Dysphagia in Two Cases of Fibrodysplasia Ossificans Progressiva

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Abstract

Fibrodysplasia Ossificans Progressiva (FOP) is an autosomal dominant genetic disorder caused by a heterozygous mutation in the ACVR1 gene. It is characterized by progressive heterotopic ossification (HO) and developmental skeletal defects. In this study, we assessed the swallowing function in two patients with FOP presenting the limited mandibular opening.

The computed tomography scans of case 1, a 56-year-old female, and case 2, a 66-year-old male, demonstrated HO of the medial pterygoid muscle between the mandibular ramus and lateral pterygoid plate. With limited mandibular movements, they usually ate a puree diet through their teeth with assistance. In case 2, HO of the suprathyroid and infrahyoid muscles between the mentum and collarbone, including the hyoid bone, was observed. On the fiberoptic endoscopic evaluation of swallowing and modified barium swallow, some foods were found to be retained in their pharynx even after repeated swallowing with the limited laryngeal elevation.

These findings suggest that dysphagia in patients with FOP may be caused not only by the limited mandibular opening but also by the limited laryngeal elevation. However, further studies are required to generalize dysphagia in patients with FOP based on these findings.

Keywords: Fibrodysplasia ossificans progressiva; Limited mandibular opening; Limited laryngeal elevation; Swallowing disturbance; Modified barium swallow.

Abbreviations

CT: Computerized Tomography; FOP: Fibrodysplasia Ossificans Progressiva; HO: Heterotopic Ossification; TMJ: Temporomandibular Joint; MBS: Modified Barium Swallow; FEES: Fiberoptic Endoscopic Evaluation of Swallowing.

Introduction

Fibrodysplasia ossificans progressiva (FOP) is a very rare inherited connective tissue disorder characterized by progressive heterotopic ossification (HO) and developmental skeletal defects [1–3]. This autosomal dominant genetic disorder is caused by a heterozygous mutation in the ACVR1 gene (OMIM135100) with R206H and some variant mutations currently reported [4–6]. The prevalence of FOP is estimated to be approximately 1 in 2 million [1–3]. During early childhood, most patients with FOP develop inflamed swellings which transform into HO, typically in the axial regions [7,8]. Typical symptoms are severe limitations of movement owing to the progressive immobilization of the limbs, jaw, and chest wall. Most patients die in their fifties and sixties frequently due to respiratory failure. A previous report recommended the high-calorie food pureed or semisolid to compensate the masticating and swallowing difficulty and minimizes weight loss as a result of submandibular flare-ups [9].

Although ankylosis of the temporomandibular joint (TMJ) is involved in approximately 70% FOP, it does not cause dysphagia. However, submandibular flare-ups, which are common at any age, frequently lead to swallowing problems and dysphagia [7–9]. Several reports suggest that not only ankylosis of the TMJ but also HO of the pterygoid muscles is involved in the limited mandibular opening with nutrition problems and weight loss [10,11]. However, precise causes underlying swallowing difficulty have not been clarified to date. Conversely, no cases involving the extracutaneous muscles, facial muscles, tongue, larynx, esophagus, diaphragm, intestines, sphincter muscles, or skin have been reported [12].

We reported two patients with FOP assessing the cause of the limited mandibular opening and swallowing dysfunction using the modified barium swallow (MBS) and fiber optic endoscopic evaluation of swallowing (FEES). This is the first report analyzing the mechanism of dysphagia in two patients with FOP and proposing an effective way to adjust the diet form based on the pathomechanism.

Case Reports

Case 1

At the age of 10 years, the female patient demonstrated neck hypomotility and experienced a gradual progression of HO and ankylosis of the joints throughout the body. She needed crutches in high school and was diagnosed with FOP in a university hospital based on the clinical symptoms. Since then, she had lived in a care facility. From the age of 39 years, she presented with jaw hypomotility and gradually decreased food intake by eating. At the age of 56 years, she was admitted to the Department of Neurology, Omuta National Hospital (Fukuoka Japan), for seeking medical care for the limited mandibular opening.

She was found to carry the R206H mutation in the ACVR1 gene and was diagnosed with classic FOP. She weighed 37.3 kg and exhibited rigidities and fixed contractures in joints throughout the body. She was bedridden the whole time. Although she had bilateral short hallux and her hearing difficulty required her to wear an acoustic aid, she did not have respiratory disturbances. The limitation of mandibular movement was severe with a range of motion within 1mm and allowing her to eat only a puree diet through her teeth with assistance.

Case 2

The male patient demonstrated stiffness and hypomotility surrounding the bilateral axilla at the age of 10, claudication due to stiffness in the right hip joint at the age of 13, ankylosis in the right knee at 15, the left elbow at 18, and the right elbow at 25. After 33 years, he exhibited jaw hypomotility and trismus. At 36 years, he was unable to walk due to ankylosis of the left hip and knee joints, left thigh swelling, and pain and was admitted to the Department of Neurology, Omuta National Hospital for medical care.
He was found to carry the Gly356Asp mutation in the ACVR1 gene and was, thus, diagnosed with FOP. Owing to the limited mandibular opening, his diet was gradually changed from soft rice and chopped side dishes to puree. He weighed 32.2 kg and exhibited rigidities and fixed contractures in joints throughout the body. He was bedridden the whole time. Although he had deficits at the bilateral hallux and bilateral sensorineural hearing loss, he did not present respiratory troubles. His mandible hardly moved, and he ate a puree-based diet through his teeth with assistance.

The computerized tomography (CT) images revealed HO of the medial pterygoid muscle between the mandibular ramus and lateral pterygoid plate (Figure 1a and b) on the left side of case 1 at the age of 56 and on the right side of case 2 at the age of 66. Moreover, the images of case 2 revealed HO of the suprahyoid and infrahyoid muscles between the mentum and collarbone, including the thyroid and cricoid cartilages, and the hyoid bone (Figure 2).

They underwent the MBS at the 15° reclining position corresponding to their usual eating position. Since their axial regions were rigid in the 15° reclining position because of multiple HO, it was challenging to adjust the trunk posture to the reclining 30°position as a measure for dysphagia. Both cases swallowed 3–5mL of liquid and jelly, which could be crushed by the tongue, without pharyngeal retention. In case 1, tracing of the mentum movement and the hyoid bone excursion was completed by analyzing the recordings frame-by-frame or in slow motion using the motion analysis software in two dimensions (Dipp-Motion Pro; Ditect, Tokyo, Japan; Figure 3a) [13]. The relative coordinates of the lowest point of the hyoid bone to the two points on the cervical vertebrae were followed, and distances were calibrated by imaging.
the radioactive marker. Presumably, the association of the hyoid movement with the laryngeal movement prevents the passage of food through the upper esophageal sphincter. Reportedly, the range of the hyoid bone movement was 7–8 mm which is similar to that of patients with neuromuscular disorders, who frequently demonstrate obstruction to the passage of bolus at the esophageal entrance [13]. On the FEES, a small piece of a hard cracker remained on the tip of the epiglottis even after repeated swallowing. In case 2, ungrounded rice gruel partially remained in the pyriform sinus even after repeated swallowing in the absence of the mentum movement and hyoid bone excursion (Figure 3b). The laryngeal elevation was assumed to be inhibited by HO of the suprahyoid and infrahyoid muscles between the mentum and collarbone. Owing to the 15° reclining position, neither penetration nor aspiration was observed.

Currently, at the age of 66, case 1 continues to eat a puree diet orally in conjunction with nasoesophageal tube feeding to compensate the insufficient intake caused by anorexia. At the age of 70, case 2 continues to eat a puree diet orally. Nutrition management of these patients is under the guidance of nutritionists and speech therapists to minimize the risk of malnutrition and aspiration.

This study was approved by the ethics committee of the National Hospital Organization Omuta National Hospital. Informed consent for this study was obtained from both participants.

Discussion

This is the first report to evaluate dysphagia in patients’ with FOP. Previously, some case studies have reported the limited mandibular opening in patients with FOP presumably because of HO of the pterygoid muscles [10,11]. However, ankylosis of the TMJ is not necessarily required as a cause of the limited mandibular opening [10]. Notably, CT scans of both patients in our study did not demonstrate ankylosis of the TMJ but HO of the medial pterygoid muscles. It is still unclear which muscles have priority to lead to HO excluding involuntary or visceral muscles, i.e., the extraocular muscles, facial muscles, tongue, esophagus, diaphragm, intestines, sphincter muscles, or skin [12]. HO appeared in jaw-opening muscles and the medial pterygoid muscles in both patients and the suprahyoid and infrahyoid muscles in case 2. In FOP, HO is likely to develop in any muscle beyond limb muscles classified as skeletal and voluntary muscles. Although we could not detect apparent submandibular swelling in both cases [9], we cannot deny the existence of minute swelling. Conversely, we can also not deny the possibility that long-term limited mandibular opening and laryngeal elevation induce swallowing disturbance.

Some case reports have suggested swallowing difficulty in FOP and recommended the high-calorie food, either pureed or semisolid [9], but the swallowing function and causes of dysphagia have not been analyzed. Although case 1 demonstrated laryngeal elevations within 7–8 mm, which is about half of those in healthy individuals [13], a small piece of hard food could not pass through the esophageal entrance. Case 2 did not exhibit any laryngeal elevation due to the widespread HO in the larynx involving the hyoid bone and could not make soft solid food, i.e., rice gruel, pass through the esophageal entrance. Difficulties in passing the bolus through the esophageal entrance in these elderly patients were obviously caused by the limited laryngeal elevation which decreases the swallowing pressure and the upper esophageal sphincter relaxation. Arguably, the limited laryngeal elevation can be considered a type of disuse syndrome in FOP. In possible rare causes of dysphagia [14,15], pathology affecting the TMJ can impair the formation of a food bolus and cause oropharyngeal dysphagia [16]. However, the long-term limited mandibular opening in FOP will induce various peculiar swallowing dysfunctions. Many cases in previous reports did not undergo the MBS or FEES and most were young patients, in the age of 10–30 years [9,10], therefore they possibly did not present clear symptoms underlying the swallowing dysfunction.

The swallowing dysfunction in both patients may be caused not only by the limited mandibular opening but also by the limited laryngeal elevation. However, further studies are required to generalize dysphagia in patients with FOP based on these findings. Our results highlight the need for medical staff to be aware of difficulties in passing foods through the pharynx in addition to trismus. Prevention of malnutrition in patients with FOP requires HO sites identification using CT images, swallow function evaluation by the MBS, and diet adjustment based on dietary guidance by nutritionists and speech therapists.

Acknowledgments

We are grateful for the support of this work by the Japan Society for the Promotion of Science and Grants-in-aid for Scientific Research (17K12069).
Conflict of Interest

Authors have no competing interest.

References


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Received Date: May 14, 2017, Accepted Date: June 30, 2017, Published Date: July 05, 2017.

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