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Investigation of septum pellucidum and its variations with magnetic resonance imaging

Keziban Karacan [1], Alper Karacan [2]

[1] Department of Anatomy, Faculty of Medicine, University of Sakarya, Turkey
[2] Department of Radiology, Faculty of Medicine, University of Sakarya, Turkey

ORCID ID of the author(s)
KK: 0000-0001-8861-1647
AK: 0000-0001-8930-9546

Corresponding Author
Keziban Karacan
Department of Anatomy, Faculty of Medicine, University of Sakarya, The neighborhood of Korucuk, The campus of Korucuk, Adapazarı, Sakarya, Turkey
E-mail: kkaracan@sakarya.edu.tr

Ethics Committee Approval
The study protocol was approved by the local ethics committee of Sakarya University, Faculty of Medicine (71522473/050.01.04/113). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The septum pellucidum (SP) is the thin layer formed by the two laminas that form the medial wall of the lateral ventricle. When the laminas do not fuse, a cavity called cavum septum pellucidum (CSP) or Cavum Vergae (CV) forms. CSP is a developmental anomaly with unclear pathological significance and is common in people with neuropsychiatric diseases, especially schizophrenia, as well as post-traumatic stress disorder, Tourette's disease, and patients who suffer from recurrent and severe head trauma. However, few studies in the literature examine the CSP morphology among healthy individuals. Therefore, we aimed to evaluate the morphology and variations of septum pellucidum in healthy individuals.

Methods: In this retrospective cohort study, the septum pellucidum was morphologically evaluated in 509 patients who underwent brain Magnetic Resonance Imaging (MRI) at Sakarya University Faculty of Medicine, Sakarya Training and Research Hospital. We classified the anatomical variations of the septum pellucidum as CSP, CV, CVI and evaluated their dimensions.

Results: CSP was detected in 11.98% of the cases, and CV, in 1.38%. While 55.74% of individuals with CSP were male, 44.26 % were female. The mean CSP length and height were 7.71 (2.95) mm (P=0.103), and 2.80 (1.12) mm (P=0.649), respectively, and the mean length and height of the SP were 30.98 (7.36) mm (P=0.001), and 11.89 (3.32) mm (P=0.042), respectively.

Conclusion: Knowledge of CSP, one of the septum pellucidum variations, is of great importance in the differential diagnosis of midline cystic mass lesions. Its volumetric changes may be related to the development of psychiatric disorders in childhood and adulthood.

Keywords: Septum pellucidum, Cavum septum pellucidum, Cavum vergae, Magnetic resonance imaging

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Introduction

Septum pellucidum (SP), considered a part of the limbic system, is a vertically extending closed cavity between the lateral ventricles, covered with ependyma on both sides, consisting of a thin pia layer with white matter and gray matter [1]. It is attached cranially to the corpus callosum and caudally to the columna of fornix on the front between the rostrum and truncus corporis callosi [2, 3]. The thickness of this partition is usually 1-3 mm, and it is formed by the union of two separate leaves during fetal life [4, 5]. There may be a potential gap between the two leaves, sometimes detected at autopsy or radiological imaging [6, 8]. If the cavity extends rostrally, it is called Cavum Septum Pellucidum (CSP), and is in front of the foramen interventriculare. When the cavity extends caudally and is behind the foramen interventriculare, it is called Cavum Vergae (CV). The cavum veli interpositi (CVI) is in front of the quadrigeminal (superior) cistern above the roof of the third ventricle. Cisterna interventricularis, ventriculi tertii, transverse fissure and sub-trigonal fissure are also used instead of CVI. It develops because of the abnormal separation of the limbs of the fornix and is independent from the septum pellucidum [9].

The defect in the SP structure may indicate a disruption in the development of the hippocampus or corpus callosum during the embryological period because the development of CP is synchronous with the hippocampus, corpus callosum or nucleus septalis, all limbic system structures. During the embryological period, the growth of the hippocampus and corpus callosum pushes the SP leaves and allows the leaves to adhere from the back to the front. Therefore, it is thought that dysgenesis occurring in neighboring structures will also affect SP and may cause CSP, CV or CVI by disrupting the adhesion process of leaves [10]. It is clearly emphasized in the literature that the presence of CSP or CV may be an indicator of a disruption in limbic system embryology and may be associated with schizophrenia, obsessive-compulsive disorder or other psychotic disorders [11-13]. Based on this information, we aimed to evaluate SP and its variations in our study.

Materials and methods

Participants

The present retrospective study included 640 patients who were admitted to Sakarya University Faculty of Medicine Training and Research Hospital between 2013 and 2016. The study protocol was approved by the local ethics committee of Sakarya University, Faculty of Medicine (71522473/050.01.04/113). The patients presented with headache, dizziness, tinnitus, hearing disturbance, hemisensory disturbance, and seizures. Initial neurological examination and interviews confirmed that none of the 509 patients had a history of previous intracranial hemorrhage, cerebral infarction, meningitis, ventriculitis, neurodegenerative disease, traumatic brain injury, intracerebral and intraventricular cysts, hydrocephalus, brain tumor, or psychotic disorders. One hundred and thirty-one patients were excluded due to operation history, structural anomaly and the presence of space-occupying lesions. Brain MRI scans of 509 (189 males, 320 females) cases aged 1-89 years were reviewed. The mean age of the patients was 44.99 (18.945) years among females and 49.98 (20.46) years among males.

Magnetic Resonance Imaging

Examinations were performed using a 1.5 T MRI unit (Signa Voyager; GE Healthcare, Milwaukee, WI) with spine coil, in supine position. The cranial MRI protocol included coronal T2-weighted TSE images (TR/TE, 5102/102 ms; slice thickness/interslice gap, 5/1.5 mm and NEX, 2), sagittal T2-weighted TSE images (TR/TE, 4410/102 ms; slice thickness/interslice gap, 5/1.5 mm and NEX, 2), and axial T2-weighted Propeller images (TR/TE,6335/125 ms; slice thickness/interslice gap, 5/1.5 mm and NEX, 1).The T2WIs at the level of the foramen of Monro and that at the lowest level of the body of the lateral ventricles were used as references for identifying the CSP, CV, and CVI.

Measurements

The presence of CSP, CV and CVI investigation with length and height measurements were made for these variations when detected. The shape and extent of the CSP, CV and CVI were assessed on the coronal and sagittal images. In addition, the study group was divided into four age groups as 0-20, 21-40, 41-60 and 60+ years to better reveal the development of CP. The present study was performed per our institution's guidelines for human research. Ethics committee approval (71522473/050.01.04/113) was obtained before starting the measurements. All authors declare that the study was conducted in accordance with the World Medical Association Helsinki Declaration, "Ethical Principles for Medical Research on Human Subjects".

Statistical analysis

Data management and statistical analysis were performed with the statistical package for social sciences (SPSS) version 18 for Microsoft Windows. After descriptive statistical analyses (frequency, percentage distribution, mean (standard deviation)) were performed, normal distribution of continuous variables was assessed by Shapiro-Wilk and Kolmogorov Smirnov Tests. Chi-square test was conducted to evaluate the group difference in terms of discrete variables. Independent t-tests were used for continuous variables meeting parametric assumptions. The data were compared by gender. Statistical significance was indicated by a *P*-value of less than 0.05.

Results

Among all, 84.64% of the cases had normal CP anatomy. The CSP and CV incidences were 11.98% (n=61) (Figure 1), and 1.38% (n=7) (Figure 2), respectively; however, no CVI was not found in these cases. The incidence, length, and height of CSP were insignificantly higher in males, while those of CV were higher among females (71.43% vs. 28.57%) (Table 1). In the comparison of the length and height of SP, the values of men were significantly higher than that of women (Table 1) (Figure 3).

CP length was similar between individuals aged 0-20 years and 21-40 years (P=0.277). However, significant differences existed between individuals aged 0-20 years and those aged 41-60 years and 61+ years (P=0.001). Those in the 21-40-year age group significantly differed from those aged 41-60 years and 61+ years (P=0.001). The CP length of individuals

aged 41-60 years significantly differed from all other groups (P=0.001). Similarly, there was a significant difference between the CP lengths of those over the age of 61 and all other age groups (P=0.001) (Table 2).

Figure 1: Presence of cavum septum pellucidum (CSP) on coronal MR image

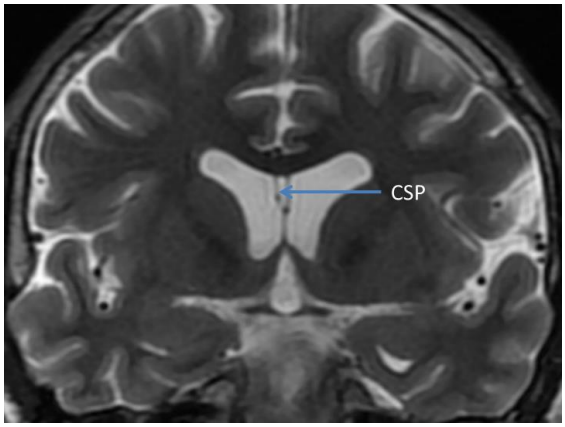

Figure 2: Presence of cavum vergae (CV) on axial MR image

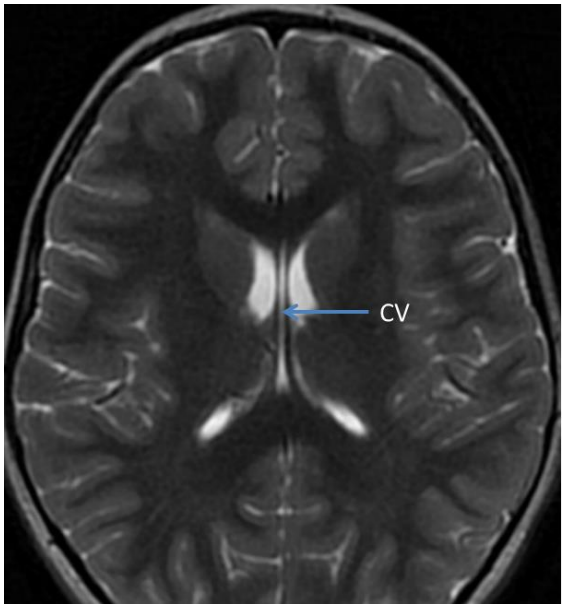

Figure 3: Presence of septum pellucidum (SP) on coronal MR image

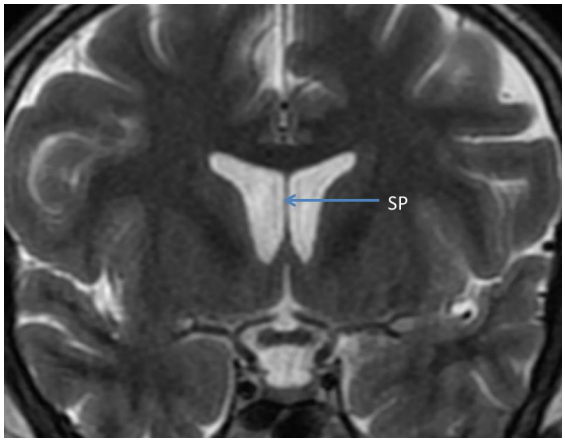

Table 1: Evaluation of cavum septum pellucidum (CSP), cavum vergae (CV) and septum pellucidum in terms of length, height, and width according to gender

		Male	Female	Total	*P*-value
CSP	n (%)	34(55.74)	27(44.26)	61(11.98)	
	Length Mean(SD)	8.26(3.29)	7.02(2.34)	7.71(2.95)	0.103
	Height Mean(SD)	2.86(1.37)	2.73(0.72)	2.80(1.12)	0.649
CV	n (%)	2(28.57)	5(71.43)	7(1.38)	
	Length Mean(SD)	12.04(3.06)	14.80(2.34)	14.01(1.43)	0.456
	Height Mean(SD)	51.13(1.98)	47.50(0.72)	48.54(5.78)	0.505
	Width Mean(SD)	5.43(1.43)	8.77(5.17)	7.82(4.56)	0.432
SP	n (%)	153(34.7)	288(65.3)	441(100)	
	Length Mean(SD)	32.59(7.36)	30.13(7.23)	30.98(7.36)	0.001*
	Height Mean(SD)	12.33(3.55)	11.66(3.17)	11.89(3.32)	0.042*

SD: Standard deviation, *P<0.01 statistically significant

Table 2: Evaluation of septum pellucidum (SP) in terms of length and height according to age groups

Age Groups	n(%)	SP length	height
0-20	47(10.7)	25.49(6.42)	10.14(2.74)
21-40	131(29.7)	27.40(5.63)	10.60(2.26)
41-60	144(32.6)	31.43(6.57)	11.78(2.93)
61+	119(27.0)	36.54(6.42)	14.15(3.73)
Total	441(100)		

CP height was similar between individuals aged 0-20 years and 21-40 years (P=0.811). There were significant differences between individuals aged 0-20 years and those aged 41-60 years (P=0.007) and 61+ years (P=0.001). The CP length of individuals aged 41-60 years significantly differed from all other groups. Similarly, there was a significant difference between the CP heights of those over the age of 61 and all other age groups (Table 2).

Both CP length and height were insignificantly lower in females (P>0.05) (Table 3).

Table 3: Evaluation of septum pellucidum (SP) in terms of length and height according to gender

Age Groups	Gender	SP				
		n(%)	length	*P*-value	height	*P*-value
0-20	Male	14(29.8)	28.24(6.87)	0.055	11.01(2.92)	0.164
	Female	33(70.2)	24.33(5.94)		9.78(2.62)	
21-40	Male	36(27.5)	28.17(6.43)	0.341	10.61(2.46)	0.952
	Female	95(72.5)	27.11(5.30)		10.59(2.19)	
41-60	Male	52(36.1)	32.25(6.91)	0.263	11.87(3.28)	0.764
	Female	92(63.9)	30.97(6.36)		11.72(2.73)	
61+	Male	51(42.9)	37.24(5.77)	0.304	14.37(3.71)	0.568
	Female	68(57.1)	36.01(6.87)		3.98(3.76)	
Total		441	p>0.05			

Discussion

The development of the septum pellucidum is synchronized with the development of the corpus callosum, hippocampus, amygdala, and septal nuclei, all of which are limbic system structures. Therefore, possible variations of septum pellucidum can be accompanied by the variations of these structures [8].

CSP, an indication of the abnormal development of the brain's midline structures, is a closed space that is generally not connected to the ventricular system and cisterna. Septum pellucidum agenesis is seen at a frequency of 2-3/100,000 and associated with some congenital brain anomalies, especially holoprosencephaly, septo-optic dysplasia and schizencephaly [14-16]. There were no individuals with septum pellucidum agenesis in our study. The rate of CVI variation, which was also not found among our patients, was reported as 5.54% by Alessandro et al. [17]. Meanwhile, Satoshi et al. [18] reported an unusually high and controversial rate of 50%. CSP volume increases until the 32nd week of gestation and then decreases [19]. D Addriove et al. [20] found the average size of midline cysts to be 12.4 mm prenatally. Behnaz et al. [21] reported the cut-off value of CSP width as 7.1 mm for indicating a probability of brain anomaly during the prenatal period. However, the generally accepted view is that if the CSP width is 10 mm in any period of pregnancy, it should be called a cyst instead of an anatomical variation [18]. Dremmen et al. [22] found the incidence of CSP to be 4.6% in their study on school-age children. Studies on the prevalence of CSP in healthy adults have revealed vastly different numerical results (0.1-85%). This difference was attributed to the sensitivity of the imaging method in many articles. Studies with a low incidence of CSP are generally performed with CT, and those reporting higher incidences of CSP are performed with MRI. In the study of

Oktem et al. investigating the MRIs of 3128 patients, the incidence of CSP was reported as 3.7% [8]. In our study, the incidence of CSP is 12%. Some studies indicate that the association of neurological diseases with CV is much more common than CSP. Oktem et al. reported the incidence of CV as 3.1% (8). In our study, this rate was 1.2%. Raine et al. showed that adult patients with large CSP had significantly more antisocial activities than patients with normal CSP [23]. Filipovic and Teofilovski-Parapid [24] found a CSP rate of 68.63% in the autopsy series of cases with neuropsychiatric disorders. In the same study, the incidence of CSP in asymptomatic cases was 10.61%, and 22.96% in total. In addition, CSP length and width are significantly higher in the symptomatic group. Cystic lesions in the midline such as arachnoid cysts can be confused with CSP, CV, and CVI variations due to their localization. In these cases, distinction can be made by evaluating their relationship with the surrounding anatomical structures, especially the third ventricle-lateral ventricle and cisterns. Arachnoid cysts and other cystic lesions are not related to these structures and usually present with compression findings [25]. Most CSPs are asymptomatic and considered anatomical variations [26]. Symptomatic CSP is rare; its diagnosis is both difficult and controversial [27]. In symptomatic cases, the cause is increased intracranial pressure and the most common symptom is headache [28]. Endoscopic fenestration is used in the safe and effective treatment of CSP [29].

Limitations

Our study contains some limitations, one being its retrospective nature, including results from a single center, and the relatively small sample size.

Conclusions

SP variations which are indetectable in CT may be detected by MRI. We wanted to share the frequency of CP variation and detailed morphometric evaluation in the Turkish population in this study we conducted on healthy individuals using MRI. We think that the age-grouped data we shared for CSP, and CV will contribute to the literature. Patients with SP variations should be evaluated in detail in terms of other accompanying anomalies. Due to the superiority of showing anatomical details in the anatomy of the septum pellucidum region, the preferred imaging method should be MRI.

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