A case of cryptogenic localization related epilepsy with Asperger's syndrome

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Background: We report on the possible link between localization-related epilepsy of origin around the left temporal lobe and Asperger's syndrome (AS).

Clinical Details: A 13-year-old boy, born of normal delivery, was diagnosed with Asperger's disorder at 7 years old based on the criteria laid out by the Diagnostic and Statistical Manual of Mental Disorders-IV, due to the presentation of characteristic clinical symptoms and the results of the Wechsler Intelligence Scale for Children-III assessment. Just after the time of diagnosis, he experienced complex partial seizures and status epilepticus. Antiepileptic drugs were prescribed for epilepsy, after which, his convulsions disappeared. Presently, he attends a special support class at a public junior high school due to his AS. In a single photon emission computed tomography (SPECT) of the brain with Tc-99m ethyl cysteinate dimer, the abnormal findings of perfusions around the left temporal lobe and the bilateral cerebral ventricles were recognized. The patient also has presented no neurological symptoms, such as paralysis. Electroencephalogram (EEG) at 9 years old showed bilateral and occipitotemporal paroxysmal discharge.

Conclusions: Abnormality in the left occipital and post-temporal areas, which was strongly indicated by the EEG and brain SPECT findings, could be a cause of epilepsy and pervasive developmental disorder, including AS.

Key words: Asperger's syndrome, cryptogenic localization related epilepsy, electroencephalogram, single photon emission computed tomography

Abbreviations: AS, Asperger's syndrome; ECD, ethyl cysteinate dimer; EEG, electroencephalogram; MRI, magnetic resonance imaging; SPECT, single photon emission computed tomography

Introduction

Epilepsies among patients with autism have been reported in many studies. However, few combined cases of Asperger's syndrome (AS) and epilepsy have been reported. The mechanism which is common to AS and epilepsy, of pathogenesis and pathophysiology requires further elucidation, and the conclusion is yet unknown. In our combined case of AS and epilepsy, the electroencephalogram (EEG) and brain single photon emission computed tomography (SPECT) findings indicated the possibility of abnormality in the left occipital and post-temporal areas. We suggest the possibility of a link between the localization-related epilepsy of origin around the left temporal area and AS with some reports as evidence.

Case study

A 13-year-old boy, who was born by normal delivery, started visiting our hospital for febrile seizures from 3 years of age. He was diagnosed with Asperger's disorder at 7 years of age based on the Diagnostic and Statistical Manual of Mental Disorders-IV criteria, due to the presentation of characteristic clinical symptoms and the results of the Wechsler Intelligence Scale for Children (WISC)-III assessment. Four months after the diagnosis, he experienced complex partial seizure. This seizure started as the partial seizure which was dominant on the right side with unconsciousness, and continued over 40 minutes. The author diagnosed him with status epilepticus, therefore, he received antiepileptic drugs, after which his convulsions disappeared. He is currently

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attending a special support class at a public junior high school because of his AS.

WISC-III
The WISC-III which was used at 7 years old in the present study, consists of 6 verbal subtests and 7 performance subtests, and yields verbal intelligence quotient (VIQ) (from information, similarities, arithmetic, vocabulary, comprehension, and digit span), performance intelligence quotient (PIQ) (from picture completion, coding, picture arrangement, block design, object assembly, symbol search and matrix reasoning), and full scale intelligence quotient (FIQ) scores (Figure 1). The patient's VIQ was 105, PIQ was 85, and FIQ was 95. The point of each subtest was dispersed. The category of digit span increased and the category of picture arrangement decreased remarkably.

Cranial MRI and Tc-99m ECD Brain SPECT
On the sagittal plane of the MRI at 7 years old, abnormal findings including the thinning of the corpus callosum or the cerebellar atrophy, were not observed (Figure 2A). Moreover, on the horizontal plane at the level of the cerebellum and the brainstem, these findings were similar except that an arachnoid cyst was discovered in the left middle cranial fossa (Figure 2B). The abnormal findings showed a high signal in the periventricular white matter and irregularity of the lateral ventricle wall at T2WI (Figure 2C).

On the sagittal plane of SPECT of the brain with Tc-99m ethyl cysteinate dimer (ECD) in the present case, the increased perfusion of the frontal lobe and the decreased perfusion of cerebellar hemisphere that have been reported in the literature, were not observed (Figure 2D, E). We recognized that the abnormal findings of perfusions around the left temporal lobe and the bilateral cerebral ventricles were decreased (Figure 2F).

Interictal EEG
In the EEG findings of drug-induced sleep at 10 years old, there were extensive spikes, polyspikes and waves (Figure 3). In the portion of the paroxysmal discharge, the spikes, or spikes and waves that were found in the occipital and post-temporal areas, preceded the others. Clinical convulsions were recognized as the partial seizures which were dominant on the right side. However, in the interictal EEG findings, the laterality was not clear because the paroxysmal discharges were present on both sides.

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**Figure 1.** The patient's verbal intelligence quotient (VIQ) was 105, performance intelligence quotient (PIQ) was 85, and full scale intelligence quotient (FIQ) was 95. The category of digit span and working memory indices increased, and the category of picture arrangement decreased.

VCI, verbal comprehension indices; POI, perceptual organizational indices; WMI, working memory indices; PSI, processing speed indices.
Figure 2. (B) The horizontal plane of T2 weighted image shows an arachnoid cyst in the left middle cranial fossa and (C) a high signal in the periventricular white matter and irregularity of the lateral ventricle wall. (F) On the horizontal plane of SPECT, the perfusions around the left temporal lobe and the bilateral cerebral ventricles were decreased.

Figure 3. The spikes or spikes and waves that were found in the occipital and post-temporal areas, preceded the other portion. The laterality of paroxysmal discharge was not clear.
Discussion

There are fewer recent reports on Tc-99m ECD SPECT findings of combined cases with epilepsy than there are on autism including AS. There are, however, a few Japanese research papers on the subject. Kawasaki et al. reported that the autistic patients, in their study, displayed increasing blood flow at the left medial frontal region and decreasing blood flow at the left cerebellar hemisphere, compared with the control group. Alternatively, Ohnishi et al. showed that decreases of regional cerebral blood flow in autistic patients compared with the control group were identified in the bilateral insula, superior temporal gyri, and left prefrontal cortices. And Ito et al. found significant left less than right perfusion in the temporal region in the high functioning autism group. In each report, it was common that the left superior temporal cortex which showed anatomical connectivity between the frontal lobe, limbic system, parietal lobe, auditory cortex, and visual cortex could be related in the presence of autism. Therefore, they were attempting to discover the cause and to recognize the abnormal findings as the decreasing perfusion of the left temporal lobe. Our findings in the present case were similar to those of Ito et al. Generally, partial seizures produce increased cerebral blood flow in the region of seizure onset, and the interictal regional cerebral blood flow in the patient is reduced in the ascribable lesion. Our findings on interictal SPECT corresponded with this point.

The results in another Kawasaki et al. study revealed that 47.5% of individuals with autism display spikes or spikes and waves in the bilateral frontal areas. Nezu et al. reported on cases of AS with paroxysmal discharge in the bilateral midtemporal area. The other reports showed that individual cases with epilepsy and AS had significantly increased EEG slow activity. Our EEG findings in the present case are similar to those of Nezu et al., and the kind of paroxysmal discharges of our case are similar to those of Kawasaki et al.

Based on the evidence from the literature, the pathogenic causes of the symptoms of autism and AS may have their loci in the superior temporal sulcus and effect the frontal and parietal lobes, the auditory and visual cortex, and the limbic system. Regarding the frontal lobe dysfunction in autism, Chugani et al. showed that in autistic children, serotonin synthesis capacity increased, especially, in the left frontal cortex. In SPECT of people with AS, Murfy et al. reported a reduction in serotogenic 2A receptor binding in the bilateral frontal and temporal lobes, and the left parietal lobe. This speculate revealed that an abnormal

Figure 4. The loci in the superior temporal sulcus that effect the frontal and parietal lobes, the auditory and visual cortex, the limbic system, and vice versa, while the frontal lobe also effects the parietal lobe and the limbic system, and vice versa, may be the pathogenic causes of the symptoms of Asperger's syndrome.
connection of frontal, temporal, and parietal lobes might cause AS. As the reports about the connection of the temporal area and auditory or visual cortex, Gervais et al. explained that autistic children lack the activation of the superior temporal sulcus to vocal sounds,15 and McAlonan et al. reported that in autistic children, there was a decrease of reactivity in the superior temporal gyrus for phonic stimulations.16 Moreover, we refer to the reports about the abnormal findings of the hippocampus in the limbic system.17 The present case results did not conflict with the evidence in the literature. Based on the evidence of the present case and the literature, we hypothesize the relationships between AS and brain dysfunction in the schema (Figure 4).

The authors described a case of AS in which the patient concurrently suffered from cryptogenic localization related epilepsy after the time of diagnosis presentry. The abnormal findings of Tc-99m ECD brain SPECT and interictal EEG were observed around the left temporal lobe. There were several other similar signs observed in the same region. We formulated the relationships between AS and brain dysfunction as shown on the schema (Figure 4) based on the evidence from the present case and the literature. We believed that the area of brain dysfunction was likely the focus of the paroxysmal discharge and was the cause of the epilepsy. It will be imperative that other reports of combined cases such as this one be considered to further elucidate the pathogenesis of AS.

References