Multidisciplinary approach for treating malocclusion of patient with basal cell nevus syndrome: A case report

ABSTRACT

Basal cell nevus syndrome (BCNS) is a rare genetic disorder that can be caused by mutation of multiple genes, including *PTCH1*, *PTCH2* and *SUFU*. in an autosomal dominant manner. The symptoms include some craniofacial features such as keratocystic odontogenic tumors (KCOTs), macrocephaly, and cleft lip and/or palate. Although comprehensive orthodontic treatment is frequently required for some of these craniofacial deformities, there are few reports which show the outcomes of comprehensive orthodontic treatment. Here we report a case of BCNS with multiple KCOTs, macrocephaly, skeletal Class III malocclusion, asymmetric dental arch, and mandibular crowding, which was successfully treated with comprehensive orthodontic treatment.

KEY WORDS

Macrocephaly, Orthodontics, Genetics, Dental anomalies

INTRODUCTION

Basal cell nevus syndrome (BCNS) is a generalized disorder which shows autosomal dominant inheritance. It was described initially by Jarisch in 1894 and classified as a distinct syndrome by Gorlin and Goltz (1960). The characteristic craniofacial clinical features include multiple basal cell carcinomas, keratocystic odontogenic tumors (KCOTs) and cleft lip and/or palate. KCOTs usually appear during the first decade of life (in 65% to 86% of patients), more commonly in the mandible than in the maxilla, and most of them are associated with displaced or impacted permanent teeth (Gorlin et al., 1971; Endo et al., 2012). These cysts are typically lined with uniform, stratified squamous epithelium with variable degrees of keratinization. Satellite cysts and epithelial islands, strongly resembling basal cell clusters of the skin, are usually found in the fibrous cyst wall. This suggests that these keratocysts arise from the basal cell layer of the oral epithelium (Stoelinga et al., 1975; Bala et al., 2015; Gorlin 2004). By observing these characteristic features, dentists may be the first clinicians to detect these symptoms. Early diagnosis is important since it minimizes the spread and recurrence of cysts, and it also minimizes consequent loss of teeth and malpositioning of teeth. In the course of dental treatment of BCNS, KCOT enucleation is sometimes performed in association with removing dentition. There is also sometimes a need to retract severely displaced, impacted teeth, and the orthodontist must consider how to manage these situations in order to obtain ideal occlusion. However, there are still only a limited number of case

reports about orthodontic treatment in BCNS, and additional reports are essential for expanding our knowledge and developing optimal methods for managing the occlusion in BCNS (Maroto et al., 1999).

In this case report, we describe a case of BCNS that we treated using a multidisciplinary approach starting with cyst enucleation by oral and maxillofacial surgery, and followed by orthodontic treatment including retraction of impacted teeth and edgewise treatment. A prosthodontic approach was also utilized to fill the gap of dentition after the active orthodontic treatment. At the end of the treatment the patient obtained mutually protected occlusion with improved profile and high satisfaction. Since BCNS is associated with other general medical symptoms which require continuous attention, comprehensive long-term follow-up with occlusal stability management is necessary.

DIAGNOSIS AND ETIOLOGY

A 12-year-old girl was referred to the Department of Oral and Maxillofacial Surgery at ********* with a complaint of swelling in the upper right deciduous canine area. The X-ray examination showed that she had 6 cysts and impacted teeth in the upper right canine area, second molar area, upper left canine area, lower left lateral incisor and canine area, second premolar area and third molar area (Fig 1A, B). Based on other symptoms such as pits palmar,

macrocephaly and hypertelorism, she was diagnosed with BCNS. Genetic testing was not performed.

After all of the surgical procedures (described below) and waiting for possible spontaneous eruption of impacted teeth at the age of 13, diagnostic records were taken in preparation for orthodontic treatment. The extraoral examination showed a straight type profile with long lower facial height and moderate hypertelorism (Fig 2A). Intraoral examination showed that molar relationships were both Angle Class I, and both overjet and overbite were acceptable. The maxilla showed high-arched palate and constricted dental arch with spacing. The mandible dentition showed mild crowding with asymmetrical dental arch and lingually inclined right second molar (Fig 2B). The cephalometric analysis showed large cranial base length (SN, 71.7 mm), the maxilla was anteroposteriorly long (PTM-ANS/PP, 56.8 mm) and ramus length and mandibular body length were long (Ar-Go, 55.6 mm, Go-Me, 76.0 mm) with skeletal Class I relationship (ANB, 3.6º). Although the gonial angle was large (GoA, 134.7º), the mandibular plane angle was within average range (Mp-SN, 38.8º). The maxillary incisors were palatally inclined, while the mandibular incisors showed average inclination (U1-FH, 106.0º, L1-Mp 91.7º) (Fig 2D, Table). The position of the upper right canine had not reached the occlusal plane (Fig 2B, C). The upper right second premolar and lower left second molar were impacted.

After the diagnostic procedures, the patient underwent enucleation of KCOTs and

extraction of associated teeth, including the upper right deciduous canine, second deciduous molar, impacted second molar, upper left deciduous canine, impacted canine, lower left second deciduous molar and third molar. At the same time, the cysts in the lower left lateral incisor area were removed, and fenestration was performed for the cysts in both sides of the maxillary molar area and lower left molar area by an oral and maxillofacial surgeon.

TREATMENT OBJECTIVES

The patient was diagnosed with BCNS with skeletal Class I relationship associated with impacted upper right second premolar and lower left second molar. The treatment objectives were to (1) retract and align the upper right second premolar and canine, and the lower left second molar, (2) correct the lingual inclination of the lower right second molar, (3) relieve the crowding in the mandible by extracting the lower left lateral incisor, (4) expand the maxillary arch and close the extra space to create a proper prosthodontic space for the upper left canine (5) obtain mutually protected occlusion, and (6) retention and prosthodontics for the upper left canine.

TREATMENT ALTERNATIVES

For managing the spaced arch in the maxilla, molar medialization could be utilized to close all of the space instead of using prosthodontics. Additionally, the cleft that had been created in the upper right canine area could have been repaired by closing the space orthodontically (Borzabadi-Farahani 2012; Borzabadi-Farahani et al., 2015). Since the upper left first premolar was already medially inclined, special consideration needed to be taken for medialization, such as using a long hook and TADs for bodily movement. Mild crowding of the lower arch could be treated by interproximal reduction to obtain space. At this time, the patient showed mandibular growth and exhibited a skeletal Class III tendency before the treatment with an edgewise appliance and thus required lingual inclination of lower incisors, which demanded more space than we could get by interproximal reduction. Extraction of the lower premolar on the left side instead of the incisor could have been considered to match the extracted upper left canine, and to prevent center line discrepancy.

TREATMENT PROGRESS

At the age of 13, after the orthodontic diagnosis, the upper right canine and second premolar started to be retracted and aligned by a lingual arch which had an auxiliary hook. At the age of 14, the patient underwent removal of recurrent cysts in the upper right canine area, upper right second molar area, upper left premolar area and lower left second molar area by an oral and maxillofacial surgeon. At the age of 15, her lower right second molar started to be

aligned by a lingual arch to correct the scissors bite. As a result of treatments until this time, midline deviation, spacing in the upper arch, asymmetrical lower dental arch, crossbite of the left second molar, Angle Class III molar relationship on the right side and lower mild crowding remained as orthodontic problems.

After a maxillary and mandibular growth spurt, immediate edgewise orthodontic treatment was recommended. However, she preferred to start the treatment after finishing her university entrance examination. For this reason, the second phase of treatment was started at the age of 18 (Fig 3A-D). To relieve the crowding in the lower arch, the left lateral incisor was extracted. After that, edgewise appliances were attached on the entire arch in order to align the upper and lower arch. Prosthodontic space was created at the position of the upper left canine. After the orthodontic treatment continued for 3 years, all appliances were removed and a Begg type retainer on the upper arch and a fixed retainer on the lower arch were placed for retention. Posttreatment records were taken after the prosthodontic treatment was finished with an adhesive extension bridge (Fig 4A-D).

TREATMENT RESULTS

After the first phase of orthodontic treatment using a lingual arch, the upper right canine and second premolar were erupted and retracted into the level of the dental arch. However, some of the problems still remained at the time of the second phase of orthodontic

treatment. Cephalometric superimposition indicated vertical and horizontal mandibular growth from the first phase until the beginning of the second phase treatment, which resulted in a concave type facial profile (Fig 3, 5).

After the active edgewise orthodontic treatment, mutually protected occlusion was obtained with a comprehensive approach. The posttreatment photographs showed proper overjet and overbite. The molar relationship was Class III on the right side and Class I on the left side (Fig 4B). The upper dental arch was expanded and space was accumulated at the area of the upper left canine for prosthodontic treatment. The dental midline of the maxilla coincided with the facial midline. Mandibular crowding was eliminated by extraction of the lower left lateral incisor. The cross bite on the left second molar remained. The upper incisor showed labial inclination, as U1-FH changed from 110.3º to 114.2º. The upper molar showed mesial movement, which contributed to improving the spaced arch of the maxillary arch. The lower incisor showed slight lingual inclination (L1-FH 54.5° to 57.8°) and extrusion after lateral incisor extraction, which contributed to maintaining positive overjet and overbite. The lower molar showed mesial movement and resulted in an Angle Class III relationship on the right side. We could have reinforced the molar anchorage in the lower arch to obtain a better overjet and molar relationship. Adequate prosthodontic space was created at the upper left canine (Fig 4B).

DISCUSSION

Congenital craniofacial defects frequently result in severe malocclusion and require comprehensive dental treatment, including orthodontics (Nakatsugawa et al., 2019). BCNS is one of the genetic diseases which exhibit multiple craniofacial deformities (Maroto et al., 1999). The causative genes (*PTCH1*, *PTCH2* and *SUHU*) for BCNS are known to work as mediators for the Sonic Hedgehog (*SHH*) signaling pathway. It is well known that disrupting the *SHH* signaling pathway can cause a wide range of craniofacial phenotypes to occur (Hu et al., 1999; Kurosaka et al., 2014; Kurosaka et al., 2015).

BCNS is a congenital disease that is associated with elevated *SHH* signaling, and with a variety of craniofacial phenotypes including facial clefting and dental anomalies such as delayed eruption with KCOTs (Mui et al., 2017; Smith et al., 2014). Despite the fact that BCNS frequently requires orthodontic treatment, there are still few case reports which show the process of the comprehensive dental treatment. Among many craniofacial symptoms, one of the most significant phenotypes for causing malocclusion in BCNS is multiple KCOTs in the jaw bone, which generally develop in the first decade of life and severely displace teeth. These keratocysts may remain symptom-free but can become very large before they are detected. Frequently, these keratocysts can disrupt adjacent teeth.

In this case report, swelling of the upper right deciduous canine area was observed without pain, and many cysts and ectopic impacted teeth in both sides of the maxilla and in

the left mandible were detected by X-ray examination. A large KCOT in the left side of the mandible probably contributed to development of an asymmetrical lower dental arch. Enucleation of the cysts and associated teeth is frequently required in order to prevent jaw fracture or infection. After these procedures, orthodontic treatment can be effective for correcting the malpositioned teeth and associated malocclusion.

In the present case, some of the impacted teeth spontaneously erupted after the cyst enucleation. These results suggest that one possible solution for impacted teeth in BCNS patients would be waiting for a certain amount of time for the teeth to change their position after the enucleation of KCOTs. However, some of the teeth did not erupt into the oral cavity, and their eruption required orthodontic force. It is important to monitor individual tooth movement after enucleation to identify the teeth which need orthodontic treatment.

Since there are some cases in which permanent teeth have to be removed during the course of KCOT enucleation, the way to close the resultant spaces has to be considered during the orthodontic treatment. In the present case, we decided to utilize an adhesive extension bridge in order to replace the extracted upper left canine. Orthodontic space closure could also be considered for closing the space. Asymmetric extraction would sometimes result in a different occlusal relationship between left and right, which should be taken into consideration when making the treatment plan.

In the present case, an asymmetrical lower dental arch form remained even after the active orthodontic treatment. For this reason, cross bite of the left second molar was not improved even at the end of the treatment. The long-term stability of retracted teeth or the corrected dentition in BCNS has not been well investigated and needs to be carefully monitored. In addition, the general symptoms of BCNS, such as basal cell carcinoma and recurrence of KCOTs, have to be followed during the retention period from an interdisciplinary point of view.

CONCLUSIONS

In this case report we showed successful craniofacial management of BCNS by an interdisciplinary approach. It began with the treatment of KCOTs, which was followed by orthodontic treatment and a prosthodontic approach. Since there is a wide variety of defects among individual patients with BCNS, continuing reports of various cases will be required to expand our knowledge and optimize the orthodontic treatment outcome in BCNS patients.

REFERENCES

Bala Subramanyam S, Naga Sujata D, Sridhar K, Pushpanjali M. Nevoid Basal cell carcinoma syndrome: a case report and review. *J Maxillofac Oral Surg* 2015;14:11-15.

Borzabadi-Farahani A. Orthodontic Considerations in Restorative Management of Hypodontia Patients With Endosseous Implants. J Oral Implantol. 2012;38(6):779-91

Borzabadi-Farahani A, Zadeh HH. Adjunctive Orthodontic Applications in Dental Implantology. J Oral Implantol. 2015;41(4):501-8.

Endo M, Fujii K, Sugita K, Saito K, Kohno Y, Miyashita T. Nationwide survey of nevoid basal cell carcinoma syndrome in Japan revealing the low frequency of basal cell carcinoma. *Am J Med G*enet A 2012;158A:351-357.

Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib. A syndrome. *N Engl J Med* 1960;262:908-912.

Gorlin RJ, Sedano HO. The multiple nevoid basal cell carcinoma syndrome revisited. *Birth Defects Orig Artic Ser* 1971;7:140-148.

Gorlin RJ. Nevoid basal cell carcinoma (Gorlin) syndrome. Genet Med 2004;6:530-539.

Hu D, Helms JA. The role of sonic hedgehog in normal and abnormal craniofacial morphogenesis. *Development* 1999;126:4873-4884.

Kurosaka H, Iulianella A, Williams T, Trainor PA. Disrupting hedgehog and WNT signaling interactions promotes cleft lip pathogenesis. *J Clin Invest* 2014;124:1660-1671.

Kurosaka H, Trainor PA, Leroux-Berger M, Iulianella A. Cranial nerve development requires co-ordinated Shh and canonical Wnt signaling. *PLoS One* 2015;10:e0120821.

Maroto MR, Porras JL, Saez RS, de los Rios MH, Gonzalez LB. The role of the orthodontist in the diagnosis of Gorlin's syndrome. *Am J Orthod Dentofacial Orthop* 1999;115:89-98.

Mui Lee L, Ma L, Jun Li T. Clinical Finding and Management of 12 Orofacial Clefts Cases With Nevoid Basal Cell Carcinoma Syndrome. *Cleft Palate Craniofac J* 2017;54:338-342.

Nakatsugawa K, Kurosaka H, Mihara K, Tanaka S, Aikawa T, Kogo M et al. Orthodontic-Surgical Approach for Treating Skeletal Class III Malocclusion With Severe Maxillary Deficiency in Isolated Cleft Palate. *Cleft Palate Craniofac J* 2019 Mar;56(3):400-407.

Smith MJ, Beetz C, Williams SG, Bhaskar SS, O'Sullivan J, Anderson B et al. Germline mutations in SUFU cause Gorlin syndrome-associated childhood medulloblastoma and redefine the risk associated with PTCH1 mutations. *J Clin Oncol* 2014;32:4155-4161.

Stoelinga PJ, Cohen MM, Jr., morgan AF. The origin of keratocysts in the basal cell nevus syndrome. *J Oral Surg* 1975;33:659-663.

FIGURES

Fig 1. Pretreatment radiographic records of the patient. A, panoramic radiograph; B, frontal radiograph.

Fig 2. Diagnostic records of first phase treatment. A, pretreatment facial photographs; B, pretreatment intraoral photographs; C, panoramic radiograph; D, lateral cephalogram.

Fig 3. Diagnostic records of second phase treatment. A, pretreatment facial photographs; B, pretreatment intraoral photographs; C, panoramic radiograph; D, lateral cephalogram.

Fig 4. Posttreatment records. A, posttreatment facial photographs; B, posttreatment intraoral photographs; C, panoramic radiograph; D, lateral cephalogram.

Fig 5. Superimposition of pretreatment of first phase (black), before the initiation of second

phase (blue), and posttreatment of second phase (red) cephalometric tracings.