mouth opening was normal and no respiratory and cardiovascular abnormalities were found.

The patient had been treated with ibuprofen and was currently on montelukast, which has been shown to decrease the intensity of FOP flare-ups. There is some evidence that a 4-day course of high-dose corticosteroids, started within the first 24 h of an acute flare-up, may reduce lymphocytic infiltration and tissue oedema. Therefore, the day before the procedure montelukast was stopped and prednisone 2 mg kg⁻¹ day⁻¹ orally in a single daily dose was started. The following day, an equivalent dose of dexamethasone (prednisone 1 mg=dexamethasone 0.15 mg) was administered i.v. during surgery. Prednisone was given for 2 more days after the procedure and then gradually discontinued over the next 2 days.

In the preoperative holding area, the patient was premedicated with rectal atropine 0.125 mg and midazolam 7 mg. Lidocaine 2% (2 ml) was nebulized through an aerosol mask. Then, in the operating room, routine monitors (ECG, arterial pressure cuff and pulse oximeter) were placed and a 22G i.v. cannula inserted, taking particular care to avoid tissue trauma. The patient was then sedated with fentanyl 25 μg and incremental doses of midazolam (total dose 6 mg) and propofol (total dose 80 mg) slowly injected in order to maintain spontaneous breathing. Although the patient could open his mouth normally, no attempt to perform a direct laryngoscopy was made. A fiberoptic bronchoscope was introduced through the right nostril, previously instilled with neo-synephrine one drop and lidocaine 2% (1 ml), and, under direct vision, the vocal cords and the trachea were sprayed with an additional 1 ml of lidocaine 2%.

The trachea was then intubated with a 4.5 uncuffed tracheal tube which had been previously softened by keeping the package under the air warming blanket. Rocuronium 8 mg was administered. End tidal CO₂ and neuromuscular transmission monitoring were started. Anaesthesia was maintained with sevoflurane 1 MAC and remifentanil 0.1–0.25 μg kg⁻¹ min⁻¹ and muscle relaxation with rocuronium 0.6 mg kg⁻¹ h⁻¹. Two more 20G peripheral i.v. lines were established, keeping the 22G line solely for the infusion of remifentanil. Femoral vein access, common during neurosurgical procedures in children, was intentionally avoided, because of the proximity to a major joint.

Special precautions were taken to avoid traumatic injury in every part of the body: to this purpose silicon carpets and headrest were used and every point of contact was padded with cotton wool.

Vital signs remained stable during surgery, which lasted 1 h and 20 min. Half an hour before the end of the procedure, ketorolac 7 mg and tramadol 20 mg were given for postoperative analgesia. At the end of the procedure, sevoflurane, remifentanil and rocuronium were discontinued and neuromuscular block was antagonized; the tracheal tube was removed when the patient was fully awake. The postoperative period was uneventful. The child was discharged from hospital 1 week after the procedure and came back 2 months later for a routine neurosurgical consultation: he was in good health and showed no sign of progression of the disease.

**Discussion**

FOP, sometimes called ‘Myositis ossificans progressiva’ or ‘Stone Man Syndrome’, is a very rare disease. Its prevalence in the United Kingdom has been estimated at 1 case per 1.64 million and less than 400 cases have been reported worldwide. It is an inherited, autosomal dominant disorder in which heterotopic bone progressively replaces skeletal muscle and connective tissue. Ossification usually begins in the occipital, cervical and upper paravertebral muscles, as in our patient, and then involves muscles around all the major joints, producing progressive immobilization. Certain muscle groups are spared, including tongue, larynx, diaphragm, abdominal wall, face, extracutaneous muscles, sphenoid and visceral smooth muscle.

Because of the ankylosis of the costovertebral joints and ossification of the chest wall, the patients eventually develop restrictive respiratory failure. Atelectasis and ineffective cough often determine recurrent pulmonary infections.

Ossification of the cardiac muscle has never been described, but it has been suggested that cardiac connective tissue may be involved in the disease. ECG abnormalities (right bundle branch block, T-wave inversion, left axis deviation with ST segment changes, supraventricular tachycardia) have been observed in 29% of the patients. Right ventricular dysfunction has been reported in older patients with longer disease duration, higher haemoglobin and more impaired pulmonary function.

Careful preoperative evaluation of these patients is essential. Nutrition may be poor if there is impaired ability to eat caused by temporo-mandibular joint ankylosis.

Pulmonary and cardiovascular status should be assessed: chest X-rays, ECG and, if possible, spirometry should be obtained; CT scan may be helpful. Cervical spine status needs to be investigated, as fusion of the cervical vertebrae is a common feature of the disease and atlanto-axial subluxation has been described in one patient.

Drugs currently used in the treatment of FOP include corticosteroids, non-steroidal anti-inflammatory agents, leukotriene inhibitors (montelukast), Cox-2 inhibitors and mast-cell stabilizers. To date, no treatment has been proven to modify the natural history of FOP. Corticosteroids are usually restricted to early treatment of flare-ups involving major joints or mandibular area. We preventively administered prednisone in order to avoid flare-ups connected to the surgical trauma, following the guidelines that have been recently revised by Kaplan and colleagues and that can be downloaded from the FOP website (www.IFOPA.org).

All the previous reports regarding anaesthesia in FOP patients recommend awake fibroptic endotracheal intubation as the preferred method of airway management. However, in a selected group of patients, the awake intubation approach may not be feasible. Anaesthesia with fiberoptic bronchoscopy is a promising alternative that allows the performance of awake tracheal intubation. The advantage of this technique is that it allows the anaesthetist to position the endotracheal tube under direct vision and confirm correct placement before ventilation is started. It is a technically demanding procedure that requires specialized training and experience. However, it has been shown to be safe and effective, even in patients with difficult airways. In this case report, we describe the successful use of awake fiberoptic endotracheal intubation for the anaesthesia of a patient with FOP.
intubation\textsuperscript{5,8–10} which, in paediatric patients, requires deep sedation. Tracheostomy should be avoided because of possible ossification in the site of incision that could result in airway obstruction.\textsuperscript{8} Direct laryngoscopy may overstretch the temporo-mandibular joint and cause ossification and ankylosis. Therefore, laryngoscopy must be avoided, even if mouth opening is normal, unless the trachea needs to be intubated under emergency conditions.

The airway should be carefully anaesthetized; transtracheal injection of local anaesthetic must not be performed because of the risk of ossification, nebulized or sprayed or directly instilled local anaesthetics are preferred. Jaw displacement manoeuvre to open the airway should be avoided, as it significantly stimulates the temporo-mandibular joint.

I.M. injections should not be performed (ossification at the site of injection has been observed after routine immunizations in children).\textsuperscript{11} S.C. injections and venipuncture pose no significant risk, but dysfunctional i.v. catheters are a well-known cause of heterotopic ossification. It has been suggested that disuse atrophy characteristic of advanced stages of the disease could contraindicate the use of succinylcholine.\textsuperscript{9} At present, no adverse reactions have been reported with neuromuscular blocking agents such as vecuronium and rocuronium.

Careful positioning and padding of the patient during surgery are needed to prevent soft tissue injury. If a flare-up develops in the postoperative period, ice application for 24 h and steroids are recommended. Chest physiotherapy and pulmonary toilet should be instituted after operation in order to prevent respiratory infections.

FOP, although a very rare disorder, may pose significant challenges to the anaesthetist. There is a great variability in FOP progression, but, as a general rule, the oldest patients are the most disabled. In children there may not be severe impairment, but it is important that anaesthetic management follows adequate protocols. Every effort should be made to avoid situations that may put the patient at risk of new localizations of heterotopic ossification, as that may have a substantial impact on their quality of life.

References