Relationship between Cavum Septum Pellucidum and Epilepsy

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Objective: The authors study a relationship between the presence of cavum septum pellucidum (CSP) and the development of epilepsy by comparing the presence of CSP, which has been known to be a normal variation, in normal control group and epilepsy patients.

Methods: This study included 377 patients with epilepsy and 252 controls without epilepsy. Of epilepsy patients, 168 patients underwent surgery due to intractability and 209 patients was on medication of antiepileptic drugs. Control group had only headache and no visible lesion in MRI. Of 168 surgical patients, 102 patients had temporal lobe epilepsy and 66 patients had extratemporal lobe epilepsy. Ninety five patients showed a neuronal migration disorder in histopathologic findings. Definition of "CSP" and "partial CSP" was followed by Pauling’s classification.

Results: CSP was present 8.2% of epilepsy patients and 1.6% of control group (p<0.01). CSP was detected in 11.3% of patients with surgical treatment and in 5.7% of patients with medical treatment. CSP was noticed in 8.9% of temporal lobe epilepsy, in 15.2% of extratemporal lobe epilepsy, in 13.7% of patients with neuronal migration disorder, and in 8.2% of patients with no neuronal migration disorder.

Conclusion: Presence of CSP is statistically higher in epilepsy patients than in control group. This results indicates that the presence of CSP may not be a simple normal variation, and it can be considered a developmental anomaly that may contribute to epileptogenesis.

KEY WORDS: Cavum septum pellucidum - Epilepsy.

Introduction

Septum pellucidum refers to a thin translucent plate of two laminae that parallels interhemispheric fissure. It forms the medial wall of both lateral ventricles and extends from the lamina terminalis to the splenium of the corpus callosum. It is posteroinferior to the corpus callosum and antero-superior to the fornix and hippocampal commissure. Lateral aspect of septum pellucidum is a triangular shape with its base locating anteriorly and with its apex locating posteriorly. Septum pellucidum is part of the limbic system and play as a relay station connecting the hypothalamic autonomic system to hippocampus, amygdala, habenula and brain stem reticular formation.

A cavity between two leaflets of septum pellucidum is called cavum septum pellucidum (CSP), and it can be also called the fifth ventricle because it is filled with cerebrospinal fluid (CSF). But the cavity is not connected to leptomeningeal or ventricular spaces. CSP normally exists in the fetal period but begins to close from the posterior part starting the 6th month of gestation. It remains as a small slit but usually becomes to close completely around the 2nd month of birth as brain develops. However CSP can be occurred on an acquired basis. Higher presence of CSP in boxers than that of ordinary people indicates that CSP can be occurred even by repeated brain damage.

Investigation into presence of CSP was started by autopsy at the initial period, and subsequently continued by means of pneumoecephalography, computed tomography (CT) and magnetic resonance image (MRI). But, it failed to attract attention on a clinical basis and CSP has been considered as normal variation. Recently, research was conducted for patients with psychotic disorders such as schizophrenia and mood disorder compared with normal control groups regarding presence of CSP but none was made for epilepsy patients with control groups.

As CSP was observed frequently in MRI of epilepsy patients, we have launched this investigation on the idea that existence of CSP may have an impact on epileptogenesis.

Materials and Methods

Three hundred and seventy seven epilepsy patients were included for this study. Out of them, 168 patients underwent operation due to intractable epilepsy from May 1998 to
June 2003 and could be traced, and the remaining 209 were outpatients on medication for epileptic seizures.

Epilepsy patients caused by head trauma, tumors, parasite and vascular malformation which were not related to epilepsy that broke out in course of brain development were excluded from this study.

Control groups included 252 who have come to hospital for headache from January 2001 to June 2003 and had no visible lesion in MRI.

Epilepsy patients were composed of 220 males (58.4%) and 157 females (41.6%), and 30.3±11.9 years old on average, while control groups were made up of 133 males (52.8%) and 119 females (47.2%), and 44.3±12.6 years old on average. Of patients who underwent operation for epilepsy, there were 102 patients (60.7%) with temporal lobe epilepsy and 66 patients (39.3%) with extratemporal lobe epilepsy. In biopsy, 95 patients (56.5%) were diagnosed as neuronal migration disorder and 73 patients (43.5%) were not.

MRI scans were obtained on a 1.5 Tesla imager (Siemens Magnetom Vision, Erlangen, Germany). T1-weighted images were acquired using spin echo technique with a repetition time(TR) 520msec, echo time(TE) 12 msec in axial and coronal, and sagittal planes. T2-weighted images were obtained with a RT of 4600msec and TE of 99msec. The thickness of the contiguous slices were defined as 5mm. The number of excitation(NEX) was 2.

According to the classification of Pauling\textsuperscript{22}, when the leaves of the septum were separated by at least 2mm from the rostral-superior attachment to the corpus callosum to the caudal-inferior attachment to the columns of the fornix, it was defined as “CSP”. When two laminae were partly connected or divided and length from anterior to posterior was longer than width, it was defined as “partial CSP”(Fig. 1, 2). Additionally, when signal intensity in CSP was different from that in cerebrospinal fluid of both lateral ventricles, it were excluded from this research even though there was a cavity.

Pearson’s $\chi^2$ and Fisher's exact test of SPSS were used for a statistical analysis.

**Results**

As epilepsy patients recorded CSP presence of 8.2% (31/377) and control groups posted 1.6%(4/252) respectively, epilepsy patients showed significantly higher ratio(p<0.01). With partial CSP presence standing at 13%(49/377) for epilepsy patients and 10.7%(27/252) for control groups, epilepsy patients have more partial CSP than control groups, but there was no statistical significance(p=0.389).

Presence of CSP reached 11.3%(19/168) for epilepsy patients who underwent operation and 5.7%(12/209) for patient who did not, and thus those who underwent operation showed higher presence ratio(p=0.060). Presence of partial CSP amounted to 14.9%(25/168) for patients who underwent operation and 11.5%(24/209) for patients who did not(p=0.330). Of patients who underwent operation, temporal lobe epilepsy patients stood at 8.8%(9/102) and extratemporal lobe epilepsy patients commanded 15.2%(10/66), showing higher presence ratio (p=0.206) in terms of presence by lesion. As patients who were diagnosed as neuronal migration disorder in biopsy accounted for 13.7%(13/95), and patients who were not reached 8.2% (6/73), patients with neuronal migration disorder showed higher presence ratio of CSP(p=0.268). In terms of presence of partial CSP, temporal lobe epilepsy patients accounted for 11.8%(12/102) and extratemporal lobe epilepsy patients held 19.7%(13/66) and thus extratemporal lobe epilepsy patients showed higher presence of partial CSP(p=0.158). In patients with neuronal migration disorder showed a 12.6%(5/39) and patients who were not accounted for 17.8%(13/73)(p=0.350). In epilepsy patients, CSP presence by age stood at 16.7%(3/18) from 1 to 10, 8.8%(5/57) from 11 to 20, 10.7%(13/121) from 21 to 30, 5.4%(6/112) from 31 to 40 and 5.8%(4/69) from 41 and older(p=0.365). By sex, control groups' CSP presence was 1.5%(2/133) for male and 1.7%(2/119) for female, while that of epilepsy patients was 8.2%(18/220) for male and 8.3%(13/157)
for female, showing similar presence in both control groups and epilepsy patients.

According to the investigation result on presence of CSP or partial CSP, CSP showed statistically higher ratio in epilepsy patients than in control groups. In terms of the location of the epileptogenic zone and pathologic substrate, patients with extratemporal lobe epilepsy or neuronal migration disorder showed higher ratio. Presence of CSP by age and sex was highly observed in patient groups but both cases had no statistical significance(Table 1).

**Table 1. Incidence of cavum septum pellucidum in control and patient groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Absent(N, %)</th>
<th>Partial(N, %)</th>
<th>Complete(N, %)</th>
<th>Total(N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>221(87.7%)</td>
<td>27(10.7%)</td>
<td>4(1.6%)</td>
<td>252</td>
</tr>
<tr>
<td>Patients</td>
<td>297(78.8%)</td>
<td>49(13.0%)</td>
<td>3(8.2%)</td>
<td>377</td>
</tr>
<tr>
<td>Operation</td>
<td>124(73.8%)</td>
<td>25(14.9%)</td>
<td>19(11.3%)</td>
<td>168</td>
</tr>
<tr>
<td>NMD</td>
<td>70(73.7%)</td>
<td>12(12.6%)</td>
<td>13(13.7%)</td>
<td>95</td>
</tr>
<tr>
<td>No NMD</td>
<td>54(74.0%)</td>
<td>13(17.8%)</td>
<td>6(8.2%)</td>
<td>73</td>
</tr>
<tr>
<td>TLE</td>
<td>81(79.4%)</td>
<td>12(11.8%)</td>
<td>9(8.8%)</td>
<td>102</td>
</tr>
<tr>
<td>ETLE</td>
<td>43(65.1%)</td>
<td>13(19.7%)</td>
<td>10(15.2%)</td>
<td>66</td>
</tr>
<tr>
<td>No Operation</td>
<td>173(82.8%)</td>
<td>24(11.5%)</td>
<td>12(5.7%)</td>
<td>209</td>
</tr>
</tbody>
</table>

* p<0.01 NMD: neuronal migration disorder, TLE: temporal lobe epilepsy, ETLE: extra temporal lobe epilepsy, N: number

**Discussion**

In this study, presence of CSP showed a statistically higher ratio in epilepsy patients. It implies that existence of CSP in epilepsy patients could have implications for epileptogenesis in a previously unknown form. According to other studies on CSP presence of normal people, the rates of CSP in CT were reported to reach 1.3–3.3% by MRI studies, they reported CSP in 1.1% to 84.8% (Table 2). Classifying the size of the width of CSP, Shunk announced that CSP presence stood at 16.3% when it was less than 2mm-wide, 8.4% when it was less than 3mm-wide, 5.4% when it was less than 4mm-wide and 0.3% when is more than 5mm-wide. The reason why there is a discrepancy between investigation result is that there is a difference between definition and investigation method of CSP and the number of targeted groups, but presence of CSP is usually around 2%, based on large or complete CSP.

On CSP presence of patients with brain disease, there are a group of researchers who have made the comparative study on schizophrenia and control groups. They reported that patients and control groups showed a similar CSP presence when size of width of CSP was not taken into consideration, and deemed partial CSP as anatomical normal variation. Nopoulos et al. studied 44 schizophrenic patients without CSP and 10 patients with CSP. In this study, the schizophrenic patients with abnormal CSP showed volume reduction in the left temporal lobe, as well as a less severe decrease in total brain tissue. This finding may reflect developmental abnormality of hippocampus and corpus callosum in schizophrenic patients with CSP.

There are some reports that CSP were more common in retarded populations. They explained that the CSP serves as a marker or cerebral dysfunction manifested by neurodevelopmental abnormalities.

In our study, epilepsy patients presence of partial CSP was slightly higher than control groups, but there was no statistical significance. On the other hand, presence of CSP stood at 8.2% for patient groups and 1.6% for control groups and statistically significant difference was observed accordingly.

Akiyama et al. observed CSP from 71 patients (2.6%) by analyzing CT of 2722 patients. Of those who were observed to have CSP, 16 patients (22.5%) were those who showed symptoms of clinical epileptic seizure and 22 patients (31.0%) were those who did not have the symptoms but showed abnormal findings in electroencephalography. Bruyn said that 30 to 50% of people with CSP were found to show epileptic seizure and 15% were known to have psychosis, dementia and personality changes. Two leaflets of septum pellucidum become fused by rapid growth of hippocampal alveoli and corpus callosum in process of brain maturation, and abnormal forma-tion of this structure can hamper fusion of septum pellucidum, thereby leading to presence and continued existence of CSP.

Septum pellucidum itself cannot cause epilepsy because it does not consist of pyramidal cells, so that it can be thought that epilepsy which occurred in patients with CSP is attributable to abnormality in the

**Table 2. Incidence of CSP in normal persons**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Number</th>
<th>Incidence</th>
<th>Imaging</th>
<th>Definition of CSP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bae et al.</td>
<td>1000</td>
<td>1.3%</td>
<td>CT</td>
<td>Not described</td>
</tr>
<tr>
<td>Degreer et al.</td>
<td>46</td>
<td>15.2%</td>
<td>MRI</td>
<td>Visible space between SP</td>
</tr>
<tr>
<td>Nopoulos et al.</td>
<td>95</td>
<td>58.7%</td>
<td>MRI</td>
<td>More than 1 slice in coronal view (1mm slice thickness)</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>28</td>
<td>10.7%</td>
<td>MRI</td>
<td>With &gt;3mm in axial view</td>
</tr>
<tr>
<td>Aldur et al.</td>
<td>500</td>
<td>2.8%</td>
<td>MRI</td>
<td>Space between SP (entire length)</td>
</tr>
<tr>
<td>Pauling et al.</td>
<td>814</td>
<td>2.1%</td>
<td>MRI</td>
<td>Space between SP (entire length)</td>
</tr>
<tr>
<td>Kwon et al.</td>
<td>47</td>
<td>84.5%</td>
<td>MRI</td>
<td>More than 1 slice in coronal view (1.5mm slice thickness)</td>
</tr>
<tr>
<td>Choi et al.</td>
<td>252</td>
<td>1.6%</td>
<td>MRI</td>
<td>Space between SP (entire length)</td>
</tr>
</tbody>
</table>

CT: computed tomography, MRI: magnetic resonance image, SP: septum pellucidum, CSP: cavum septum pellucidum
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limbic system related to the formation of CSP or other accompanying abnormality in neuronal development. According to our study on the relationship between presence of CSP and epilepsy, presence of CSP stood at 8.2% for patient groups and 1.6% for control groups, and 13.7% for patients with neuronal migration disorder and 8.2% for patients without neuronal migration disorder. From this, authors think that patients with CSP may show symptoms of epilepsy in tandem with other abnormality in neuronal development.

In this study, presence of CSP stands at 11.3% for patients who underwent operation and 5.7% for patients whose seizure is well-controlled by medication and this indicates intractable epilepsy patients have higher presence ratio (p<0.06). This can be interpreted that existence of CSP may have influence on effect of antiepileptic drugs, but it is necessary to study further on this.

In our study on CSP presence according to the location of the epileptogenic zone and the presence of the neuronal migration disorder, patients with extratemporal lobe epilepsy and patients with neuronal migration disorder had more CSP even though there was no statistical significance. From the above results, it can be suggested that existence of CSP is abnormality in neuronal development associated with brain diseases such as schizophrenia, mental retardation, epilepsy, and so on.

There are some studies that agenesis of septum pellucidum, one of other abnormalities in neuronal development associated with presence of septum pellucidum, is related to epileptic seizure. Harenko et al. noted that of nine patients with agenesis of septum pellucidum, two are related to epileptic seizure. Agenesis of septum pellucidum is very rare innate or acquired abnormality that lateral ventricles are connected into one because there is no septum pellucidum. This can be occurred to boxers, patients with Tourette syndrome, and patients after neuroendoscopic surgery, the fetus exposed to anticonvulsant during gestational ages. It is known that genetic background comes from injury of nerves stemming from hypoperfusion and infection at a time when septum pellucidum forms around 7 to 8 weeks of pregnancy. Usually 2 or 3 per 100,000 are reported to have agenesis of septum pellucidum, but in our study, this abnormality have not shown from control groups but had a relatively higher ratio of 0.8%(3/377) from epilepsy patients. However, the figure cannot be deemed general because the number of patient groups is small.

Conclusion

According to our study, presence of CSP showed statistically higher ratio in epilepsy patients than in control groups. It is found to be higher in patients with extratemporal lobe epilepsy than in patients with temporal lobe epilepsy and also higher in patients with neuronal migration disorder than in patients without neuronal migration disorder. This leads to a conclusion that CSP is not a simple normal variation but related to occurrence of epilepsy in some portions, and CSP should be considered a developmental anomaly that may contribute to epileptogenesis. More sophisticated study should be continued by increasing the number of patient groups and control groups.

References


