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Sella Volume and Posterior Fossa Morphometric Measurements in Chiari Type 1

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ABSTRACT

AIM: To retrospectively evaluate the relationships between morphometric measurements in craniovertebral junction and the possible genetic basis of the disease in Chiari 1 malformation patients undergoing surgical treatment.

MATERIAL and METHODS: We included patients who underwent surgical treatment for Chiari 1 malformation with unknown etiology between 2013-2018 in the Neuosurgery Clinic of Eskişehir Osmangazi University. Morphometric and volumetric measurements of the posterior fossa from cranial and cervical radiological imagings of patients with Chiari 1 malformation were performed by a single experienced observer. The results were independently reviewed by two experienced observers who supervised the process and verified the calculations.

RESULTS: It was observed that basal angle was greater in the group of patients with Chiari 1 malformation (125.29° ± 9.522° Vs. 112.33° ± 9.09°), and a significant difference was observed (p=0.000). In patient group, it was also found that the basion-dens distance (3.51 mm ± 1.695mm Vs. 5.27 ± 1.695 mm) (p=0.000), and cerebellar hemispher height were shorter (58.47 ± 5.143 mm Vs. 52.05 ± 5,008 mm) (p=0.000). Tentorium angle was greater in the patient group (97.95° ± 11.321° vs. 87.79° ± 9.891°) (p=0.034). In patient group, dens height was found to be longer (13.9 ± 2.46 mm vs. 14.79 ± 1.631mm) (p=0.041). Sella volume was found to be smaller (41.4 mm^3 Vs. 53.3 mm^3) in the patient group compared to the control group (p=0.034), and foramen magnum plane was larger (64.6° vs. 31.1°) (p=0.000).

CONCLUSION: It is concluded that many parameters including BA, FMP, BDD, CHH, TA, DH, and cellar volüme are abnormal, suggesting the need for focussing to the hormonal metabolism - related synchondral changes.

KEYWORDS: Cellar volume, Chiari malformation, Morphometric measurements

INTRODUCTION

Chiari malformation (CM1) is a congenital malformation defined as varying degrees of herniation of posterior fossa structures from the foramen magnum downwards. It is a disease that has been emphasized since its definition, and new information is added to the literature every day. In parallel with the effect of both the development of imaging methods and the increase in genetics in recent years, different types have been defined for CM and different theories have emerged about these classifications (1,4,9,11). However, the severity of tonsillar herniation is insufficient to explain the etiology and pathophysiology of CM1s today (2). Morphometric evaluation of the posterior fossa (PF) with tonsillar herniation may help resolve this deficiency. Incidentally detecting individuals with low tonsil positions has become more common because the number of cranial and cervical imaging studies has been increasing in recent years (4,9). In addition to the tonsillar position, parameters such as the accompanying basillary invagination, the presence of an occipitoatlantal or atlantoaxial instability, whether a relationship exists between the clivus and

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the foramen magnum and the density, and the position of the foramen magnum led to data creation that will help establish a cause–effect relationship in the herniation of the tonsils and/or in the clinic of patients. This study aims to make the 3D volumetric analysis of the morphometric structure of the PF and the volume of the sella in patients with CM1 and compare these data with the data of normal individuals.

MATERIAL and METHODS

Patient Population

Eighty-four patients were operated on for CM1 in the clinic of the current study between 2013 and 2018. Patients with hydrocephalus, basilar invagination, intracranial mass, tethered cord syndrome, or previous spinal dysraphism were excluded from the study. Consequently, 46 patients meeting the criteria were included in the study. The radiological data of 46 patients were compared with the data of 48 asymptomatic individuals.

Analyses of patient data were approved by the Faculty Board of Eskişehir Osmangazi University Faculty of Medicine, Eskişehir, Turkey, dated 06.12.2018 and numbered 45425468/46. The abbreviation of the analyzed parameters is given in Table I.

All parameters are shown in Figure 1. Cellar volume was measured using the Di Chiro-Nelson method ($v = 0.5 \times h \times w \times l$) (3).

Statistical Analysis

For independent samples, the *t*-test (independent sample *t*-test) was utilized to detect the difference between the groups whose normal distribution assumptions were provided. The Mann–Whitney *U*-test was utilized in cases where normal distribution assumptions could not be achieved.

RESULTS

Of the CM1 patients included in the current study, 16 (34.78%) and 30 (65.21%) were males and females, respectively. The mean age of the patients was 35.3 (age range, 18–62 years old). In the control group, 18 (38.29%) and 29 (61.71%) male and female patients, respectively, were included. The mean age of the control group was 35.4 years old.

Clinical Assessment

All patients complained of headaches and dizziness. Nineteen (41%) patients complained of numbness in the arms along with a feeling of headache and dizziness that was exacerbated by cough, sneezing, and straining. One (2.1%) patient stated to have bitten the left side of his tongue unknowingly, especially during eating, together with a feeling of numbness in the tongue.

In the examination of the patients, 11 (23%) patients had completely normal cerebellar tests. However, cerebellar system examination was abnormal in 35 patients. Moreover, 10 of 12 patients with syringomyelia had a cape-style sensation defect, accompanied by a minimal loss of strength in arm abduction, and described hypoesthesia toward the shoulders and the occipital region.

Radiological Assessment

In the evaluation of 46 patients, tonsillar herniation from FM varied between 9.7 and 13.3 mm (average, 11.8 mm).

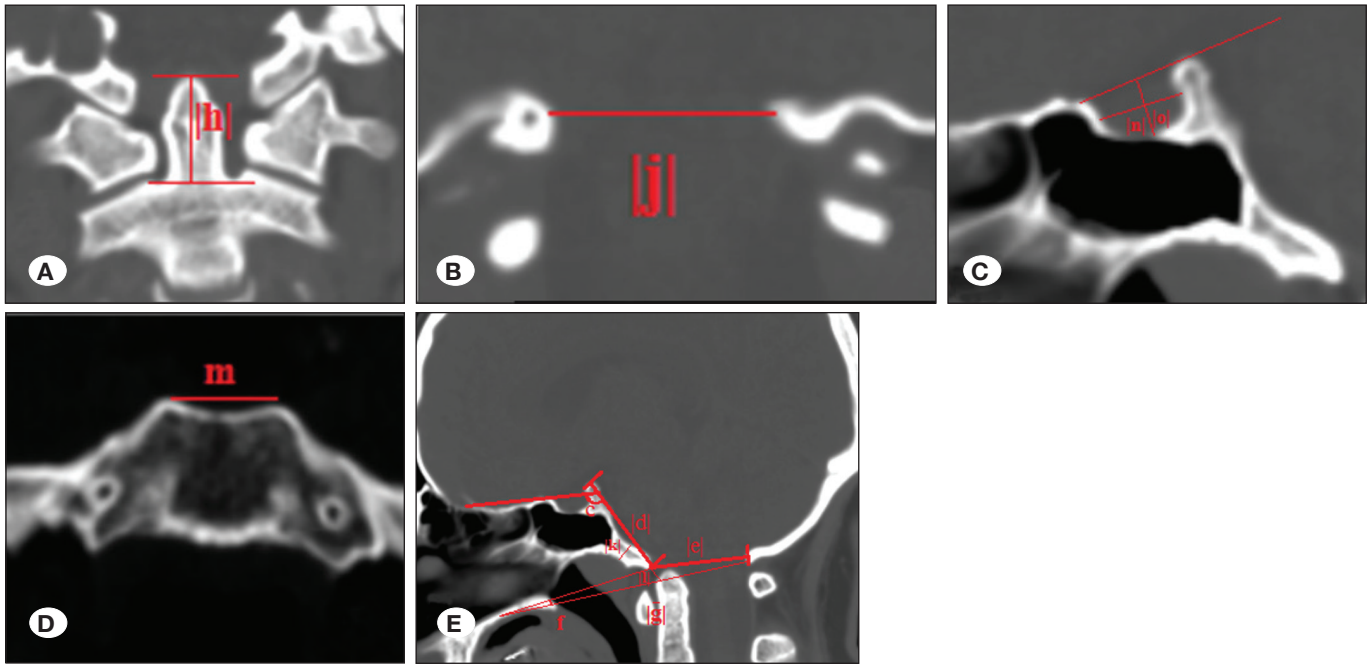

Figure 1: Measured parameters**. A)** Dens height **(h), B)** Foramen magnum lateral distance at the level of juguler tubercle **(j), C)**Cellar depth **(n),** Cella A-P lenght **(o), D)** Cellar lateral lenght **(m), E)** basal angle **(c),** clivus lenght **(d)**, foramen magnum AP distance **(e),** Plane of the foramen magnum according to the hard palate **(f)**, atlantodental distance (**g),** clivus thickness at the level of midsagittal plane (**k),** and distance between basion and dens **(l).**

As an additional pathology, 12 (26%) of the patients have syringomyelia and related symptoms.

Compared to the control group, BA was greater in the patient group (125.29 ± 9.522 vs. 112.33 ± 9.09), and a significant difference was present between the two groups (p=0.000). BDD (3.51 mm 5.27 ± 1,695 mm vs. 5.27 ± 1.695 mm; p=0.000) and CHH were determined to be shorter (58.47 ± 5.143 mm vs. 52.05 ± 5.008 mm; p=0.000). The TA was found to be greater (97.95 ± 11.321 vs. 87.79 ± 9.891 p=0.034) in the patient group, and the DH was longer (13.9 ± 2.46 mm vs. 14.79 ± 1.631 mm; p=0.041).

No significant difference was found for both the independent t-test in CV and FMP. In the Mann–Whitney U-test, a significant difference was observed between the two groups. Sella

Table I: Results of Analysis of the Morphometric Measurements in Patients with CM1 (Group 1) and Control Group (Group 2)

Variable	Group	n	Average	Standart Deviation	sd	t	p
Atlanto-dental distance	1.00	46	0.91	0.458	92	1.112	0.27
	2.00	48	0.81	0.438			
Basal angle	1.00	46	125.29	9.522	92	6.748	**0.000**
	2.00	48	112.33	9.097			
Clivus thickness	1.00	46	7.19	1.835	92	-2.643	0.1
	2.00	48	8.34	2.358			
Clivus lenght	1.00	46	26.94	6.633	92	-1.631	0.106
	2.00	48	29.17	6.600			
Distance between basion and dens	1.00	46	3.51	1.443	92	-5.403	**0.000**
	2.00	48	5.27	1.695			
FM Lateral distance	1.00	46	30.38	5.351	92	-0.039	0.969
	2.00	48	30.43	8.190			
FM A-P distance	1.00	46	34.45	6.317	92	-0.731	0.467
	2.00	48	35.21	3.378			
Cerebellar hemispher height	1.00	46	58.47	5.123	91,604	6.141	**0.000**
	2.00	48	52.05	5.008			
Tentorial angle	1.00	46	97.95	11.321	92	4.640	**0.000**
	2.00	48	87.79	9.891			
Dens height	1.00	46	13.90	2.460	92	-2.076	**0.041**
	2.00	48	14.79	1.631			

Table II: Results of CV and FMP in Patients with CM1 (Group 1) and Control Group (Group 2)

	Group	n	Mean Rank	Sum of Ranks	Mann-Whitney U	p
Cella Volume	1	46	41.4 mm^3	1904.5	823.50	**0.034**
	2	48	53.3 mm^3	2560.5		
	Total	94				
Foramen Magnum Plane	1	46	64.6°	2970.5	318.50	**0.000**
	2	48	31.1°	1494.5		
	Total	94				

volume in the patient group was smaller than in the control group (41.4 mm^3 vs. 53.3 mm^3; p=0.034), and FMP was found to be greater (64.6 vs. 31.1; p=0.000).

DISCUSSION

This study revealed that, compared to the normal population, BA and FMP are greater; BDD, CHH, and DH are longer; and TA is greater in CM1 patients. This study has shown for the first time in the literature that the volume of sella in CM1 is smaller than in the normal population.

Morphometric evaluations of PF in 46 patients with Chiari malformations are an important indicator OF the etiology and pathophysiology of CM. In recent years, morphometric studies comparing radiographic PF parameters between CM1 patients and control individuals in the general population have been published (7). A combination of several parameters has been proposed as an alternative diagnostic criterion other than the tonsillar position. This study examined the differences between healthy individuals that can potentially differentiate patients with symptomatic CM1.

CM1 is a pathology that develops primarily in the bones that will form the skull base (craniovertebral junction and sphenoid bone). A synchondrosis is a cartilage growth plate that consists of a chondrocyte resting zone between proliferating and hypertrophic zones. In humans, sphenoccipital synchondrosis characteristically shows a postpartum closure.

Basicranial synchondrosis fusion begins at 14-15 years and 11–12 years old in men and women, respectively, and is the beginning of puberty (10). Basicranial synchondroses are similar to the epiphyseal growth plates of long bones. The PF growth is affected by hormones and related disorders are not fully understood. However, in some studies, basiocciput is shorter in patients with growth hormone deficiency (14). In a study conducted on a several patients with rickets, the PF was found to be significantly smaller than healthy controls, and CM1 was found in ~30% of the patients (13). These data indirectly show that various hormones regulate the development of the PF. In another study, 5-20% of CM1 patients had growth hormone deficiency (6). This endocrine deficiency in children reveals a physiological mechanism for insufficient development in the PF together with the tonsillar herniation.

In the current study, the reason for finding CV in CM1 patients that were smaller than in healthy individuals is that the hormonal influence is not limited only to the PF. In a study involving 3D measurement of the sphenoid sinus and 2D measurement of the sella, the area of the sella volume is narrower in patients with CM1 (8). Evaluating the volume instead of the area measurement will reveal the change of sella turcica in CM1 patients more. Another study in the literature revealed the presence of pituitary hormone deficiency, narrow sella turcica, ectopic PF, and CM concerning the mutation in the *LHX4* gene (12). A narrow CV in CM1 patients can lead to PF insufficiency with a hormonal response.

Publications show TA changes in PF measurements performed in patients with CM1 (16). The superior displacement of the anterior part of the tentorium may not always develop secondary to compression in the PF. Bony structures may cause the widening of the angle of the tentorium to the opisthion (Figure 2). Therefore, as mentioned in the literature, TA is higher in CM1 patients compared to healthy individuals (15). However, with the influence of hormonal factors and genetic features, the effect on the occipitoparietal synchondrosis, which forms the bone structures of the PF, can change the TA due to the change in protuberantia externa–opistion distance. The effect that will occur here may not only change the angle of the tentorium but also lead to a narrower and shorter PF.

FMAP and FMLD did not change in CM1 patients. This may be caused by the effect of growth factors as a result of the effects on sphenooccipital and occipitoparietal synchondrosis. Rather than evaluating CM1 as a tonsillary herniation hanging down from the basion–opistion line, it should be considered as a result of the basion–opistion line not being caudally located sufficiently (Figure 3). CL is shorter in patients with CM1. This situation can be explained by the density of the PF due to the occipital hypoplasia and shortening of the basioxyptus. Along with the BDD shortness, the longer DH in patients with CM is a response to the dense structure of the disease. It is a response that occurs to protect the instability and neural structures that may develop with the cranial placement of FM. DH increases in response to the herniation caused by the placement of FM in the cranium.

As a result of the measurements made, the FMP was observed to be wider in CM1 patients compared to the hard plate, due to the basion and opistion line remaining more caudal than the facial bones. As the basion and opisthion remained caudal, the FMP widened compared to the hard plate and prepared the ground for “tonsillar herniation”. Here, the complaints arising due to the presence of a short clivus, an FM that is not sufficiently located in the cranial direction, and caudal herniation of the cerebellum and other possible neural structures, are related to the congenital basis of the

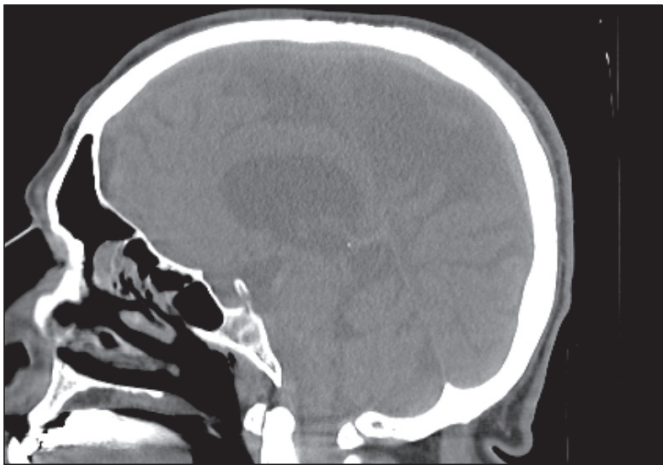

Figure 2: Tentorium position of an adult patient without CM. Tentorium-opistion angle: 96.70. It is observed as a value close to the average (97,950) of patients with CM1. Despite the wide-angle placement of TA compared to normal individuals, CM1 does not exist.

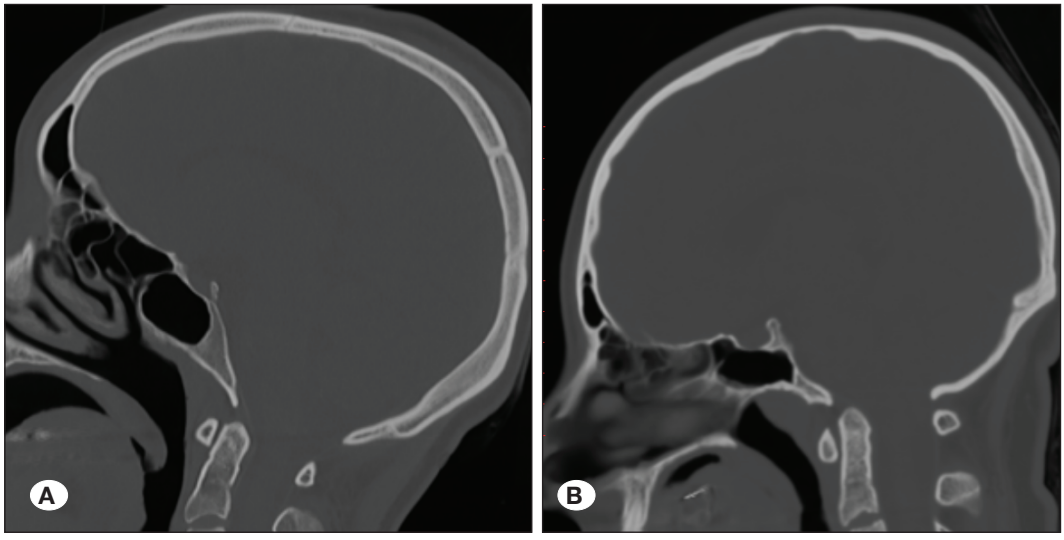

Figure 3: A) CT examination of the normal adult in the midsagittal axis **B)** CT examination of the patient with adult type CM in the midsagittal axis.

disease at the craniovertebral junction in patients with CM1, which was evaluated as "inherent" in light of recently acquired information.

The mean height of the operated patients with CM1 is shorter than the normal adult group, their neck is shorter and some other skeletal anomalies may accompany (5,6). Some studies show that hormonal imbalance conditions associated with growth factors were considered especially in the pediatric age group, such as the aggregation of CM after growth hormone replacement and Paget's disease in CM patients, a positive correlation between them may be observed. However, not enough studies in the literature exist evaluating the relationship between CM and pituitary hormones. However, not only growth hormones but also the characteristics of the sex hormones and growth factors in the synchondral joints, which are associated with the growth pattern, should be considered. In both intrauterine and postnatal life, examining growth factors, to which basicranial synchondroses are exposed or unresponsive is important. Another problem is revealing whether a hormonal response is a cause or effect. In FMP, the angle was observed to be wider in CM patients. In the developmental process, it is proportional to the facial bones in the cranium, the development of the paranasal bones, and other body structures.

CONCLUSION

This study revealed that BA, FMP, BDD, CHH, TA, and DH in CM1 patients are different from the normal population, and sella volume is also lower than normal. All these differences reveal that the unknowns are more than what is known in Chiari 1 and the hypotheses should be reviewed. This study is suggesting that further studies should focus on the embryogenetic basis of the Chiari 1 patients.

AUTHORSHIP CONTRIBUTION

Study conception and design: GB
Data collection: GB
Analysis and interpretation of results: EO
Draft manuscript preparation: ZO
Critical revision of the article: SN
Other (study supervision, fundings, materials, etc...): AA
All authors (GB, EO, ZO, SN, AA) reviewed the results and approved the final version of the manuscript.

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