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CLASSIFICATION OF FIRST AND SECOND BRANCHIAL ARCH SYNDROME: STUDY REPORT 1 - DEVELOPMENT OF A MEASUREMENT METHOD USING THREE-DIMENSIONAL COMPUTED TOMOGRAPHY DATA

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Synopsis

The first and second branchial arch syndrome is a congenital anomaly syndrome that causes morphological abnormalities of the maxillofacial region, especially significant deformity of the mandible. The classification method for mandibular deformity reported so far has some problems, such as differences in evaluation among examiners.

Therefore, in this study, we devised a method to measure the distance and volume of each part of the mandible in order to devise a new numerical classification method using CT data. As a result, the distance and volume measurements showed that each region could be compared. In addition, hypoplasia was observed, and in some cases, hyperplasia of the coronoid process was also observed in the volume.

The method of measurement developed in this study enabled us to quantify and objectively evaluate the degree of mandibular deformity.

Key words: first and second branchial arch syndrome, 3D measurement, CT analysis

Introduction

The first and second branchial arch syndrome, a congenital anomaly of the maxillofacial morphology, develops at 4-5 weeks of gestation due to some dysfunction of the first and second branchial arches. Grabb[1)] in 1965 first named it as the first and second branchial arch syndrome. This syndrome affects 1 in 5,000 people, with a 3:2 male-to-female ratio[2)]. Patients with this condition have dysplasia of the maxillofacial skeleton, including the maxilla, mandible, and zygomatic bone. There is a particularly noticeable mandibular deformity that affects both occlusion and facial appearance. Classifications by Pruzansky[3)] and Murray[4)] have been widely used to evaluate mandibular deformity in this syndrome. However, since these classifications are based on standardized lateral head radiographs, it is difficult to make an appropriate classification due to the overlap of anatomical feature points. The need for a more objective classification method was noted by Furukawa et al.[5)] due to the interrater variability across examiners in the evaluation of the syndrome, particularly between Grade I and II. Therefore, an

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objective classification method that can evaluate mandibular deformity without interrater variability is required for the diagnosis of the first and second branchial arch syndrome. Using computed tomography (CT) images from patients with the first and second brachial arch syndrome, a three-dimensional assessment method of mandibular morphology was developed in this study. By comparing the data with the skeletal data of healthy participants, this study aimed to clarify the characteristics of mandibular deformity seen and to obtain fundamental data for classifying the severity of this syndrome according to the degree of dysplasia.

Materials and Methods

1. Ethics approval and consent to participate

The study was conducted in accordance with the principle laid out in the Declaration of Helsinki and approved by the Ethical Committee of the School of Dentistry, Aichi Gakuin University (Approval No. 638, September 2nd, 2021). Every effort was made to protect patient confidentiality and personal information. All participants provided comprehensive agreement.

2. Participants

Seven patients were included in the study (four men, three women, aged 10 – 33 years old, mean age 18.1 ± 6.9 years old) who were diagnosed with the first and second branchial arch syndrome (unilateral) and who visited the Cleft Lip and Palate Center, Aichi Gakuin University Hospital between 1990 and 2021. Of the seven patients, one and six had hypoplasia of the right and left sides of the mandible, respectively. As controls, among the patients who underwent sagittal split ramus osteotomy with a diagnosis of mandibular protrusion at our center, seven patients were included in the study (four men, three women, aged 17-29 years old, mean age 22.5 ± 3.6 years old) with no significant asymmetry and a difference of 5 mm or less in the amount of set back between the left and right sides.

3. CT imaging method

From CT images recorded at the Department of Radiology and Diagnostic Imaging, Aichi Gakuin University Dental Hospital, DICOM data were obtained. Moreover, a CT value threshold of 200-2000 was used to perform a 3D reconstruction using the 3D viewer Aquarius Net (TeraRecon, San Francisco, USA).

4. Distance and volume measurement methods

1) Distance (Fig. 1)

Starting from the mandibular foramen, the distances to the head of mandible (a), coronoid process (b), angle of mandible (c), mental foramen (d), and distance from the mental foramen to the pogonion (e) were measured.

2) Volume (Fig. 2)

The growth of the mandible is noted by repeated resorption and addition of the bone[6]. In the anterior part of the mandibular body, the bone on the medial and lateral surfaces is resorbed and added, respectively. In the mandibular branch, bone resorption and absorption occur at the anterior and posterior margins. In the

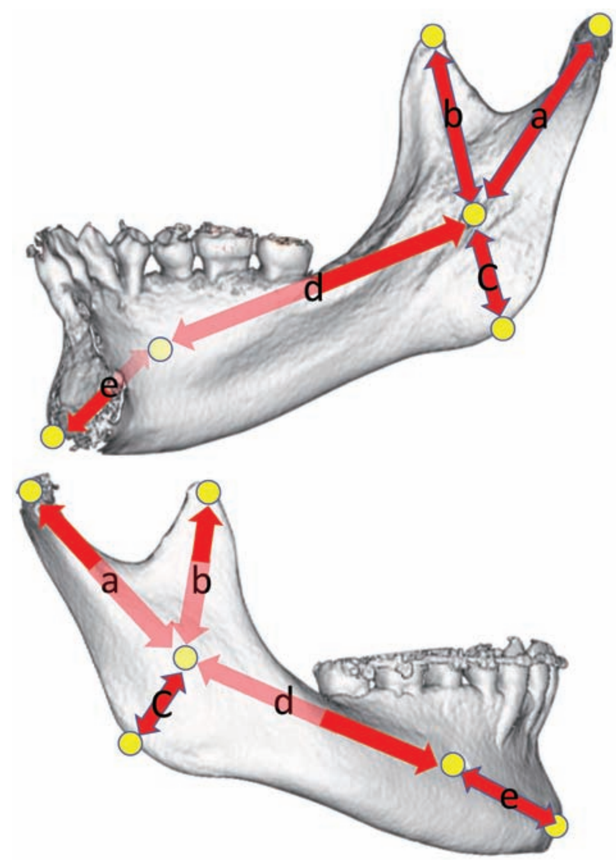

Fig. 1. Distance measurement sites of the mandible
The reference points used were the head of mandible, coronoid process, mandibular foramen, mental foramen, and ocular region. (a) The distance from the mandibular foramen to the head of mandible. (b) The distance from the mandibular foramen to the coronoid process. (c) The distance from the mandibular foramen to the angle of mandible. (d) The distance from the mandibular foramen to the mental foramen. (e) The distance from the mental foramen to the Pog (mm).

coronoid process, bone resorption occurs at the upper posterior and lower anterior margins of the mandibular branch, whereas bone addition occurs at the lower posterior margin. The medial aspect of the basal portion of the mandibular branch is resorbed, whereas bone addition occurs at the lateral aspect. Bone addition occurs at the mental ridge, and the growth of the mandible is observed with the addition of bone cortex on the medial lingual surface and resorption of bone cortex on the lateral labial surface with the mental foramen as the apex[7].

Considering the abovementioned points, a new bone segment must be defined for the mandible measurement considering the above points. A method described by Chen et al.[8] was used as a reference in this study to create a plane (Gonion [Go] and Menton [Me]), which passes through the origin of the external and internal oblique lines of the mandibular branch and intersects perpendicularly with a straight line, and the volume of the entire posterior mandibular branch (T) divided by this plane was measured (Fig. 3).

The mandibular branch was divided vertically into head of mandible (H) and coronoid process by a plane that passed through the mandibular notch and crossed perpendicularly with a line passing through the mandibular notch and foramen, as described by Lo Giudice et al.[9]. The mandibular branch was divided vertically by the plane passing through the mandibular foramen and parallel to the Go-Me, with the upper ramus of mandible (R) and lower angle of mandible (A) (Fig. 4, 5).

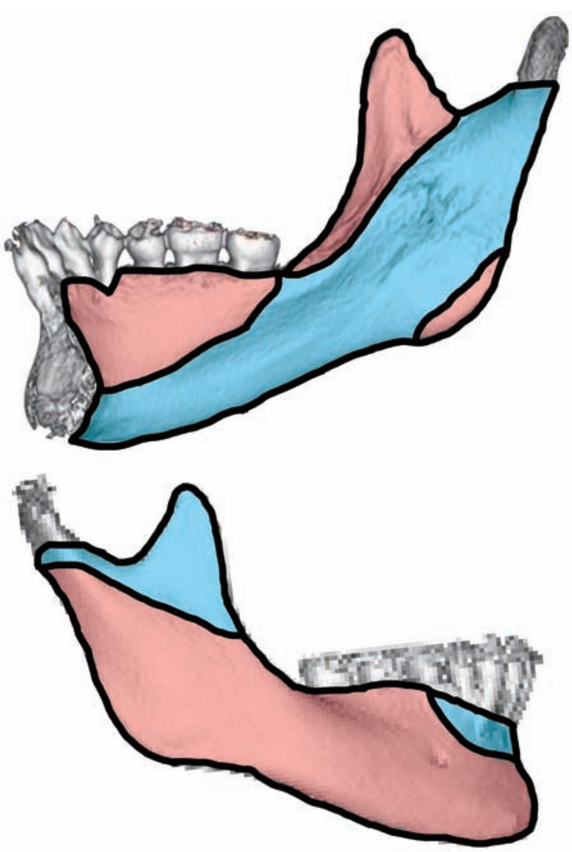

Fig. 2. Growth of mandible
The mandible grows by repeated resorption and addition. Bone addition is shown in orange and resorption in blue. The resorption area comprises the buccal ridge anterior to the processus, anterior to the most posterior molar, medial part of the mandibular branch, head of mandible, and lateral part of the processus; the bone addition area is composed of the medial part of the head of mandible and processus, angle of mandible, and lateral part from the mandibular branch to the mandibular angle and molars.

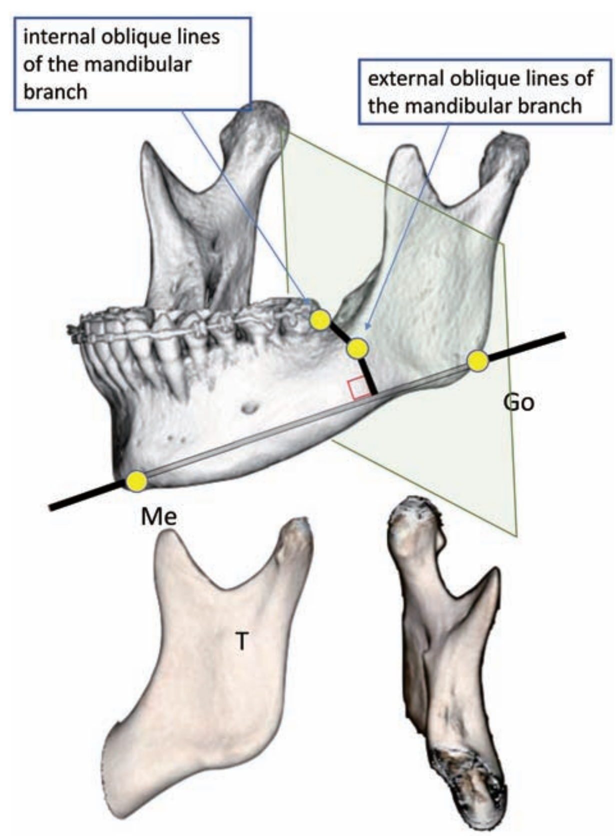

Fig. 3. Determination of the mandibular branch area
A plane was created passing through the origin of the external and internal oblique lines of the mandibular branch and intersecting perpendicularly with the straight line: Go–Me. The area including the posterior portion divided by the plane was designated as the mandibular branch (T), and its volume was measured.

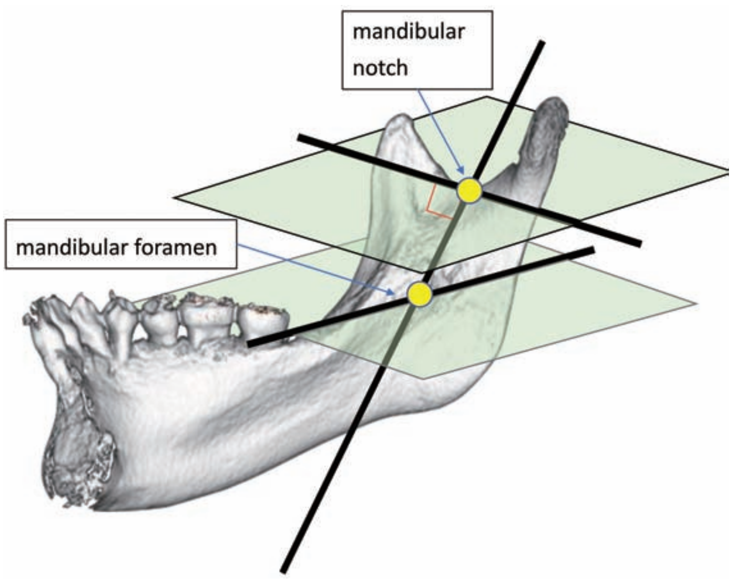

Fig. 4. Method of dividing the mandibular branch

The mandibular branch was divided vertically into head of mandible (H) and coronoid process (C) by a plane that passed through the mandibular notch and crossed perpendicularly with a line passing through the mandibular notch and mandibular foramen.

The mandibular branch was divided by the plane passing through the mandibular foramen and parallel to the Go–Me, with the upper ramus of mandible (R) and lower parts angle of mandible (A).

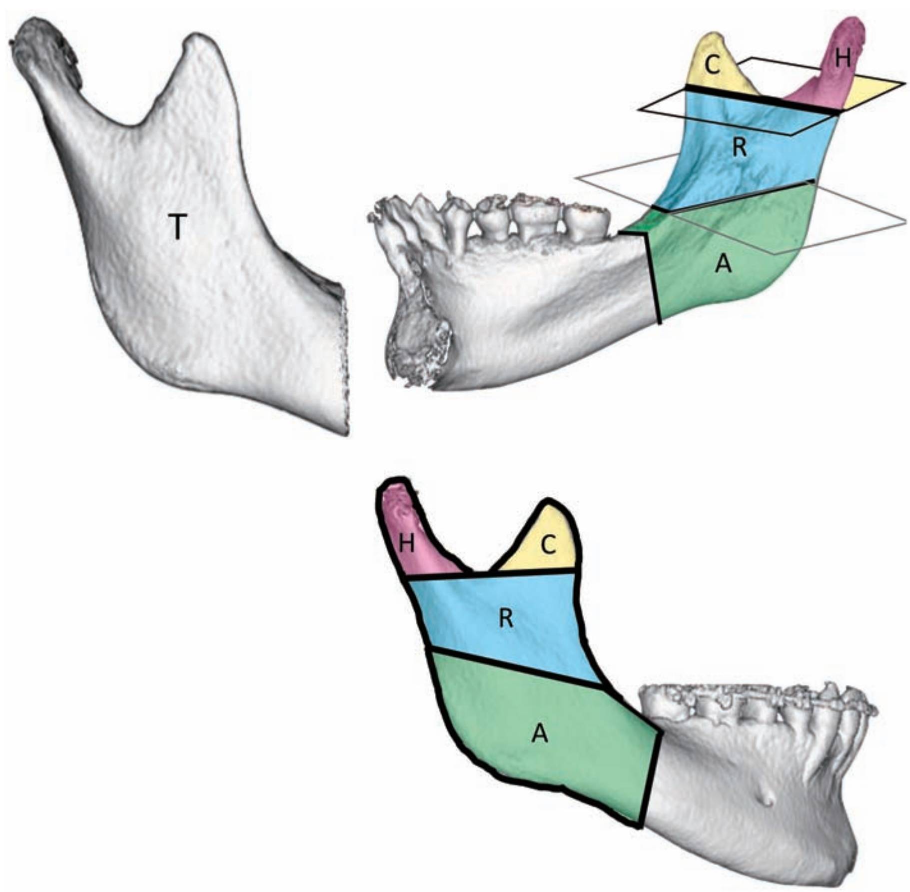

Fig. 5. Area of the head of mandible, coronoid process, and central part of the mandibular branch

The under part of the head of mandible and coronoid process were designated as "H" and "C," respectively. The upper part was divided vertically by the plane that passes through the mandibular foramen and is parallel to Go–Me, The upper part was designated as R and the lower part as A.

5. Evaluation method

1) Measurement error

The following method was used to calculate the measurement error of the distance and volume measurements in this study: Distance and volume were measured using 3D images created from the seven control participants in this study. The measurement errors were a and b for distance and T, H, R and A for volume. Each item was measured twice by the same surgeon on different days in the same case to eliminate interrater error, and the measurement error was calculated using Dahlberg's formula[10] as shown below:

Standard error = $(\Sigma d2/2n)^{1/2}$ (d is the difference between two measurements; n is the number of measurements)

2) Evaluation method

We used percentages rather than actual measurements to evaluate the degree of hypoplasia at each site of the right and left eyes because the participants in this study varied in age, sex, and affected side. In the participant group, the affected side was defined as the one with hypoplasia, and the value of affected side/healthy side × 100 (%) was used for the evaluation. In the control group, the values of the left and right sides were measured, and the value of the left side / right side × 100 (%) was used. Five measurements were taken for each item, and the average value was used.

Significant differences between the two groups were determined using Mann – Whitney's U test; $p < 0.05$ was considered significant.

6. Statistical analysis

Statistical significances between control and experimental groups were evaluated using a one-way analysis of variance (ANOVA), and the results were analyzed using the adjusted chi-square test (Microsoft® Excel for Mac Ver.16.65).

Results

1. Measurement error

The measurement error of this method was 0.25 mm in distance and 0.31 cm^3 in volume, which were acceptable for use in measurement.

2. Distance (Table 1, Fig. 6)

Table 1 shows the measurement results for the participant and control groups. Distance measurements showed differences at the 5% significance levels between (a) mandibular foramen and head of mandible, (b) mandibular foramen and coronoid process, (c) mandibular foramen and angle of mandible, (d) mandibular foramen and mental foramen, and (e) mental foramen and Pog.

Table 1. Results of distance measurement for each site

	a		b		c		d		e	
	Participant group	Control group	Participant group	Control group	Participant group	Control group	Participant group	Control group	Participant group	Control group
Average value (%)	61.7	100.8	64.6	100.8	89.4	102.6	92.2	101.4	126.2	98.5
Standard deviation	17.0	3.8	17.7	2.9	14.6	1.4	26.4	2.9	44.9	3.7
Lower quarile (%)	47.7	98.3	99.8	99.8	92.1	92.1	98.5	98.5	92.9	92.9
Median (%)	67.9	100.4	68.2	100.7	89.1	103.2	89.2	99.3	108.4	99.6
Upper quartile (%)	74.9	103.4	79.0	107.7	95.7	100.5	95.1	104.7	117.3	99.4

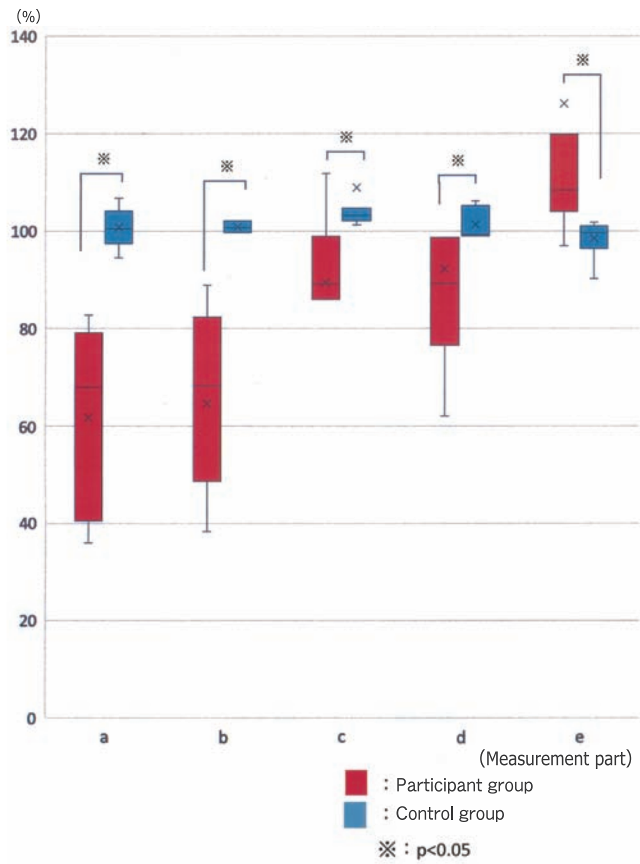

Fig. 6. Evaluation of distance measurement at each site (a) between mandibular foramen and head of mandible, (b) between mandibular foramen and coronoid process, (c) between mandibular foramen and angle of mandible, (d) between mandibular foramen and mental foramen, and (e) between mental foramen and Pog, with differences at 5% significance level.

3. Volume (Table 2, Fig. 7)

Table 2 shows the measurement results of the participant and control groups.

The volume of the entire mandibular branch (T), the head of mandible (H), and the mandible from the inferior border of the mandible to the mandibular branch (R, A) differed at the 5% level of significance. Nevertheless, no significant difference existed in the coronoid process (C), as hyperplasia was observed in some cases .

Table 2. Results of volume measurement for each site

	H		C		R		A		T	
	Participant group	Control group	Participant group	Control group	Participant group	Control group	Participant group	Control group	Participant group	Control group
Average value (%)	35.5	98.7	123.4	99.8	59.1	99.8	65.2	100.1	61.1	100.3
Standard deviation	30.7	2.6	69.0	1.8	29.1	2.4	21.0	2.5	21.7	0.9
Lower quarile (%)	10.2	96.8	76.3	98.5	39.0	98.7	54.1	98.7	47.5	99.5
Median (%)	17.3	99.6	95.1	100.6	69.3	99.2	70.1	100.4	61.8	100.4
Upper quartile (%)	61.4	100.7	173.7	100.9	84.9	100.2	76.5	101.7	78.4	101.1

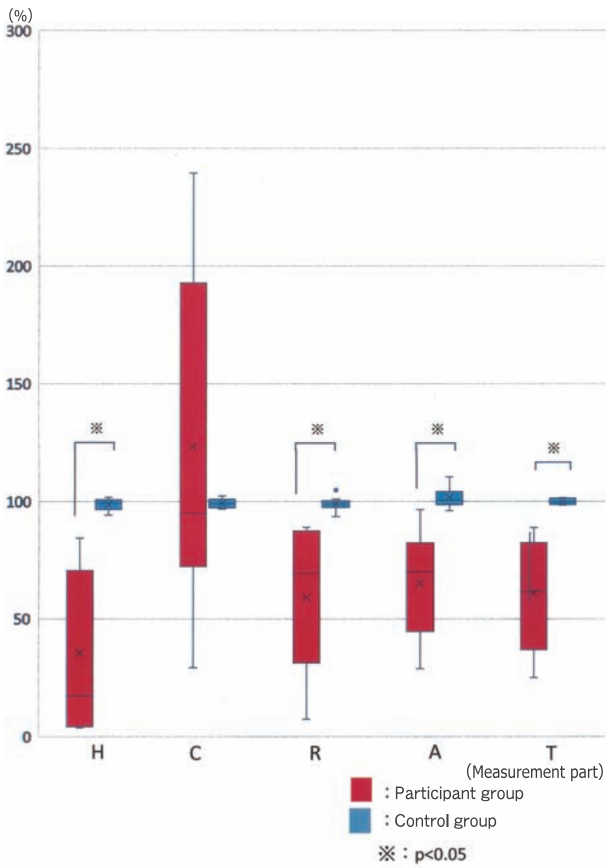

Fig. 7. Evaluation of volume measurement at each site
Differences in T, H, R, and A were observed at 5% level of significance.

Discussion

In this study, we developed a new measurement method to evaluate the degree of mandibular deformity quantitively in this syndrome, and evaluated its accuracy and usefulness. Using this method, we evaluated the mandibular morphology of patients with the first and second branchial arch syndrome.

The first and second branchial arch syndrome is a congenital disorder of the tissues originating from the first and second branchial arches. It is sporadic, with an incidence of approximately 1 in 5,000 people and a male-to-female ratio of 3:2. The affected side of the face shows a transverse facial cleft (macrostomia) and mimetic muscle hypoplasia. Additionally, microtia, auricular deformity, parotid gland malsecretion, abnormalities of the tongue and uvula, complete or partial loss unilateral cervical spine, strabismus, microphthalmia, stenosis or obstruction of the external auditory canal, hearing loss, cleft lip and palate, ventricular septal defect, Fallot's tetralogy, and patent ductus arteriosus have also been reported[2].

To classify the morphological abnormalities of the mandible, Pruzansky[3] and Murray et al.[4] employed the degree of formation of the head of mandible; however, the results sometimes vary depending on the evaluator[5]. These severity classifications were based on two-dimensional measurements using standard head radiographs, which had the drawback of being difficult to measure accurately due to the overlap of anatomical feature points. Recently, Three-dimensional bone measurement using a CT has been reported to be possible, and Ko et al.[11] reported the evaluation of treatment results for this syndrome using a CT. In the current study, we used CT data to measure the length and volume of each compartment of the mandible in a patient with the first and second branchial arch syndrome in an attempt to comprehend and objectively evaluate the severity of mandibular hypoplasia. Additionally, we attempted to determine the severity of hypoplasia of the mandible by quantifying the distance and volume of each region of the mandible using CT data. In other words, the angle of mandible was divided into two groups by the plane parallel to Go–Me passing through the mandibular foramen to avoid the boundary area of the growth style of the mandibular branch.

Significant differences in the present study were observed between the two groups in the distance of mandibular foramen to head of mandible, mandibular foramen to coronoid process, mandibular foramen to angle of mandible, mandibular foramen to mental foramen, and mental foramen to Pog, indicating that the syndrome caused hypoplasia not only in the mandibular branch but also in the mandibular body. The differences in the values of each region of the mandible may be due to mandibular development. Cranial neural crest cells migrating to the first branchial arch exist as mesenchymal cells and then differentiate into osteoblasts, dental pulp cells, dentinoblasts, cementoblasts, and chondroblasts that form Meckel's cartilage[12]. The latter initially develops anteriorly and posteriorly near mental foramen, and anterior ends face each other on both sides and fuse to form a U shape[12,13]. The anterior end of Meckel's cartilage is fused and forms a U shape[12,13]. Subsequently, membranous bone is formed on the upper and lateral surfaces of the cartilage, and the head of mandible and coronoid process are produced by membranous bone. In this case, the mandibular branch and mental foramen may also be hypoplastic.

Additionally, the volume evaluation revealed significant hypoplasia in the mandibular branch and head. However, in the three of the seven cases, the coronoid process was more hyperplastic than the healthy side. This phenomenon was also reported by Terasaki et al.[14]. According to Sarnat et al.[15], when the head of mandible was surgically resected, the coronoid process grew excessively during subsequent mandibular growth. The cause of this phenomenon was reported to be that as the head of mandible grows, the mandible shifts downward throughout the process, and the coronoid process grows in parallel to prevent the head of mandible from shifting downward, thereby maintaining equilibrium. This indicates that the enlargement of the coronoid process may have occurred in the first and second branchial arch syndrome because of hypoplasia or deficiency of the head of mandible. This implies that the new classification system must take the status of the coronoid process into account.

There are some limitations in this study. First, seven cases of the first and second branchial arch syndrome were examined in this study. The male-to-female ratio was 4:3, and the age of the seven cases ranged from 10 to 33 years old. However, owing to the rarity of the first and second brachial arch syndrome, it is challenging to assess a large number of cases in a single study. Hence, using this method could aid in the creation of a new classification method. Second, in this syndrome, not only mandibular deformity but also maxillary deformity, such as the inclination of the occlusal plane, is observed. Only the mandible was evaluated in this study, but it is necessary to consider a method to evaluate the maxillary deformity in the future.

Conclusion

In order to develop an objective classification method for the first and second branchial arch syndrome, we developed a new method of measuring mandibular morphology using CT data and compared the mandibular morphology of patients with the first and second branchial arch syndrome with that of healthy individuals. As a result, we were able to objectively examine the pathophysiology of this disease and assess the degree of mandibular deformation in patients with the first and second branchial arch syndrome. In addition to the first and second branchial arch syndrome, this approach may be used to treat various disorders that cause mandibular deformities. Furthermore, this method may serve as a basic measurement technique for the development of a new classification method for the first and second branchial arch syndrome.

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