SUMMARY

A 14-yr-old boy with fibrodysplasia ossificans progressiva (FOP) presented for surgery for bilateral division of his ossified masseter muscles. Patients with FOP may present problems to the anaesthetist, including difficulties with tracheal intubation, restrictive pulmonary disease and abnormalities of cardiac conduction. With our patient sedated the trachea was intubated using a fibroscope and anaesthesia was induced and maintained with nitrous oxide and enflurane in oxygen. Ventilation was controlled throughout surgery and recovery was uneventful.

KEY WORDS

Complications: fibrodysplasia ossificans progressiva. Intubation: complications.

Fibrodysplasia ossificans progressiva (FOP) is an inherited disorder of connective tissue in which physical handicap caused by progressive soft tissue ossification accompanies characteristic skeletal malformations. In 1982, Connor and Evans published a survey identifying all patients in the U.K. with FOP [1]. Forty-four patients were identified, of whom 30 were still alive. Although this is a very rare disease, patients with this condition may frequently require surgery and cause problems for the anaesthetist, including restrictive pulmonary disease, limited neck movement and limited mouth-opening. There may also be abnormalities of cardiac conduction. There has been one report of atlanto-axial subluxation.

CASE REPORT

A 14-yr-old boy with a confirmed diagnosis of FOP presented for division of ossified masseter muscles which had resulted in complete trismus. It was hoped that this would improve feeding and halt progressive weight loss. He had enjoyed good health until, at the age of 4 yr, he developed a large painful lump on the back of the neck associated with fever. This was biopsied uneventfully under general anaesthesia and was suggestive of malignancy. Within a few weeks he developed further similar lumps on his neck and back which were associated with pain and stiffness. These lumps were also biopsied under general anaesthesia at a specialist hospital and were reported as consisting largely of "immature fibroblasts interspersed with bands of collagen". These histological findings, together with the classical radiological appearances of thoracic soft tissue opacities extending up into the neck, monophalangeal big toes and shortened 1st metacarpals confirmed the diagnosis of FOP. One year later his condition had deteriorated and he developed a rigid thoracolumbar spine with marked upper thoracic kyphoscoliosis. Neck movements were severely limited. Over the next 9 yr his condition continued to deteriorate despite many forms of treatment, which included calcitonin, prednisolone and disodium etidronate.

On the present admission at the age of 14 yr, he was cachetic, weighing only 24 kg, and had complete trismus. He was able to walk unaided, but had slight reduction in exercise tolerance and suffered frequent chest infections. Examination revealed a gross chest deformity, with kyphoscoliosis, and fixation of chest wall musculature. Ventilatory movements were diaphragmatic, with no visible excursion of the ribs. There were no abnormalities in the cardiovascular system. His neck was fixed completely in a neutral position.

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His shoulder joints were fixed also and he had fixed flexion of both elbows.

Current treatment included prednisolone 20 mg on alternate days, warfarin 1 mg daily, disodium etidronate 400 mg daily and a low calcium diet. All biochemical and haematological investigations, including coagulation studies, were within normal limits. A preoperative chest x-ray (fig. 1) confirmed a gross upper thoracic scoliosis with marked ossification of soft tissues and associated rib deformities. Cervical spine x-rays (fig. 2) showed hypoplasia of the cervical vertebral bodies, with almost complete fusion of the spinous processes. Pulmonary function studies confirmed a severe restrictive defect (table I). ECG was unremarkable except for a sinus tachycardia.

He was premedicated with i.m. papaveretum 5 mg, hyoscine 0.1 mg and hydrocortisone 50 mg. On arrival in the anaesthetic room he was given a gargle of 4% lignocaine. ECG monitoring was commenced and he was sedated cautiously with droperidol 1 mg i.v., fentanyl 50 µg i.v. and midazolam increments totalling 7 mg i.v. Cocaine paste (25%) was applied to both nares. The trachea was intubated with a 5.5-mm tracheal tube (Portex Ltd) introduced nasally over a fibreoptic bronchoscope (Olympus ENF-P). Following confirmation of correct placement of the tracheal tube, anaesthesia was induced and maintained with enflurane and 50% nitrous oxide in oxygen. Ventilation was controlled without difficulty during the 30-min operative procedure.

### Table I. Respiratory function test results (test performed sitting)

|                      | Predicted | Actual |
|----------------------|-----------|--------|
| PEFR (litre min⁻¹)   | 314       | 122    |
| FEV₁ (litre)         | 2.14      | 0.58   |
| FVC (litre)          | 2.61      | 0.54   |
| FEV₁/FVC (%)         | 82        | 93     |
Arterial pressure, ECG, pulse oximetry and end-tidal carbon dioxide measurements remained within normal limits throughout the procedure.

At operation, bilateral intra-oral buccal incisions were made until sufficient mouth opening had been achieved for a throat pack to be inserted. The coronoid processes and fibro-osseous attachment of the temporalis muscles were sectioned, as were fibrous bands in the masseters and medial pterygoids. At the end of the procedure mouth opening to 5 cm was possible. With the patient still anaesthetized, direct laryngoscopy was attempted to assess future ease of intubation, but it was not possible to visualize the epiglottis (Cormack and Lehane grade 4 intubation) [2]. Following pharyngeal toilet, a mouth prop was placed between the molars to prevent recurrence of trismus. The nasotracheal tube was removed uneventfully when the patient awoke.

The following day, after removal of the mouth prop, the patient was noted to have a dislocated jaw. It was decided to relocate the jaw under general anaesthesia. The patient was anaesthetized uneventfully in the manner described above and his jaw was successfully repositioned. On recovery he was able to open the mouth 5 cm. After operation the patient rapidly gained weight with nasogastric tube feeding, although he was diagnosed later by a psychiatrist as having anorexia nervosa. Despite intensive physiotherapy, the masseter muscles re-osified after 5 months, resulting again in complete trismus and weight loss. Ten months after operation he developed a chest infection which was unresponsive to treatment, and he died.

**DISCUSSION**

Fibrodysplasia ossificans progressiva was noted first in 1648 by Guy Patin [3], who described a woman “qui est devenue dure comme du bois”. In 1736 John Freke, a surgeon at St Bartholomew’s hospital gave a more accurate description of “a Boy of healthy Look, and about Fourteen Years old,...of many large swellings on his Back...They arise from all the Vertebrae of the Neck, and reach down to the Os Sacrum; they likewise arise from every Rib of his Body, and joining together in all Parts of his Back, as the Ramifications of Coral do, they make, as it were, a fixed bony Pair of Bodice” [4].

The term “myositis ossificans progressiva” was applied to the disease in 1868, although the term favoured currently is “fibrodysplasia ossificans progressiva”, as the disease is a disorder primarily of connective tissue rather than muscle [5].

The aetiology of the disease remains unknown, although recent work in patients with fibrodysplasia ossificans circumspecta, a non-hereditary disorder in which the pathology appears to be identical, suggests that it may be caused by a defect in the muscle capillary endothelium [6]. Biochemical screens are always normal [7]. FOP is inherited as an autosomal dominant trait with full penetrance, but variable expression. However, patients with FOP rarely reproduce, because of physical handicap, and the majority represent fresh dominant mutations [1]. The sex ratio of affected individuals is equal, and the few patients with FOP who have reproduced have affected offspring [8].

Typically, patients with FOP are asymptomatic until early childhood (mean age of presentation is 3 yr 11 months) when invariably they present with a painful swelling, classically in the neck region. This shrinks gradually in size over several days or weeks and may be succeeded by other lumps in the same area. These represent the earliest stages of ossification within the connective tissue of the muscles, and biopsies taken at this stage show considerable proliferation of fibroblasts which may be misdiagnosed as fibrosarcoma. Within 2–8 months, the lumps become fully ossified. They usually appear spontaneously, but trauma (including i.m. injections, lump biopsies, excision of ectopic bone and dental extractions) is a common precipitating factor.

Initially, the areas of ossification develop within the musculature of the neck and back, but secondary attachment to the skeleton is common. Ectopic ossification in tendons, ligaments and joint capsules, in addition to muscular involvement, causes joint immobilization and associated osteoporosis. Occasionally, pathological fractures occur which, paradoxically, may benefit the patient by formation of a false joint in a previously fixed area.

The cervical spine is frequently abnormal. In one series [9], all 11 patients had a history of neck stiffness, usually from early childhood. In two of these patients, neck stiffness had been noted as early as 6 months of age. Most of these patients had subsequently developed complete rigidity of the cervical spine, but in some, a limited range of movement was possible. No patient had evidence
of nerve compression. All 11 patients had radiological abnormalities in the cervical spine, but the findings depended on the age of the patient. However, all had varying degrees of cervical fusion; in addition four had small cervical vertebral bodies with enlarged pedicles. In some patients, serial radiographs from early childhood demonstrated progressive cervical fusion with increasing age. Fusion was associated occasionally with ossification of the adjacent neck muscles. There has been one reported case of partial atlanto-axial subluxation in FOP, found at autopsy [10].

In our patient, mild neck stiffness was documented first at the time of his first lump biopsy at the age of 4 yr 3 months. Within 3 months, neck movements were limited severely, and by the age of 6 yr, x-rays revealed fusion of C4–8. At the time of operation for division of his masseters, complete cervical spine fusion had occurred. The difficulty of intubation that this may cause was compounded by complete trismus consequent on ossification of the masseters. This is a common finding and has been reported in 71% of these patients [10]. Interestingly, the temporomandibular joints in our patient had been reported previously as abnormal, with a flat and broadened mandibular condyle. This is thought to be a primary skeletal abnormality and has been reported in other patients with FOP [11]. This may explain the dislocation that occurred after operation in our patient.

The other major problem presented by our patient was severe restrictive pulmonary disease because of ankylosis of the costovertebral joints, ossification of the chest wall and kyphoscoliosis. In 21 patients with FOP in whom cardio-pulmonary function was assessed [12], a restrictive ventilatory defect caused by chest wall fixation was common. Patients eventually become dependent on diaphragmatic ventilation. Abnormal pulmonary function is an early feature of FOP and our patient had been dependent on diaphragmatic breathing at the age of 4 yr. Respiratory monitoring (especially end-tidal carbon dioxide concentration) is mandatory and postoperative respiratory support may be necessary in patients undergoing major procedures.

This restrictive defect does not appear to progress to chronic respiratory failure during adult life; diaphragmatic function is adequate for these patients with restricted mobility [12]. Patients with FOP usually die in their third or fourth decades, commonly from pneumonia, and attention should be directed to prevention and prompt treatment of chest infections.

Cardiac assessment usually reveals no signs of failure on physical examination, but an abnormal ECG may be present [12]. There have been reports of left axis deviation with ST segment changes and minor degrees of intraventricular block [13] and supraventricular tachycardia [14]. Bone formation has never been recorded in the heart or lungs, but it has been suggested that cardiac connective tissue may be involved by the disease process, resulting in conduction abnormalities [13].

Certain muscle groups are not involved in FOP, including tongue, extraocular muscles, larynx, diaphragm, sphincter muscles and visceral smooth muscle.

Treatment aimed at halting the progression of FOP has been largely unsuccessful, mainly because the pathogenesis remains unknown. Many therapies have been tried, but none are of proven benefit. Our patient was treated with prednisolone, disodium etidronate and warfarin. Corticosteroids decrease bone formation by inhibiting periosteal cell proliferation and have been reported to decrease the rate of progression in a few subjects, although it is doubtful if they have any effect on eventual outcome. Disodium etidronate is a diphosphonate which inhibits calcification but does not seem to halt the disabling production of the ectopic bone matrix [7]. In addition, the diphosphonates inhibit mineralization of normal bone and may result in undesirable skeletal side effects. Warfarin is used because of reports of subjective improvements in mobility in patients with ectopic calcification [15]. One of the most important aspects of treatment is to remind patients of the need to avoid factors which precipitate ossification.

FOP has a tendency to progress erratically and the oldest patients are the most disabled. Most patients are chair-bound or bed-bound by the age of 30 yr [10], with an average age at death of 34.7 yr [7], the end result being a literal "stone-man".

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