Bone Mineral Density in Hemifacial Microsomia

Minoru Yamaoka¹, Masaaki Nakamura¹, Norimasa Okafuji², Kouichi Yasuda¹, Hiroko Naramoto¹, Toshikazu Shiba³, Takashi Uematsu¹, Saburo Kurihara² and Kiyofumi Furusawa¹

¹Oral and Maxillofacial Surgery, Matsumoto Dental University Dental Hospital (Chief: Professor Kiyofumi Furusawa)
²Orthodontic Department, Matsumoto Dental University Dental Hospital (Chief: Professor Saburo Kurihara)
³ Regenetiss Co. (Director: Dr. Toshikazu Shiba)

Abstract: We aimed to assess whether patients with hemifacial microsomia can be quantitatively identified using bone mineral density information. Mandibular bone mineral density was studied using computer assisted analysis between the nonaffected (r) and the affected (l) sides with an orthopantomograph in a patient with hemifacial microsomia with median mandibular cleft, and four patients who suffered from hemifacial microsomia in the left side. Fifty controls without bone diseases were randomly selected.

Bone mineral density r/l ratios in the controls ranged from 0.479 to 2.064, and those in two patients that were associated with and without median mandibular cleft were higher than those in the controls, with a maximum of 8.622 in a particular male with median mandibular cleft after bone graft, whereas the r/l ratios in the other three cases were similar to the controls. Our findings indicate that the quantitative character in the case with median mandibular cleft reveals a large discrepancy of bone mineral density between the nonaffected and the affected sides. This may suggest a compensatory mechanism for bone hypertrophy from regulated bone mineral density with underdevelopment in hemifacial microsomia.

Key words: bone mineral density, mandible, hemifacial microsomia

Introduction

Hemifacial microsomia¹ is known as first and second branchial arch syndrome², otomandibular-facial dysmorphogenesis³ and lateral facial dysplasia⁴, and the incidence of the disease is about 1 per 5642 births² or 1 per 4000 births⁵. The pathogenesis has been described as sporadic⁶, the formation of a hematoma in the primate embryo⁷, a defect of the stapedial artery⁸, and vaginal bleeding in the second trimester⁹. The clinical appearance is characterized by varying degrees of underdevelopment of the craniofacial structures derived from the first and second branchial arches⁴⁻¹¹ and facial involvement is limited to one side in many cases²⁻¹². The disease has a progressive nature of deformities¹³⁻¹⁷, although Polly et al. (1997)¹⁸ described that the growth of the affected side paralleled that of the nonaffected side. Underdevelopment and malformation depend upon the combination of the initial defect and abnormalities secondary to the initial defect⁹, and secondary changes are due to the mechanical environment, such as muscular maturation¹⁹,²⁰. In general, it is difficult to study the influences on the markers of longitudinal bone growth, as the skeletons grow very slowly²¹. However, Pruzansky (1969)³ described a case in which the difference in size compared with the healthy side was dimin-
ished because of the greater increments of growth on the affected side, and noted that the severity of the deformity present at birth is not always predictive of the ultimate condition at maturity. Gross overdevelopment of the affected side and differential development in each mandibular segment were observed from our longitudinal analysis of the case with a median mandibular cleft, as shown by Wolf and Dubrauszky (1949). The magnitude of variations in the apparent matrix stiffness was small, within the physiological range of density for healthy bone, whereas the variations can be profound in certain pathological cases. In hemifacial microsomia, mandibular duplication, accessory mandible, double intermaxillary bone, or accessory mandibular rami are found accompanying the presence or absence of teeth. Such occasionally occurring phenomena raise important questions regarding bone metabolism in the development of hemifacial microsomia. However, little is known about the material quality of the bone in hemifacial microsomia. We report a case which revealed gross development with a change of bone mineral density in the affected side compared with four hemifacial microsomia and 50 controls.

Methods

1. Subjects

A man with hemifacial microsomia with a lateral facial cleft and median mandibular cleft was observed at 4, 5, 6, 7, 8, 9, 15 and 21 years of age, as was previously reported. Four patients with hemifacial microsomia in the left side were selected from the patients who visited our Oral and Maxillofacial Surgery or Orthodontic Department for treatment or consultation. Two male children of 7 and 8 years of age with hemifacial microsomia without median mandibular cleft, and two young females of 13 and 17 years of age with hemifacial microsomia without median mandibular cleft were studied together with a man with hemifacial microsomia with a lateral facial cleft and median mandibular cleft. Forty males (5 from each age at 4, 5, 6, 7, 8, 9, 15 and 21 years) and 10 females (5 in each age at 13 and 17 years) were randomly selected as age-matched and sex-matched controls, but individuals with mandibular bone diseases were not included as controls. Informed consent was obtained from all patients.

2. Methods

Subjects were studied as to changes of the cortical and trabecular bone mineral density with panoramic radiograms taken with an orthopantomograph (Panorammax Auto I, 20 mA, 80-84KVP, Asahi, Kyoto, Japan). The films were processed with an automatic developing machine (Konica SRX-501, Konica, Tokyo, Japan). Cortical and trabecular bone mineral densities were measured with a computerized radiograph analysis system, and were evaluated by a single examiner. The orthopantomographic images were digitized using an image scanner G780B, ES-2200 (Seiko Epson, Japan) and processed with Adobe Photoshop 7.0 (San Jose, CA, USA). Four regions of interest with a range of 2901-3240 pixels were bilaterally selected for measurements of bone density and demarcated in the cortical and trabecular portions. The cortical portion was measured at the frontal margin of the ramus behind the third molar, or the cortical portion behind the place where the third molar is supposed to be erupted if the third molar is not present, and the cortical portion at the lower border of the mandible below the first molar apices because of identifiable landmarks due to a grossly distorted ramus. The other two regions were measured at the trabecular portion corresponding to the root apices when it was supposed that the third molar was erupted, anteriorly angled at -45° against the extension of the occlusal plane, and the trabecular portion below the first molar apices (Fig. 1). Regions of interest were defined using the cursor. The pixel size was determined for each film, and those projected in the region of interest were also used in the other regions of interest in that particular case. Within the windows, the means of the gray level averages were recorded. The measure-

![Fig. 1 Localization of the regions of interest for measurement of the gray level histogram of cortical and trabecular bone in the mandible on the orthopantomogram.](image-url)
ments of the mean gray level histogram achieved two readings of each site, and the average was taken. The difference in the averages between the left and right sides was compared and shown as the r/l ratio. We assessed the differences between the patients and age-matched and sex-matched controls using a box-and-whiskers plot for a visual representation of the median, range, and interquartile range of the data in the controls.

**Results**

We calculated the r/l ratios to compare the discrepancy of the values between the nonaffected side (r) and the affected side (l) in the patients and the controls. Orthopantomographs of a male with hemifacial microsomia with a median mandibular cleft are shown in Fig. 2. The r/l ratios in the follow-up of the case, those of two males without median mandibular cleft and those of the controls are shown in Figs. 3-6. Those for the controls are shown as box plots. Among the control males, the r/l ratio levels ranged from 0.585 to 2.064. The r/l ratios of the case with a median mandibular cleft were clearly above the values of the controls for the cortical region of the lower border of the mandible in the eight (r/l = 103.98/34.47) and nine year-olds (r/l = 108.36/41.04) (Fig. 4). These were similar for the trabecular bone of the region corresponding to the third molar apices in the nine (r/l = 184.41/97.00). 15 (r/l =
118.19/22.08) and 21 year-olds (r/l = 44.50/29.04) (Fig. 5), and for the trabecular bone of the region below the first molar apices in the seven (r/l = 185.59/58.30), eight (r/l = 130.51/37.90), nine (r/l = 134.76/15.63) and 15 year-olds (r/l = 95.72/40.98) (Fig. 6). However, the other two males, aged seven and eight years, with hemifacial microsomia revealed approximately equal ratios to the control males. The 13-year-old out of the two females with hemifacial microsomia demonstrated a higher r/l ratio (cortical bone behind the third molar: 155.04/91.81, cortical bone at the lower border of the mandible below the first molar: 97.71/15.63, trabecular bone at the first molar: 152.52/100.95) than the control females, but the other female who was 17 years of age was close to the normal range compared with the control females, excluding the somewhat lower ratio than the controls for the region of the trabecular bone at the first molar (r/l = 130.51/37.90)
Fig. 7  R/L ratios of the gray level histogram in females with hemifacial microsomia and the control females for the cortical bone at the distal region of the crown of the third molar, for the cortical bone at the lower border of the mandible below the first molar, for the trabecular bone at the region corresponding to the third molar apices, and for the trabecular bone at the first molar apices region.

□ Female with hemifacial microsomia at 13 years of age
〇 Female with hemifacial microsomia at 17 years of age

84.82/110.00 (Fig. 7). Moreover, the two males and two females without median mandibular clefts showed underdevelopment of the left side. Normal dental development was seen in all five cases with hemifacial microsomia.

Discussion
There is no quantitative evidence of bone mineral density on the hemifacial microsomia. Our particular interest was in studying the bone mineral density between the affected side and the nonaffected side, and the difference from healthy populations to determine the contribution of bone mineral density to hemifacial microsomia. We observed large changes of bone mineral density of the affected side compared to the nonaffected side in a follow-up of a case with a median mandibular cleft. The trabecular and cortical bone was studied since these compartments may be independently modulated by metabolic and mechanical stimuli28, 29. Measurements were achieved of the cortical and trabecular bone around the third molar and the first molar and the region of the lower border of the mandible. A computer assisted densitometric image analysis system displays the image on a much larger gray shade scale than can be seen by the human eye, and is a widely used method of assessing bone mass30-32 as a sensitive and non-invasive technique to assess the hard tissue in the detection of changes of the mineral tissue33 in periodontal surgery34 and peri-implant tissue35.

Hypertrophy in a case with a median mandibular cleft showed an increased r/l ratio, indicating relative porosity in the thicker affected side, suggesting a compensatory local mechanism, which is likely to occur in the young, for bone fragility due to a decrease in bone mineral density. The increase in bone volume with the relative decrease in bone mineral density is different from the regulatory mechanism that increases bone mineral density and is due to consolidation of the skeleton with no further increase in bone size, as shown by Henry et al. (2004)36, and it differs from the decrease of all of the structural elements of bone through aging37. A relative loss of bone mineral density of the trabecular bone at the first molar and the third molar and that of the cortical bone at the lower border of the mandible contributes to relative bone loss. Therefore, it is likely to define a distortion dependent on the bony displasia and compensatory thickening. In adolescents, growth may result in profuse excessive thickening, as shown by Ross (1999)38 in the case of unbalanced bone mineral density between the affected and the nonaffected side. This has important implications for the understanding of future bone change. However, these remodeling changes cannot be quantified by simple linear measurements and cannot be predicted by the growth of microsomia39 and there is little evidence that a single procedure at any age is capable of restoring the face to an ideal symmetry38. A persistent widening of the affected side throughout childhood and adolescence may be induced by transplanted iliac bone into median mandibular cleft at 6.1 years of age, since some growth can take place after suture closure40. However, relatively lower levels of bone mineral density were found in a male with hemifacial microsomia with a median mandibular cleft. There seems to be a morphological disorder or shaping disorder that elongates the antero-posterior aspect of the mandible, in particular, the ramus, although the extrinsic force for extension may be generated within the tissues. In the present case, significant relative decreases of bone mineral density were confirmed after eight years of age. D’Amelio et al. (2000)41 described that a high correlation was detectable between the bone mineral density values and age in a group with decidual dentition, while the bone mineral density values were somewhat less correlated with age in a group with mixed dentition. The cause of the marked bone mineral density changes in the present case may be also related
to the eruption of permanent teeth which alters occlusal forces in the pathogenesis of asymmetric bone density. Although the case of a female revealed a relative decrease in bone density around the third molar region and the first molar region in the affected side accompanied with underdevelopment of the affected side, two other male cases and a female showed a balanced bone density, similar to the controls. The latter may indicate consolidation in the underdevelopment of the affected side. Thus, the pattern of r/l ratios involved an r/l ratio increase with hypertrophy, a controlled r/l ratio with underdevelopment and a r/l ratio decrease with underdevelopment. The variability is interpreted to reflect not only structural underdevelopment, as shown by Pruzansky (1969), but also bone metabolic disorders regarding bone mineral density. Different processes from the growth mechanism are likely to be associated with the density variables under the status with or without compensatory mechanism, although it is unknown whether a deficiency of proliferation and condensation of the mesoderm, as shown by Stark and Saunders (1962), is continually associated with a decreased bone mineral density as its essential quality. Changes of bone growth and bone mineral density need to be confirmed by a number of cases through the following-up of bone maturation for the classification of stage, and data from the regulatory mechanism of left and right symmetry will be required for clinical effectiveness.

Acknowledgments
The authors thank Ms. Hitomi Koike for secretarial assistance.

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