The Relationship between Carabelli's Trait and Tooth Crown Size in 45,X Females

Mitsuko Nakayama,¹ Raija Lähdesmäki,² Eisaku Kanazawa,¹ and Lassi Alvesalo²

¹Department of Anatomy and Physical Anthropology, Nihon University School of Dentistry at Matsudo, Matsudo, Chiba 271-8587, Japan

²Department of Oral Development and Orthodontics, University of Oulu, Oulu, FIN-90014, Finland

Correspondence to :

Mitsuko Nakayama

E-mail : nakayama.mitsuko@nihon-u.ac.jp

Abstract

The purpose of this research is to study the relationship between Carabelli's trait and tooth crown size in 45,X females and to clarify the effect of the shortage of X chromosome to the dental crown. The subjects comprised eighty-one 45,X females in the Kvantti research collection and Finnish female controls. Dahlberg's reference plaque (1956) was used to determine the score of the Carabelli's trait which was divided into three classes. The scores were compared with the maximum mesiodistal and buccolingual tooth crown diameters. The result showed that the mesiodistal diameters in 45,X females were significantly smaller than control females, while no association was found between Carabelli's trait and buccolingual tooth crown diameter in 45,X females. Mesiodistal tooth crown diameter was thought to be a key factor to develop the Carabelli's trait in 45,X females.

Keywords :

Carabelli's trait, 45,X females, Turner's syndrome, tooth crown size

Introduction

The number of human chromosomes are 22 matched pairs of autosomes and one matched pair of sex chromosomes. The autosomes are the same in both males and females, however, the X and Y chromosomes are not shaped similarly, and the pair of the sex chromosome is responsible for differences in development between males and females. In the dental development, the Y chromosome promotes growth of permanent tooth crown enamel and dentin, whereas the effect of the X chromosome seems to be restricted mainly to enamel formation (1). The 45,X females (generally called Turner's syndrome) have the same number of autosomes as normal females, however, they show abnormality in their sex chromosome constitution. The fundamental karyotypes of these females are 44 autosomes and a single X chromosome. Kajii (2) reported that the rate of incidence of the 45,X fetuses in the spontaneous abortion fetus showed 19.9%. The prevalence of these females has been estimated to be 1/2500 female live births. Approximately 98%-99% of Turner's syndrome fetuses are spontaneously aborted (3). Their physical feature includes a webbed neck, short stature,

cubitus valgus and lack of secondary sex characters (4). The skeletal features in 45,X females were caused by SHOX (short stature homeobox containing gene), on the other hand, the features of the soft tissue was concerned by the gene for the formation of the lymph channel (5-8).

In dentistry, they also have unique features, like micrognathia, high-arched palate, simplified tooth crown morphology, reduced tooth crown size and low expression of the molar crown traits (9-14). However, it is not clear whether the tooth crown morphology is influenced by the lack of one X chromosome in females. We already reported that the expression of the Carabelli's trait of those females showed low frequency in the maxillary second deciduous and first permanent molars (14). The Carabelli's trait originates from the lingual cingulum region of the maxillary molars, being evident particularly in the first molar (15, 16). The appearance of Carabelli's trait showed relationship to the development of hypocone and crown size (17-21). Kondo and Townsend (22) reported that the molars with Carabelli's trait has larger mesiodistal and buccolingual tooth crown diameters, well developed hypocone and

reduced size of protocone than those of no expression molars.

The purpose of this research is to observe the relationship between Carabelli's trait and tooth crown size in 45,X females and to clarify the effect of the shortage of X chromosome to the dental crown morphology.

Subjects and Methods

The data were derived from dental casts collected as Kvantti research collection housed in Oulu University in Finland. Kvantti research collection was the collective research of Prof. Alvesalo conducted in Finland from the 1970s to the 1980s. The subjects comprised eighty-one 45,X females whose karyotypes were confirmed by cytogenetic tests of skin fibroblasts. They were the inhabitants on different area in Finland. The controls were 137 Finnish females from rural community in Hailuoto Island. All examinations were carried out with the individual agreements. The Carabelli's trait was scored on left side of the maxillary first molars. If a left side was missing or having dental treatment on the tooth crown, we used the opposite side. Dahlberg's reference plaque (23) was used to determine the traits. The Carabelli's trait was divided into three classes; grade (–) smooth surface (Dahlberg's a), grade (–+) pit or furrow (Dahlberg's b, c, d, e) and grade (+) slight protuberance or cusp (Dahlberg's f, g, h). Maximum mesiodistal and buccolingual tooth crown

diameters (24) of the maxillary first molars were measured using digital caliper (Mitutoyo) with an accuracy of 0.01 mm. All measurements were made by one person (M.N), the errors of measurement being less than 0.10 mm. The Kruskal-Wallis test was used to statistically compare mean values in 3 grades. A statistical software package, S-PLUS 2000 (Mathematical Systems Inc. Tokyo) was used for data analysis.

Results

Table 1 gives the mesiodistal diameters and Table 2 gives the buccolingual diameters of each grades and total group mean in 45,X females and population controls. The total mean values were compared between 45,X females and control females by Student's t-test. Both of the total mean values of the mesiodistal and buccolingual diameters were significantly smaller in 45,X females than control females. The reduction in mesiodistal diameters in 45,X females compared with control females was 8.1%. The reduction in buccolingual diameters in 45,X females compared with control females was 3.8%. This result gave the impression that the effect of size reduction appeared in the mesiodistal diameters were greater than the buccolingual diameters in 45,X females.

The mesiodistal diameter of grade (–) was smaller than other two grades (–+, +) and total mean value in 45,X females and control females. The reduction in

Table 1. The Carabelli's trait and mesiodistal crown diameter in 45,X females and control females.

		n	Mean	SD	CV	Min.	Max.	K-W test
• 45,X females	–	31	9.47	0.62	0.07	8.25	10.98	ns
	–+	34	9.81	0.55	0.06	8.77	10.77	
	+	16	9.69	0.49	0.05	9.14	10.85	
	total	81	9.66*** ¹⁾	0.58	0.06	8.25	10.98	
• control females	–	57	10.36	0.56	0.05	8.79	11.78	*
	–+	52	10.61	0.76	0.07	8.88	12.02	
	+	28	10.68	0.61	0.06	9.43	11.64	
	total	137	10.52	0.66	0.06	8.79	12.02	

¹⁾: Student's t-test in 45,X females and control females., CV : the coefficient of variation., K-W test : Kruskal-Wallis test in 3 grades., ns : not significant, * : p<0.05, *** : p<0.001.

Table 2. The Carabelli's trait and buccolingual crown diameter in 45,X females and control females.

		n	Mean	SD	CV	Min.	Max.	K-W test
• 45,X females	—	31	10.56	0.42	0.04	9.41	11.56	ns
	— +	34	10.60	0.57	0.05	9.48	12.12	
	+	16	10.53	0.52	0.05	9.54	11.83	
	total	81	10.57*** ¹⁾	0.50	0.05	9.41	12.12	
• control females	—	57	10.83	0.64	0.06	9.21	12.60	*
	— +	52	11.03	0.51	0.05	10.04	12.50	
	+	28	11.25	0.54	0.05	10.28	12.50	
	total	137	10.99	0.59	0.05	9.21	12.60	

¹⁾: Student's t-test in 45,X females and control females., CV : the coefficient of variation., K-W test : Kruskal-Wallis test in 3 grades., ns: not significant, *: $p < 0.05$, ***: $p < 0.001$.

mesiodital diameters of grade (—) in 45,X females and control females compared with each total mean value were 2% and 1.5%. The mesiodital crown diameters of the other two grades (— +, +) in 45,X females became greater than their total mean values, 1.6 and 0.3%, while the grades (— +) and (+) in control females showed 0.9% and 1.5% greater than their total means. The result of Kruskal-Wallis test suggested that the control females showed a statistically significant difference ($p < 0.05$), but, there was no statistically significant difference in 45,X females among 3 grades.

The buccolingual diameter in control females showed that the grade (—) was smaller than other two grades (— +, +) and their total mean values. Grade (—) showed the reduction of 1.5% compared with their total mean. Grades (— +, +) in control females became greater in the buccolingual diameters than their total mean value, 0.3 and 2.3%. The Kruskal-Wallis test showed that the control females were statistically significant ($p < 0.05$), but, 45,X females were not statistically significant.

Discussion

Generally females have two X chromosomes in every cell. The one X chromosome is keeping huge amount of the genetic information as three times larger than Y chromosome (25). To reduce the imbalance in an amount of sex chromosome between X and Y, the most of females inactivated one X chro-

mosome on the early stage of prenatal period (26). But the some part in X chromosome escaped the inactivation. Carrel et al (27) reported that about 20% was saved by X chromosome inactivation including major pseudoautosomal region (PAR1) and minor pseudoautosomal region (PAR2). In recent years, a short stature homeobox gene (SHOX) was discovered in PAR1; this gene located at the end of the X chromosome short arm and caused a short stature and other skeletal signs in 45,X females. On the other hand, a gene for the formation of the lymph channel was estimated in the proximal part of the X chromosome. The shortage of this gene is related to the abnormalities of visceral organs and soft tissue that appear in 45,X females (5-8). These influence become a serious problem to the fetus. As a practical matter, approximately 98%-99% of Turner's syndrome fetuses are spontaneously aborted (3).

Dental crown developments also have an effect on the sex chromosome. The Y chromosome promotes formation of tooth crown enamel and dentin layers. The X chromosome have an influence on the enamel layers (1, 28-32). On the tooth crown morphology, Kirveskari and Alvesalo (11) reported that the morphological reduction of tooth crown was found in the females with a lack of the X chromosome. The Carabelli's trait originates from the lingual cingulum region of the maxillary molars, being evident particularly in the first molar (15, 16). The Western Eurasian group have high frequencies of this trait in

20 to 30% (33), but the frequencies of Finnish 45,X females showed low frequencies at 19.32% in the maxillary first permanent molars (14).

Fig. 1 showed an outline of our result about the relationship between Carabelli's trait and tooth crown size. Previous studies on normal subjects and our control females showed that the appearance of Carabelli's trait associated with tooth crown size. When the molar had the expression of the Carabelli's trait, the mesiodistal and buccolingual diameters become larger than no expression molars (17-21). The 45,X females' total mean values showed that their molars have reduced tooth crown size, especially mesiodistal tooth crown diameters suffered from reduced size more than buccolingual diameters. However, when the molar had the expression of the Carabelli's trait, the mesiodistal diameters become larger than no expression molars. There was no

change in the buccolingual diameters among the grades in 45,X females.

The process of tooth Morphogenesis has two stages, i.e., the decision of general size and form, and the formation of hard tissues. Thus, when the development of the tooth germ is not sufficient, the final form of the tooth could not be acquired even if the calcification occur properly (microdont). On the other hand, when the formation of the hard tissues is not sufficient, the tooth form would be damaged even if the tooth germ developed properly (enamel hypoplasia, dentin hypoplasia) (34). The smaller tooth crown size in 45,X females was mainly caused by a thin enamel layers. But the dentin layer in 45,X female was almost same as the normal females (28, 32). Shillingburg and Grace (35) measured the normal thickness of enamel on the mesial, labial, distal and lingual aspects of all permanent teeth. The total enamel thickness in the region of mesiodistal diameter was about 2-3 mm in average, whereas enamel thickness in those areas corresponding to maximum buccolingual diameter averaged less than 1 mm. The enamel thickness contributes considerably more to maximum mesiodistal size of the teeth than to the buccolingual diameter. If the similar tendency was shown in 45,X females, the enamel layers of buccolingual side may be thinner than mesiodistal side. Standard deviation (SD) and coefficient of variation (CV) showed that the buccolingual diameter had low variation than mesiodistal diameter, because the thinner enamel layers of buccolingual side cannot afford to have any variation.

Alvesalo et al (36). reported that the existence of the Carabelli's trait was controlled by the hereditary factor, however, the phenotype of Carabelli's trait had large variation. Kondo and Townsend (22) suggested that molars with large tooth crowns are more likely to display Carabell's trait in genetically predisposed individuals, because the fifth enamel knot, it will be Carabell's trait, that appears late during crown development will be more likely to be fully expressed. The smaller molars will tend to be associated with less developed form of Carabelli's trait. The cusp formation was thought to have two impor-

Fig.1. Schematic representation of the relationship between the appearance of Carabelli's trait and crown size in 45,X females and control females.

tant steps, i.e., the definition of the summit position by secondary enamel knot and role of the groove between cusps by growth factors such as hepatocyte growth factor (HGF) (37). Formation of the first permanent molars starts 20 weeks after the fecundation (38). The 45,X fetus had a serious problem on their skeletal and internal organs, therefore almost all Turner's syndrome fetuses are spontaneously aborted (3). The dental development and eruption in 45,X females were clearly earlier than normal females (12, 39, 40). It might be presumed that the teeth crown morphology of 45,X females could not have enough time to develop until appearance of Carabelli's trait. Investigation of more crown trait, especially development of the hypocone in 45,X females is needed in the future.

Conclusions

The molars with the Carabelli's trait in 45,X females had larger mesiodistal tooth crown diameter than those without the trait. The mesiodistal diameter also had correlation with the expression of the Carabelli's trait. On the other hand, no association was found between the expression of Carabelli's trait and buccolingual tooth crown diameter in 45,X females. It was suggested that mesiodistal diameter of the tooth crown was a key factor to develop Carabelli's trait in 45,X females.

Acknowledgments

The Kvantti collection was supported by the Emil Aaltonen Foundation, the University of Turku Foundation and the Academy of Finland. We are grateful to Prof. P. Pirttiniemi and all the staff members of the Department of Oral Development and Orthodontics, University of Oulu in Finland for their advice in conducting our research. Thanks are also all staff members of the Department of Anatomy and Physical Anthropology, Nihon University School of Dentistry at Matsudo, and Dr. Kunihiko Ohmori, Zaimokuza Dental Clinic, for their statistical and clinical advice.

References

1. Alvesalo L : Sex chromosomes and Human growth. A dental approach. *Hum Genet*, 101 : 1-5, 1997.
2. Kajii T, Ferrier A, Niikawa N, Takahara H, Ohama K, and Sugandhi A : Anatomic and chromosomal anomalies in 639 spontaneous abortions. *Hum Genet*, 55 : 87-98, 1980.
3. Kelly TL : Survival of fetuses with 45, X. An instructive case and an hypothesis. *Am J Med Genet*, 42 : 825-826, 1992.
4. Turner HH : A syndrome of infantilism, congenital webbed neck and cubitus valgus. *Endocrinology*, 23 : 566-578, 1938.
5. Rao E, Weiss B, Fukami M, Rump A, Niesler B, Mertz A, Muroya K, Binder G., Kirsch S, Winkelmann M, Nordsiek G, Heinrich U, Breuning MH, Ranke MB, Rosenthal A, Ogata T, Rappold G.A : Pseudoautosomal deletions encompassing a novel homeobox gene cause growth failure in idiopathic short stature and Turner syndrome. *Nat Genet*, 16 : 54-63, 1997.
6. Ogata T : The Genetics of Turner Syndrome (Japanese), 2003, Medical review Co., Tokyo, Japan.
7. Ogata T, and Matsuo N : Turner syndrome and female sex chromosome aberrations, deduction of the principal factors involved in the development of clinical features. *Hum Genet*, 95 : 607-629, 1995.
8. Vittay P, Bosze P, Gaal M : Lymph vessel defects in patients with ovarian dysgenesis. *Clin Genet*, 18 : 387-391, 1980.
9. Babic M : Comparative cephalometric analysis in patients with X chromosome aneuploidy. *Arch Oral Biol*, 38 : 197-183, 1993.
10. Midtbø M, and Halse A : Tooth crown size and morphology in Turner syndrome. *Acta Odont Scand*, 52 : 7-19, 1994.
11. Kirveskari P, and Alvesalo L : Dental Morphology in Turner's Syndrome (45,X females). In : Kuren B, editors. *Teeth : Form, Function and Evolution*. Columbia University Press, New York, 1982, p.298-303.
12. Filipsson R, Lindsten J, and Almqvist S : Time of eruption of the permanent teeth, cephalometric and tooth measurement and sulphation factor activity in 45 patients with Turner's syndrome with different types of X chromosome aberrations. *Acta Endocrinol*, 48 : 91-113, 1965.
13. Townsend G, Jensen BL, and Alvesalo L : Reduced tooth size in 45,X (Turner syndrome) females. *Am J Phys Anthropol*, 65 : 367-371, 1984.
14. Nakayama M, Lähdesmäki R, Kanazawa E, and Alvesalo L : Analysis of Carabelli's trait in maxillary second deciduous and permanent molars in 45,X and 45,X/46,XX females. In : Zadzińska E, editors. *Current Trends in Dental Morphology Research*. University of Łódź Press, Poland ; 2005. p.325-331.

15. Korenhof CAW : Morhological aspects of the human upper molars. Utrecht, Uitgeveramsatschappij Neerlandia, 1960.
16. Sakai T, and Hanamura H : A morphological analysis of Carabelli's cusp. *Aichi-Gakuin Dent Sci*, 5 : 60-72, 1971.
17. Scott RG : Association between the hypocone and Carabelli's trait of the maxillary molar. *J Dent Res*, 58 : 1403-1404, 1979.
18. Lombardi AV : Tooth size associations of three morphological dental traits in a Melanesian population. *J Dent Res*, 54 : 239-243, 1975.
19. Baume RM, Crawford MH : Discrete dental trait asymmetry in Mexico and Belize. *J Dent Res*, 58 : 1811, 1979.
20. Noss JF, Scott GR, Potter RHY, Dahlberg AA, Dahlberg T : The influence of crown size dimorphism on sex differences in the carabelli trait and canine distal accessory ridge in man. *Arch Oral Biol*, 28 : 527-530, 1983.
21. Hsu JW, Tsai PL, Hsiao TH, Chang HP, Lin LM, Liu KM, Yu HS, Ferguson D : The effect of shovel trait on Carabelli's trait in Taiwan Chinese and Aboriginal populations. *J forensic Sci*, 42 : 802-806, 1997.
22. Kondo S, and Townsend GC : Associations between Carabelli trait and cusp area in human permanent maxillary first molars. *Am J Phys Anthropol*, 129 : 196-200, 2006.
23. Dahlberg AA : Materials for the establishment of standard for classification of tooth characters, attributes, and techniques in morphological studies of the dentition. 1956, Zollar Laboratory of Dental Anthropology, University of Chicago, Chicago, USA.
24. Fujita T : Uder das Messungsstandard der Zähne. *J Anthropol Soc Nippon*, 61 : 27-32, 42. (In Japanese with German summary.), 1949.
25. Mizutani H : Seiwo Kimeru X to Y. (Japanese): In Newton. Newton Press, Tokyo, 2006.
26. Strachan T, Read AP : Human Molecular Genetics 3rd. ed. (Japanese ed.), 2005, Medical Sciences International, Ltd., Tokyo, Japan.
27. Carrel L, Cottle AA, Goglin KC, Willard HF : A first generation X-inactivation profile of the human X chromosome. *Proc Nat Acad Sci USA*, 96 : 14440-14444, 1999.
28. Alvesalo L, Tammisalo E : Enamel thickness of 45,X females' permanent teeth. *Am J Hum Genet*, 33 : 464-469, 1981.
29. Alvesalo L : Dental Growth in 47,XYY Males and in Conditions With Other Sex-Chromosome Anomalies. In : Sandberg AA, editors. *The Y Chromosome*, vol. 6, part B : Clinical Aspects of Y Chromosome Abnormalities. Alan R Liss, New York, 1985, p.277-300.
30. Alvesalo L, Tammisalo E, and Hakola P : Enamel thickness in 47,XYY males' permanent teeth. *Ann Hum Biol*, 12 : 421-427, 1985.
31. Alvesalo L, Tammisalo E, Therman E : 47,XXX females, sex chromosomes, and tooth crown structure. *Hum Genet*, 77 : 345-348, 1987.
32. Zilberman U, Smith P, and Alvesalo L : Crown components of mandibular molar teeth in 45,X females (Turner syndrome). *Arch Oral Biol*, 45 : 217-225, 2000.
33. Scott GR, Turner CG : The anthropology of modern human teeth. Dental morphology and its variation in recent human populations. 1997, Cambridge University press, Cambridge, USA.
34. Fukumoto S : Molecular mechanism of tooth morphogenesis regulated by extracellular matrix. *Ped Dent J*, 43 : 380-384, 2005.
35. Shillingburg HT, Grace CS : Thickness of enamel and dentin. *J South Califor Stat Dent Assoc*, 41 : 33-52, 1973.
36. Alvesalo L, Nuutila M, and Portin P : The cusp of Carabelli. Occurrence in first upper molars and evaluation of its heritability. *Acta Odont Scand*, 33 : 191-197, 1975.
37. Tabata MT, Kondo S : The way of cusp formation : A review from the development, variation, and evolution of the tooth and their molecular mechanisms. *Anthropol Sci (Japanese series)*, 114 : 57-62, 2006.
38. Antonio N : Ten Cate's oral histology : development, structure, and function. th 6ed. (Japanese). 2006, Ishiyaku Publishers, Inc., Tokyo, Japan.
39. Horowitz SL, Morishima A : Palatal abnormalities in the syndrome of gonadal dysgenesis and its variants and in Noonan's syndrome. *Oral Surg Oral Med, Oral Path, Oral Rad, and End* 38 : 839-944, 1974.
40. Jensen BL : Craniofacial morphology in Turner syndrome. *J Craniofac Gent Dev Biol*, 5 : 327-340, 1985.