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Case Report

Multiple odontogenic cysts in a patient with Neurofibromatosis–Noonan syndrome

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ABSTRACT

Neurofibromatosis–Noonan syndrome (NFNS) is an uncommon chromosomal disorder showing features of both neurofibromatosis (NF-1) and Noonan syndrome (NS). We encountered a case of NFNS with keratocystic odontogenic tumor and dentigerous cysts. A 19-year-old Japanese girl was referred to our hospital with a chief complaint of swelling in the left side of the mandible. The patient showed symptoms of both NF-1, in the form of café-au-lait spots and neurofibromatosis, and NS, in the form of short stature, intellectual disturbance, webbed neck, and hypertelorism. Panoramic radiography showed three cystic lesions, one on each side of the mandible and one on the left side of the maxilla. All cysts were removed surgically under general anesthesia. Histopathological examination revealed that both mandibular cysts were dentigerous cysts, while the maxillary cyst was a keratocystic odontogenic tumor. No recurrence has been seen as of 5 years postoperatively. Multiple jaw cysts might be added as a potential finding in NFNS.

1. Introduction

Neurofibromatosis–Noonan syndrome (NFNS) is an autosomal-dominant disorder that shows the characteristics of both neurofibromatosis type I (NF-1) and Noonan syndrome (NS) [1]. Seven diagnostic criteria for NF-1 were suggested by the National Institutes of Health in 1988, as follows: (1) six or more café-au-lait spots; (2) two or more lesions representing neurofibromatosis of any type or one plexiform neurofibroma; (3) freckling in the axillary or inguinal regions; (4) optic glioma; (5) two or more Lisch nodules; (6) a distinctive osseous lesion such as sphenoid dysplasia or pseudarthrosis; and (7) a first-degree relative (parent, sibling, or offspring) with NF-1 according to the above criteria. NF-1 is diagnosed with positive findings for two or more of these seven items [2]. Meanwhile, NS is a syndrome showing short stature, chest deformity, congenital heart disease, webbed neck, short neck, and hypertelorism [3].

Bone cysts are the most common lesion occurring in the jawbones. Jaw cysts are usually solitary, and multiple jaw cysts are rare and generally associated with certain syndromes, particularly nevoid basal cell carcinoma syndrome (NBCCS). Jaw cysts have not been identified as a specific characteristic of NFNS. We encountered a rare case of NFNS presenting with multiple jaw cysts. We present this case and discuss the possibility of an association between multiple jaw cysts and NFNS.

2. Case report

A 19-year-old Japanese girl was referred to the Department of Oral Surgery at Nagasaki University Hospital with a chief complaint of swelling on the left side of the mandible in November 2008. Nutritional status was good with a height of 151 cm and a weight of 50 kg. She showed hypertelorism, the prominent epicanthal folds, the short and broad nose with a depressed root, the distinctive upper lip with a deeply grooved philtrum, and the short and wide neck (Fig. 1A). Neurofibromatosis and café-au-lait spots were seen throughout the body (Fig. 1B). Gingival redness and discharge of pus were observed around the crown of a partially impacted mandibular left second molar. Panoramic X-ray showed cyst-like radiolucencies bilaterally in the mandible and in the left maxilla (Fig. 2A). Simple computed tomography (CT) showed cystic

☆ Asian AOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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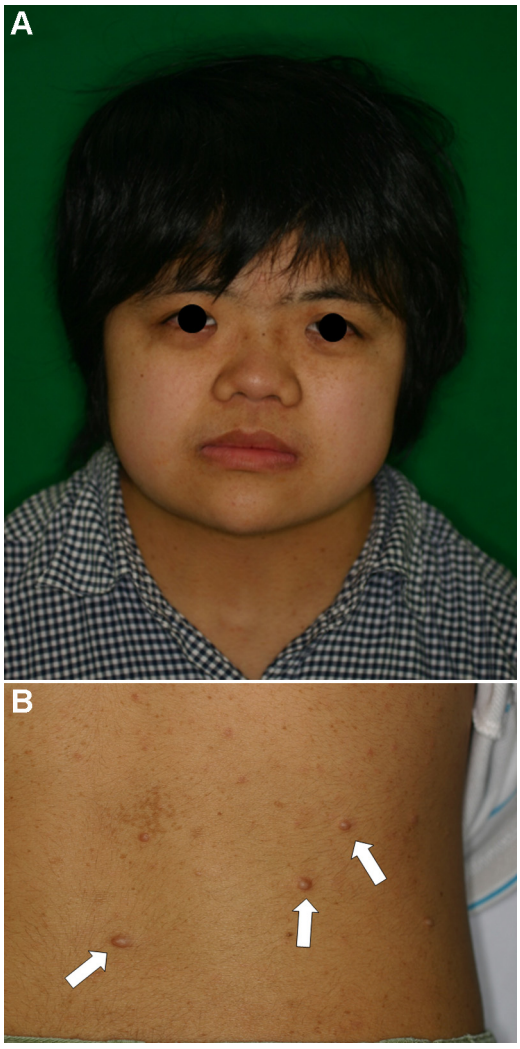

Fig. 1. (A) facial photo at the initial visit. (B) Neurofibromatosis (back).

lesions from the mandibular second molar to the condylar process involving the crown of the third molar on both sides and a cystic lesion in the posterior region of left maxilla (Fig. 3A, B).

In terms of medical history, delayed motor development had been noticed at the 3-month infant examinations. At 4 months, the patient was referred to the Department of Pediatrics at Nagasaki University Hospital due to high fever, poor suckling, and diarrhea, and NFNS was diagnosed based on clinical findings of café-au-lait spots over the whole body, short stature, webbed neck, low hairline, hypertelorism, and shielded chest, but she did not have congenital heart disease. Since her short stature had not been improved, she took growth hormone with the dose of 0.5 U/kg/week from 5 years old to 11 years old. Then, her stature was improved. Family history was non-contributory.

Swelling of the left cheek was noticed at 10 years old and she visited an oral surgery clinic at another hospital. Although panoramic X-rays and CT revealed a unilocular cyst-like lesion in the left mandible, the decision was made to observe the lesion without treatment. Unfortunately, no information was available on whether any other cystic lesions were present at that time. Although jaw cystectomy was planned in 2008, left ovarian tumor found during the preoperative general examination for cystectomy was surgically removed in the Department of Obstetrics and Gynecology at Nagasaki University Hospital in July 2008, and was histopathologically diagnosed as fibroma. Cystectomy was then performed under general anesthesia in April 2009. The mandibular second molars were extracted and the cysts with an impacted third molar on the both side of mandible were removed completely. A cyst with impacted second molar in the left maxilla was also removed. Cottage cheese-like contents were apparent in the cyst. Since keratocystic odontogenic tumor (KCOT) was suspected clinically, a surface layer of bone surrounding the cyst wall was shaved. Primary sutures were placed at each site. No findings suggestive of recurrence were observed during 5 years of follow-up (Fig. 2B).

The lesion in the left maxilla represented a cyst containing fibrosis connective tissue lined by stratified squamous epithelium of uniform thickness. The epithelium showed parakeratosis, and part had invaginated into the fibrous tissue (Fig. 4A, B). Cyst walls on both sides of the mandible represented fibrous tissue covered by thin, stratified non-keratinized squamous epithelium with epithelial processes. Round inflammatory cells had infiltrated the fibrous connective tissue (Fig. 4C), and odontogenic epithelial islands were also seen in the non-inflamed area (Fig. 4D). The cyst in the left maxilla was diagnosed as KCOT, and cysts on both sides of the mandible were diagnosed as dentigerous cyst.

3. Discussion

Odontogenic cysts are the most common lesion arising in the jawbones. These lesions are usually solitary, and multiple jaw cysts are thought to be rare and generally associated with syndromes and systemic conditions. We encountered a case of multiple odontogenic cysts in an NFNS patient, but no previous reports have described cases showing similar conditions. NBCCS is the most common syndrome presenting with multiple jaw cysts, which histopathologically represent KCOTs [4]. Other than NBCCS, orofacial digital syndrome [5], Ehlers–Danlos syndrome [6], Simpson–Golabi–Behmel syndrome [7] and NS [8] can present with multiple KCOTs reportedly in English written literatures, though only a single case report has been reported for each.

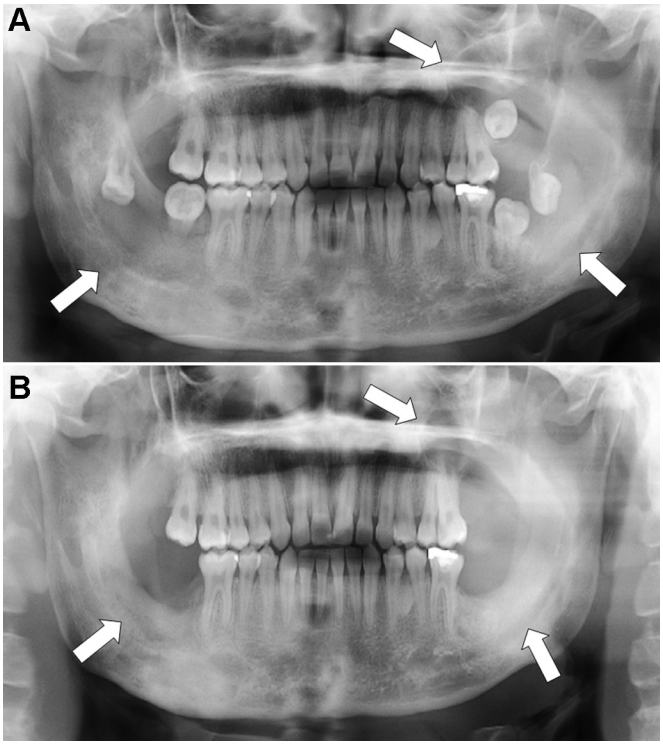

Fig. 2. (A) Pre-surgery (multiple cyst-like radiolucent images in the jaw). (B) Third month after surgery (ossification at the mandibular angle was found).