Neurosurgical management of symptomatic thoracic spinal ossification in a patient with fibrodysplasia ossificans progressiva

Case report

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Fibrodysplasia ossificans progressiva (FOP) is a rare genetic disorder characterized by heterotopic ossification of soft connective and muscle tissues, often as the result of minor trauma. The sequelae include joint fusion, accumulation of calcified foci within soft tissues, thoracic insufficiency syndrome, and progressive immobility. The authors report a patient with FOP who developed severe spinal canal stenosis in the thoracic spine causing substantial myelopathy. He underwent a thoracic laminectomy and resection of a large posterior osteophyte. Unique considerations are required in treating patients with FOP, including steroid administration to prevent ossification and anesthetic technique. The nuances of neurosurgical and medical management as they pertain to this disease are discussed. (DOI: 10.3171/2011.11.SPINE1164)

Key Words • fibrodysplasia ossificans progressiva • myelopathy • thoracic spine • neurosurgery

Fibrodysplasia ossificans progressiva is a rare genetic disorder with a prevalence of approximately 1 in 2 million individuals, without a significant sex or ethnic predilection. The majority of cases arise spontaneously, although the disease can be inherited in an autosomal dominant pattern. The genetic locus in this disease has been isolated as a recurrent mutation in ACVR1/ALK2, a bone morphogenetic protein Type I receptor, which was reported in all sporadic and familial cases of classic FOP. The hallmark of the disease is the ectopic ossification of skeletal muscle and soft connective tissues, including tendons, ligaments, aponeuroses, and fasciae after the initial formation of a cartilaginous precursor lesion. These lesions arise independently, often beginning along the upper back and neck; however, the natural progression of the disease can be altered by soft-tissue injury, which can precipitate new foci of heterotopic bone formation. Surgical removal of heterotopic bone may result in further episodes of bone growth.

Fibrodysplasia ossificans progressiva often presents with cervical spine anomalies. Neck stiffness is an early finding, even prior to the appearance of heterotopic ossification at that site. Pathological features often include large posterior elements; tall, narrow vertebral bodies; and fusion of the facet joints between C-2 and C-7. The literature currently does not report any cases of progressive myelopathy associated with this disease.

Surgical intervention in patients with FOP has the added risk of delayed ossification within the operative site, and is avoided if possible. However, when surgery is clearly necessary, there is anecdotal evidence that glucocorticoids may be used to reduce the likelihood of disease flare-up at the surgical site. Special anesthetic issues, including possible decreased pulmonary function, must also be considered in patients with FOP requiring surgery. Currently, there are no therapies that are efficacious in altering the natural history of the disease. This case study describes a patient with FOP who developed severe myelopathy from a focus of heterotopic bone formation in his thoracic spinal canal and required surgery to preserve motor function. The special considerations of the operative and perioperative treatment of this patient are discussed.
Case Report

History. This 34-year-old Asian man presented with progressive weakness of his legs and midback pain. His medical history was notable for FOP and stable, compensated hydrocephalus. Fibrodysplasia ossificans progressiva was diagnosed at the age of 26 years when he developed heterotopic bone growth with spontaneous fusion following repair of the anterior cruciate ligament in the right knee. It was determined that this was a phenotypic variant of FOP, because the patient’s advanced age at presentation and slow progression are less typical of the natural history of the disease.1 Over a period of several months he developed increasing gait difficulty with falling, to the point of requiring a walker for ambulation. He also noted decreased sensation to the level of his groin, with constipation and occasional incontinence of urine.

Examination. Physical examination showed 4/5 strength and hyperreflexia throughout both lower extremities. His left toe was upgoing. Vibratory and positional senses were decreased in both legs, while pain and temperature senses were normal. An MR imaging study of the spine revealed a T9–10 posterior osteophyte causing marked focal compression of the spinal cord, with increased cord signal on T2-weighted sequences (Fig. 1A and B). A CT scan demonstrated the focal osteophyte possibly arising from the lamina or posterior ligaments (Fig. 1C and D). He presented to the attending neurosurgeon (E.H.E.) in clinic 4 months after the onset of his symptoms.

Operation. After consultation with the anesthesiologist and neurologist previously caring for the patient, thoracic laminectomy for decompression of his spinal cord was performed. As part of a recommended protocol for patients with FOP,3,5 30 mg dexamethasone was administered intravenously immediately prior to the procedure to prevent the development of local ossification. The neurophysiology department was consulted preoperatively, and an agreement was made to do all monitoring with only surface electrodes (not needle electrodes) to reduce potential ossification sites. Transnasal fiberoptic intubation has been recommended in patients with FOP to avoid the risk of stretch injury to the temporomandibular joint, which would lead to joint ossification and inability to open the mouth. In this patient, however, his mouth opening was adequate to comfortably allow transoral fiberoptic intubation with the assistance of a Williams airway. This avoided the potential intranasal trauma caused by nasal intubation as well as the difficulties managing a nasal tube in the prone position. A single intravenous line was used throughout the surgery.

Great care was taken to minimize any potential injury from moving the patient and positioning him prone on the Jackson table. Particular attention was paid to avoiding hyperextension or excessive stretch to any joints at any time during positioning and throughout the surgery. A midline incision was performed at T9–10 and electrocautery was used for hemostasis. Once adequate exposure and localization were achieved, the decompression was performed using a high-speed drill to resect the spinous process as well as the lamina of T-9 and T-10. We identified the substantial posterior osteophyte, which was drilled and elevated using a curette. The underlying dura mater appeared to be partially calcified but very well decompressed. At the beginning of the procedure, somatosensory evoked potentials could not be elicited, but there was improvement after the decompression, especially on the left. A flat Jackson-Pratt drain was tunneled subcutaneously and placed into the wound. The wound was closed with 2 layers of Vicryl suture, and then staples.

Postoperative Course. The patient’s postoperative course showed improvement in his motor strength in both lower extremities. The drain was removed on postoperative Day 1. As per protocol,3,5 he was continued on 2 mg/kg oral prednisone for 4 days postoperatively. He was discharged to acute inpatient rehabilitation on postoperative Day 2, and he stayed there until postoperative Day 12. When he was discharged to home from rehabilitation, he had 5/5 strength in his lower extremities.

Subsequent follow-up with the patient at 2, 8, 26, and 52 weeks after surgery showed continued improvement in gait and decreased sensory symptoms. At last follow-up, 1 year after surgery, he was able to walk with a cane, whereas preoperatively he needed a walker. Postoperative MR imaging studies obtained 3 weeks after surgery showed excellent decompression with no evidence of new heterotopic bone formation. Follow-up MR imaging studies of the spine obtained at 12 months after surgery continued to show good decompression of the thoracic spine. However, there was a new subcutaneous ossified mass

![Preoperative sagittal (A) and axial (B) thoracic T2-weighted MR images, plus sagittal (C) and axial (D) CT scans showing the severe compression of the spinal cord at T9–10 by the osteophyte arising from the posterior elements.](image-url)
Surgery for symptomatic spinal ossification in a patient with FOP

measuring 1.5 × 1.9 cm seen at the tip of the T-8 spinous process in the laminectomy scar (Fig. 2). His wound at that point had healed well, with normal scar formation.

Discussion

Fibrodysplasia ossificans progressiva is characterized by ectopic bone formation within muscle and soft tissues, spontaneously or with minor trauma.1 Patients with FOP may also have thoracic insufficiency with restricted lung volumes secondary to chest wall calcification, although this was not the case in our patient. Over time, patients with FOP may lose mobility due to the progressive soft-tissue ossification. Spinal complications of FOP are generally limited to cervical fusion without compressive myelopathy. We present a patient with FOP who developed a large T9–10 posterior intraspinal osteophyte causing severe spinal cord compression and myelopathy. Although this pathology has not previously been described with FOP, the presence of ectopic bone formation within the spinal canal is consistent with other, systemic lesions seen in patients with FOP.

In our patient, a thoracic laminectomy was necessary for progressive myelopathy, with marked postoperative improvement in the patient’s neurological status. Patients with FOP who are undergoing neurosurgery require special considerations. Perioperative and postoperative glucocorticoids are recommended to minimize acute flare-ups of the disease5 and hopefully reduce heterotopic bone formation at the operative site. Because surgical trauma can lead to further bone formation, minimizing the operative exposure as much as possible should be a goal of surgery in patients with FOP. Extreme care must be taken in moving and positioning these patients to avoid even small injuries, and extra special attention to padding all pressure points is required.

Minimizing tissue trauma is quintessential in surgery for patients with FOP. Consistent with this pursuit, we used only a single intravenous line during surgery and obtained no blood draws postoperatively. We also decided to forgo the use of motor evoked potential monitoring to avoid soft-tissue trauma associated with electrode placement and the often intense muscular contractions seen with stimulation.

Our surgery successfully produced a lasting decompression that allowed significant neurological recovery for the patient. However, we were not able altogether to avoid ossification in the surgical site. Our follow-up is limited and we cannot exclude the possibility that further ossification within the surgical site may occur in the future. The patient will continue to be followed to ensure that the heterotopic ossification within the surgical area does not cause further cord compression and myelopathy.

In general, there exist several important considerations in the surgical treatment of patients in whom FOP has been diagnosed. This includes limiting surgery only to strongly indicated cases and minimizing trauma to the patient whenever possible, because unnecessary surgical intervention may lead to worsening of the patient’s condition.5,10 Management with perioperative and postoperative glucocorticoids may help decrease the incidence of disease flare-ups at the surgical site.5 Thiazolidinediones, which have a known effect of increasing mesenchymal cell differentiation from osteoblasts to adipocytes, also show some promise with reducing FOP flare-ups. Indeed, there has been a report of successful treatment of FOP with rosiglitazone.7 However, this should be used with caution due to the known side effect of increased risk of bone fractures with this drug.7 In the future, targeted molecular therapies may be used in the treatment of FOP, especially since the ACVR1/ALK2 signaling pathway has been identified as the genetic culprit for the disease. Recent studies conducted using an animal model for FOP have shown that inhibition of the signaling cascade downstream of ACVR1/ALK2 can attenuate heterotopic ossification.10 Such targeted therapies are promising, and will probably be tested clinically in the near future.

Disclosure

The authors have no competing interests to disclose. Dr. Fink is a consultant for Maquet Datascope and Procter and Gamble, and he is employed as an editor by AHC Media.

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