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Head and neck manifestations of fibrodysplasia ossificans progressiva: Clinical and imaging findings in 2 cases

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ABSTRACT

Fibrodysplasia ossificans progressiva is a rare hereditary disorder characterized by progressive heterotopic ossification in muscle and connective tissue, with few reported cases affecting the head and neck region. Although plain radiographic findings and computed tomography features have been well documented, limited reports exist on magnetic resonance findings. This report presents 2 cases of fibrodysplasia ossificans progressiva, one with limited mouth opening due to heterotopic ossification of the lateral pterygoid muscle and the other with restricted neck movement due to heterotopic ossification of the platysma muscle. Clinical findings of restricted mouth opening or limited neck movement, along with radiological findings of associated heterotopic ossification, should prompt consideration of fibrodysplasia ossificans progressiva in the differential diagnosis. Dentists should be particularly vigilant with patients diagnosed with fibrodysplasia ossificans progressiva to avoid exposure to diagnostic biopsy and invasive dental procedures. ***(Imaging Sci Dent 2023; 53: 257-63)***

KEY WORDS: Myositis Ossificans; Ossification, Heterotopic; Tomography, X-ray Computed; Magnetic Resonance Imaging

Fibrodysplasia ossificans progressiva (FOP) is a rare genetic disorder characterized by the progressive heterotopic ossification of soft tissues. This condition typically manifests in the first decade of life, with a mean age of onset of 5 years.[1] The first sign of FOP is multifocal soft tissue swelling, accompanied by fever and tenderness. As the endochondral process of lamellar bone formation progresses, symptoms progress into a rigid synostosis of major joints in the axial and appendicular skeleton.[2] Since the disease develops systemically, most patients with FOP become wheelchair-bound by their third decade of life and often experience fatal pulmonary complications in their fifth decade.[3]

As heterotopic ossification progresses in the head and neck region, it gradually restricts mouth opening and neck movement, making it challenging for patients with FOP to maintain regular oral feeding and good oral hygiene.[4] Particular care should be taken to prevent the rapid progression of heterotopic ossification, which can be triggered by traumatic dental procedures in these patients. Few reports are available on FOP in the head and neck region, and the clinicoradiological characteristics of FOP involving the head and neck remain poorly understood. The purpose of this report is to present the clinical features of FOP and the imaging findings on panoramic radiographs, computed tomography (CT), and magnetic resonance (MR) images.

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Case Reports

As this is a case report, the study was granted an exemption by the institutional review board of Seoul National Dental Hospital (IRB047/04-17) due to its retrospective nature.

Case 1

A 12-year-old boy was referred to the authors' affiliated hospital for evaluation of restricted mouth opening. One

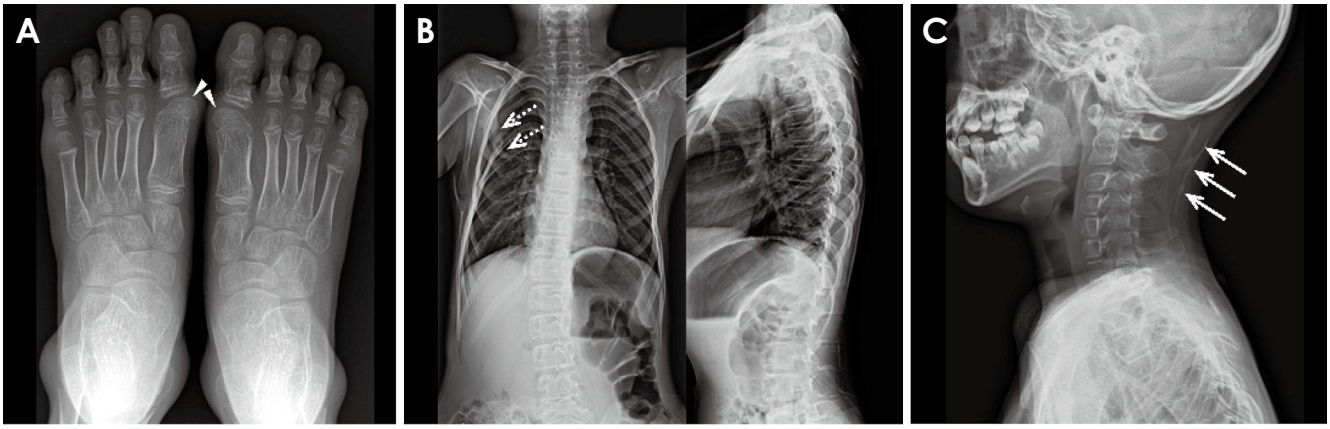

Fig. 1. A. A bilateral weight-bearing dorsoplantar radiograph shows bilateral hallux valgus characterized by medially deviated and deformed first metatarsal heads, as well as deformed first proximal phalangeal bases (arrowhead). B. Full-spine anteroposterior and lateral radiographs show large bars of heterotopic ossification connecting the right scapula to the chest wall (open arrow). C. A lateral skull radiograph reveals a focal linear area of heterotopic ossification in the posterior neck area (arrow).

week prior, he had visited a local dental clinic for multiple dental caries but could not receive treatment due to limited mouth opening. The patient had not previously experienced any issues with food intake or dental treatment. His maximum mouth opening, which was clearly restricted, measured 17 mm. The boy reported pain in his left temporomandibular joint (TMJ) when opening his mouth, and his mandible deviated to the left. Upon palpation, tenderness was observed at both TMJs and the left masseter muscle. Although no sounds were detected at either TMJ, he had a history of intermittent clicking sounds in the left TMJ.

The patient had a complex medical history. In his early childhood, he was misdiagnosed and did not receive appropriate care for FOP. At the age of 3 years, he experienced multiple swellings in the head and neck area, leading to a biopsy. However, he was incorrectly diagnosed with juvenile fibromatosis. Pathologically, the early pre-osseous stage lesions of FOP are composed of highly vascular fibroproliferative tissues that are indistinguishable from juvenile fibromatosis.[2,3] The patient underwent surgery and received postoperative chemotherapy for 6 months. Despite continuous treatment, stiffness in the right shoulder joint and scoliosis progressively worsened. At the age of 9 years, he was fitted with a scoliosis brace to prevent further disease progression. One year later, upon referral to the department of pediatric orthopedic surgery, he was finally diagnosed with FOP through genetic testing. Subsequent skeletal examination revealed bilateral hallux valgus (Fig. 1A), a bar-shaped heterotopic ossification extending from the right scapula to the chest wall (Fig. 1B), fusion of the lamina and narrowing of the disc space in the cervical spine, and linear ossifications in the posterior neck region (Fig. 1C). After his diagnosis, the patient was periodically monitored by orthopedic surgeons and experienced no acute events prior to his visit to the local dental clinic.

Standard and TMJ panoramic radiographs (Figs. 2A and B) were taken at the authors' affiliated hospital. No evidence of ankylosis was observed on either TMJ; however, an enlarged pterygoid plate was observed on the left side. To investigate the cause of restricted mouth opening, CT and MR examinations were performed.

CT images revealed bony growths originating from the left lateral pterygoid plate and subcondylar neck. These growths, which extended toward each other along the left lateral pterygoid muscle, were identified as heterotopic ossification within the lateral pterygoid muscle (Fig. 3A). Additionally, sheet-like heterotopic ossification was observed in the trapezius muscle and nuchal ligament (Fig. 3B), corresponding to the linear radiopacities in the posterior neck region on the lateral skull radiograph.

On T2-weighted and T1-weighted MR images, ossification within the lateral pterygoid muscle appeared as a hyperintense signal lesion with a dark signal intensity rim, indicative of fatty bone marrow encased by cortical bone (Fig. 4). No evidence was observed of pathological changes in either TMJ, and the position of the articular disc in each TMJ was normal in both closed- and open-mouth positions.

The ossification of the left lateral pterygoid muscle, which plays an important role in mouth opening, was determined to be the cause of the mouth restriction. The patient was referred to the department of pediatric dentistry for treatment of multiple dental caries. General anesthesia was

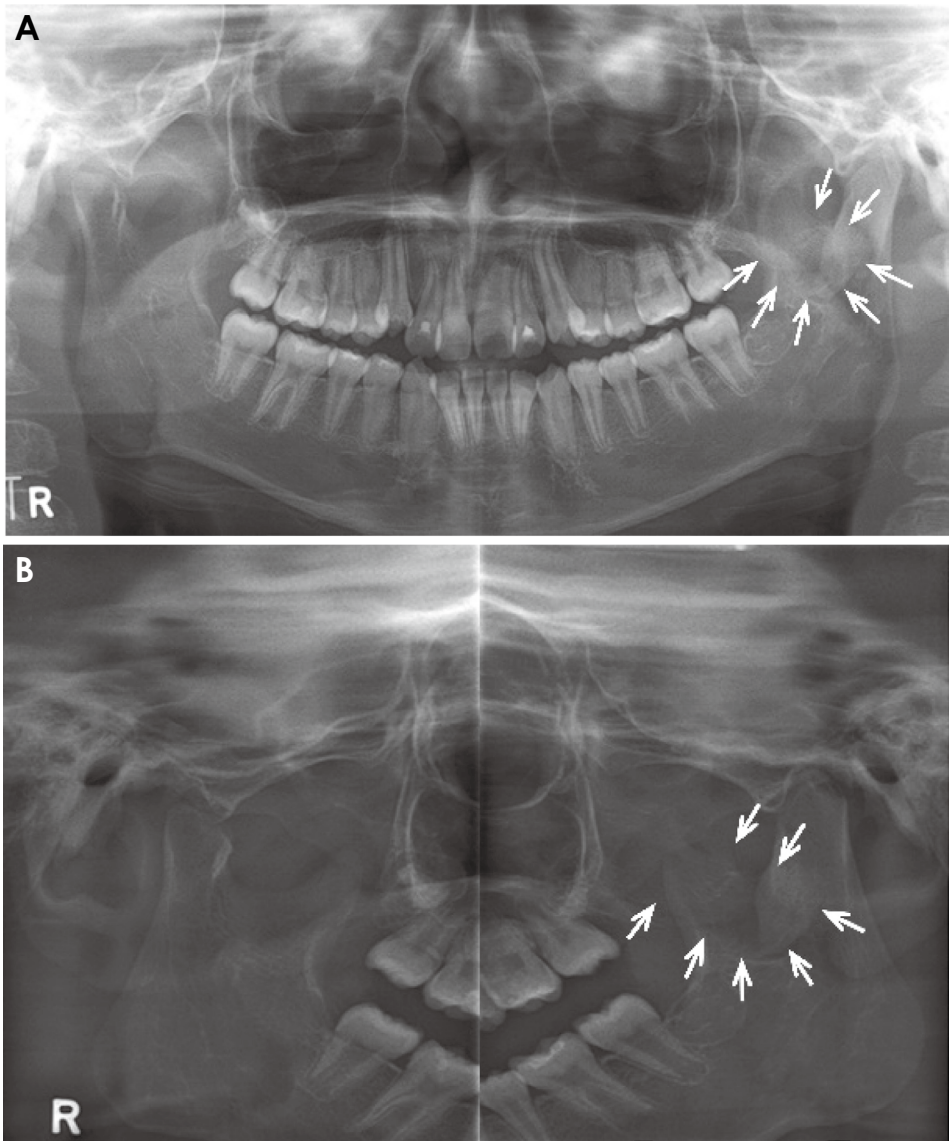

Fig. 2. A standard panoramic radiograph (A) and a temporomandibular joint panoramic radiograph (B) display an enlarged left pterygoid plate (arrow).

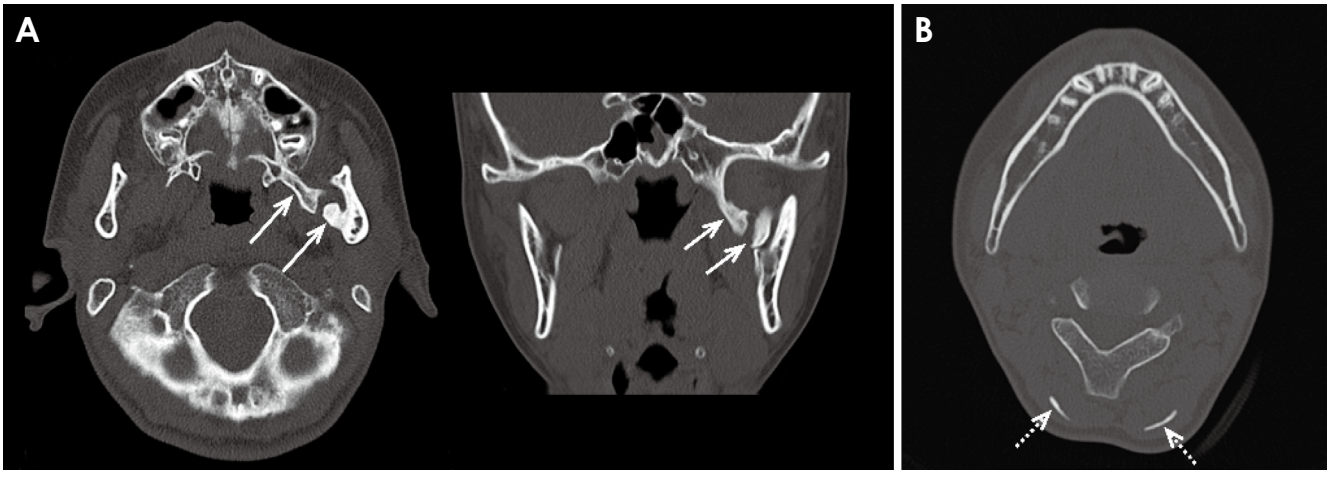

Fig. 3. A. Axial and coronal computed tomography images display heterotopic bone formation in the left lateral pterygoid muscle, extending from the left subcondylar neck to the lateral pterygoid plate (arrow). B. An axial computed tomography image reveals sheet-like heterotopic ossification of the trapezius muscle (open arrow).

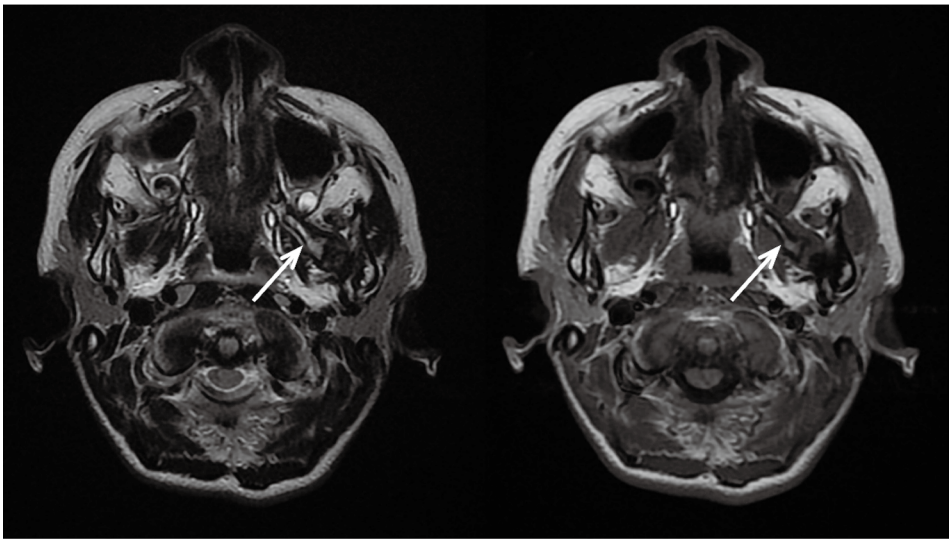

Fig. 4. Magnetic resonance images display a hyperintense lesion with T1 and T2 signals, encircled by a hypointense T1 and T2 signal rim in the inferior portion of the left lateral pterygoid (arrow).

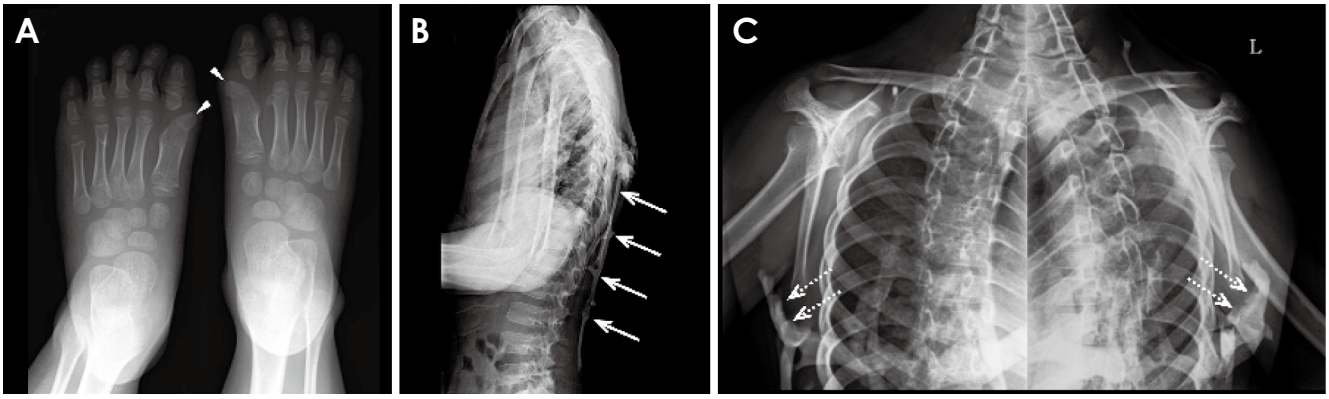

Fig. 5. A. A bilateral weight-bearing dorsoplantar radiograph displays hallux valgus on both sides (arrowhead). B. A lateral neutral radiographic view of the thoracolumbar spine reveals heterotopic ossification of the latissimus dorsi muscle (arrow). C. Bilateral scapular anteroposterior radiographs show heterotopic ossifications at the proximal humerus and chest wall (open arrow).

planned due to the difficulty in mouth opening and dental chair positioning. Several FOP-related conditions were considered before the procedure. First, any trauma during the operation could exacerbate heterotopic ossification. Second, neck extension and rotation were impossible due to instability in the atlanto-axial joint complex and scoliosis. Third, the maximum mouth opening distance was approximately 2 fingers wide. A fiber-optic bronchoscope was utilized during nasotracheal intubation, and total intravenous anesthesia was chosen over inhalation anesthesia. Composite resin fillings for 14 teeth and fluoride varnish application were conducted during the operation. The patient and his parents were advised to maintain good oral hygiene. At his last follow-up, 2 years and 7 months after the treatment, the degree of mouth opening was preserved, and no additional symptoms were reported related to the worsening of FOP.

Case 2

An 8-year-old boy with limited neck movement was referred to us by a pediatric orthopedist for the treatment of luxated deciduous mandibular anterior teeth resulting from a fall.

At the time of referral, the patient had already been diagnosed with FOP, following a complex medical history preceding this diagnosis. When the patient was 5 years old, he experienced swelling and pain in the occipital region, which gradually developed into a hard mass. A month later, another swelling appeared on his left shoulder, prompting a diagnostic biopsy. Initially, he was misdiagnosed with juvenile fibromatosis, similar to the previous case. Subsequently, multiple swellings repeatedly emerged in the neck and shoulder area. Three months after the initial swelling, the patient began to struggle with daily activities, such as

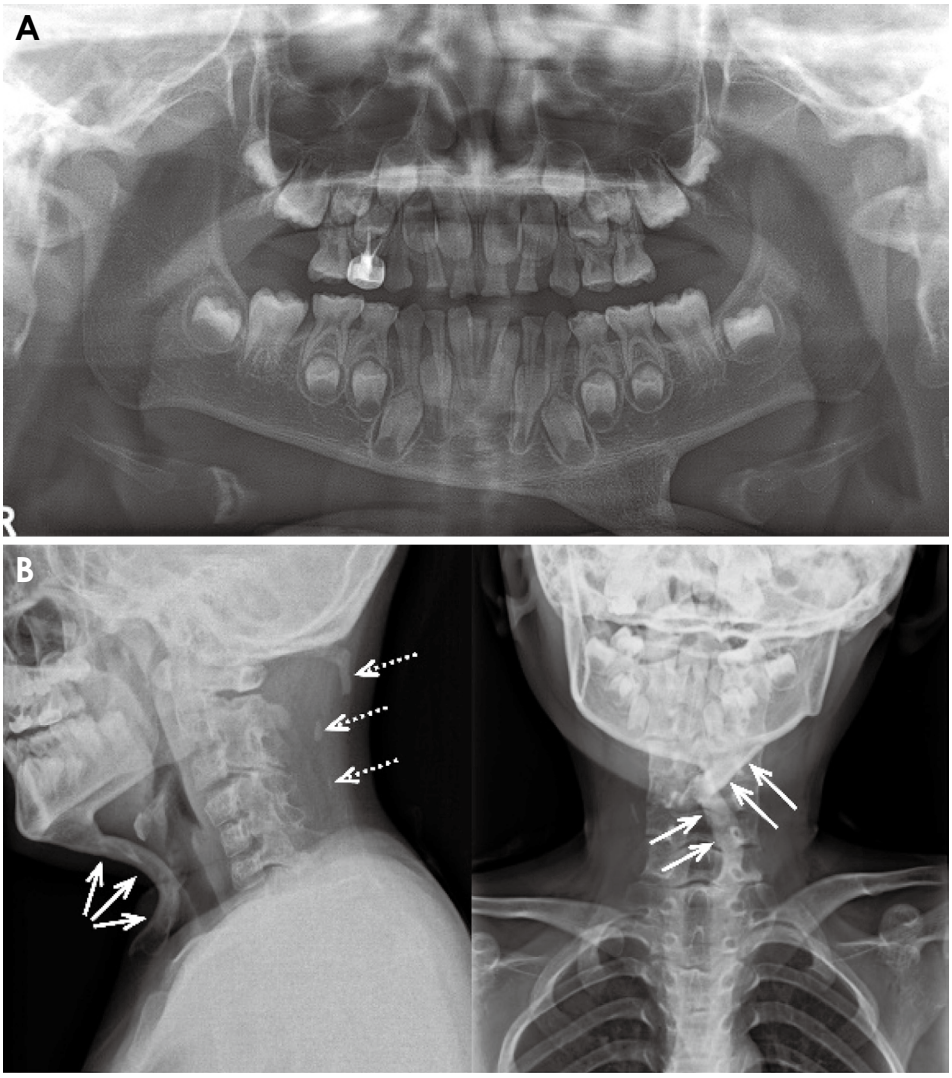

Fig. 6. A. A standard panoramic radiograph displays heterotopic triangular ossification extending from the inferior border of the mandible. B. Lateral and anteroposterior skull radiographs depict heterotopic ossifications along the ventral (arrow) and dorsal (open arrow) neck muscles.

changing clothes. At this point, a pediatric orthopedic surgeon discovered a malformation of the great toes (Fig. 5A) and suspected FOP. Following a genetic examination, the patient was ultimately diagnosed with FOP with the activin receptor type 1 (ACVR1) R206H mutation. A skeletal examination revealed partial ossification of the latissimus dorsi muscle (Fig. 5B) and ossifications between the proximal humerus and the chest wall (Fig. 5C).

At the hospital, a panoramic radiograph (Fig. 6A) was taken to assess the trauma associated with the anterior mandible. This radiograph revealed heterotopic triangular ossification extending from the inferior border of the mandible. In both lateral and postero-anterior skull projections (Fig. 6B), the ossification was observed to extend along the ventral neck muscle to the jugular notch. Additionally, heterotopic ossifications were noted on the trapezius muscle and nuchal ligament.

On MR images of the head and neck (Fig. 7), a tubular-shaped lesion exhibiting hyperintense T1 and T2 signals, outlined by a dark signal rim, was observed. This lesion extended downward from the inferior border of the left mandibular parasymphysis to the jugular notch, suggesting ossification of the platysma muscle. Additionally, a narrowing of the disc space at the C4/C5 and C5/C6 levels, as well as central canal stenosis with fusion at the C3/4 level, were revealed.

Extraction of the primary mandibular central incisors was planned. To prevent trauma from dental procedures, which can aggravate heterotopic ossification, subcutaneous local infiltration anesthesia and extraction were carefully performed. A follow-up panoramic radiograph taken 10 months after extraction showed normal eruption of the permanent mandibular anterior teeth, with no signs of advanced heterotopic ossification. Additionally, a clinical examination confirmed a normal range of mouth opening.

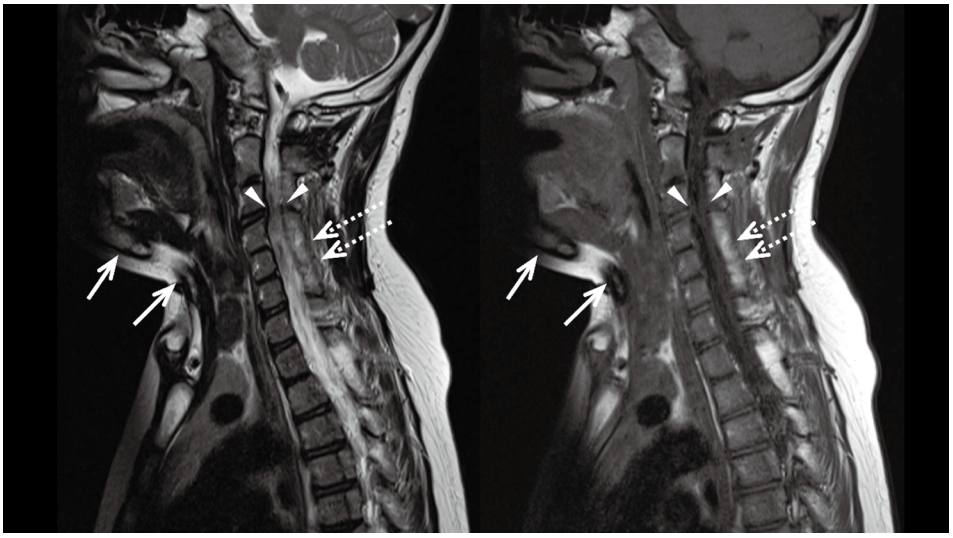

Fig. 7. A magnetic resonance image shows tubular heterotopic ossification extending downward from the inferior border of the mandible to the jugular notch (arrow), fusion of facet joints at the C4/C5 and C5/C6 levels (open arrow), and central canal stenosis at the C3/4 level (arrowhead).

Discussion

In the head and neck region of patients with FOP, heterotopic ossification typically occurs in the masticatory muscles.[4-9] This ossification can be triggered by trauma, which may lead to a progressive limitation of mouth opening. Heterotopic ossification is also frequently observed in the nuchal ligaments and adjacent dorsal neck muscles, such as the trapezius muscle.[10,11] Although rare, heterotopic ossification of ventral neck muscles, including the platysma muscle, can occur.[12] When neck muscles are affected by ossification, the range of neck motion becomes restricted. Abnormalities of the cervical spine often accompany this ossification, with characteristic anomalies including fusion of facet joints between C2 and C7.[13] Most of these features were present in the 2 cases discussed here.

Unfortunately, both patients had been initially misdiagnosed with juvenile fibromatosis. Such misdiagnoses can result in unnecessary procedures and detrimental iatrogenic outcomes for patients with FOP. Pathologically, early preosseous stage lesions of FOP are composed of highly vascular fibroproliferative tissues, which are indistinguishable from juvenile fibromatosis.[2,3] In a study involving 138 patients with FOP, only 13% received an initial diagnosis of FOP.[14] The classic FOP phenotype includes congenital malformation of the great toe, also known as hallux valgus, and phalangeal synostosis.[15] These features can be observed at birth and may serve as an initial diagnostic indicator.[16] A definitive diagnosis of FOP relies on the detection of the *ACVR1* gene mutation in the bone morphogenic protein (BMP) type I receptor. Constitutive activation of *ACVR1* increases BMP4 expression, decreases BMP antagonism, triggers ectopic chondrogenesis, and promotes joint fusion.[17] The classic *ACVR1* gene mutation was confirmed through genetic screening in both patients described in this report.

An early and accurate diagnosis of FOP is crucial before patients undergo dental procedures. Imaging plays a critical role in diagnosing FOP, but the findings may vary depending on the maturity of the lesion. On CT images, early-stage lesions appear as swellings of muscle bundles with effacement of fascial planes. In the mature stage, ossified sheets replacing entire muscles and fascial planes are clearly visible. Mature lesions typically present in 2 ways: a column of new bone replacing an entire muscle or a plate of new bone outlining the fascial plane.[15] These changes can be seen on plain radiographs, but are evident earlier on CT. MR findings also depend on the maturity of the lesions. On T1-weighted images, early lesions are isointense to normal muscles, and a mass effect can be observed only through the displacement of fascial planes. Early lesions appear as homogeneous hyperintense soft tissue masses with surrounding edema on T2-weighted images. This hyperintensity decreases as the lesion matures. Late-stage imaging reveals a hypointense signal on both T1- and T2-weighted images, resulting from fibrous or ossified tissues.[18] In the present cases, heterotopic ossification of the lateral pterygoid muscle and platysma muscle was observed as an inner hyperintense signal lesion with an outer dark signal intensity rim on both T1- and T2-weighted images. This finding corresponds to a column of new bone with fatty marrow. This type of ossification with inner fatty marrow has not been reported in previous studies. In the present authors' opinion, the fatty replacement in the inner part of the ossification is also related to the maturity of the lesion. MR imaging is not sensitive for detecting soft tissue ossification, and its findings can be nonspecific depending on the course and progression of FOP. However, MR can re-

veal the initial lesion before ossification occurs. The lesion spreads along fascial planes, and such a manifestation can be a helpful diagnostic finding on MR images.

So-called atraumatic procedures are crucial in dental treatment, especially for patients with FOP. Invasive procedures, such as dental anesthesia and surgical extraction, can cause iatrogenic damage to nearby soft tissues and exacerbate the disease. For instance, injecting local anesthesia requires careful consideration, as it may increase the risk of heterotopic ossification.[19] Subcutaneous and intravenous injections are known to pose less risk than deep intramuscular injections, which can lead to a higher likelihood of ossification in patients with FOP.[20] As a result, dental injections should be limited to subcutaneous local infiltration, and nerve blocks should be avoided. General anesthesia for these patients also presents challenges. Limited mouth opening, a stiff neck, and cervical vertebrae fusions make tracheal intubation difficult. Heterotopic ossification of chest walls and scoliosis can impede pulmonary ventilation. Utilizing a fiber-optic bronchoscope during endotracheal intubation and intravenous anesthesia is the preferred method for airway management.[4] Given these factors, preventive dentistry is strongly recommended over reparative dentistry. Regular visits, oral hygiene instruction, and nutritional counseling are essential.

In patients with FOP, ossification often occurs in the head and neck region, specifically within the masticatory muscles and superficial neck muscles, which are susceptible to minor trauma. Clinical observations of limited mouth opening or restricted neck movement, along with radiological evidence of related heterotopic ossification, should prompt consideration of FOP in differential diagnoses. Dentists must exercise particular caution regarding patients with FOP to avoid exposing them to potentially traumatic and invasive dental procedures.

Conflicts of Interest: None

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