Cavum Vergae and Schizophrenia: Brain Imaging Findings and Treatment Outcome of a Case with 25 Years of Untreated Psychosis

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SUMMARY

Psychotic symptoms and disorders can emerge due to structural brain abnormalities. The septum pellucidum is one of the midline brain structures, which consists of the fusion of two thin membranes. Cavum vergae is recognized as the most severe form of fusion defect in the membranes of septum pellucidum. Although cavum vergae is reported to be common in schizophrenia and other psychotic disorders, a significant relationship has been found only for anomalies greater than 6 mm. Large cavum vergae may be a marker of developmental anomalies in other midline structures and connections, which in turn may lead to psychotic symptoms and disorders. In this case report, we present cavum vergae in a schizophrenia case with a 25 year history of untreated psychosis, discuss the probable relation of psychotic symptoms to structural brain anomaly, and evaluate the treatment course.

Key Words: schizophrenia, cavum vergae, septum pellucidum, duration of untreated psychosis

Psychosis refers to a syndrome in which an individual has disordered thought, hallucinations, and delusions (van Os and Kapur 2009). According to studies by the World Health Organization, one in three psychotic patients receive no treatment or admission to mental health services (Kohn et al. 2004). On the other hand, admission may delay even in the case of emergence of psychotic symptoms (Norman and Malla 2001). Duration of untreated psychosis (DUP) refers to the period from the first emergence of psychotic symptoms to the first administration of antipsychotic treatment (Norman and Malla 2001). There is wide variation in mean duration of DUP, extending from 98 days to 2 years. Studies in Turkey reveal a mean duration of 8 weeks in first episode psychosis (Ucok et al. 2004) and up to 11 months in chronic schizophrenia patients (Alptekin et al. 2005). Low socioeconomic status and mild psychosocial dysfunction are main factors that lead to increase in DUP (Morgan et al. 2006). Longer DUP is associated with increased severity of positive and negative symptoms, higher treatment resistance, and disability in schizophrenia. Furthermore, it is associated with decreased response to antipsychotic treatment and poorer outcomes (Ucok et al. 2004).

Several genetic and environmental factors are associated with psychotic symptoms and disorders (van Os and Kapur 2009). Psychotic symptoms are also associated features of many somatic diseases including intracranial pathologies and injuries (Shenton et al. 2001, van Os and Kapur 2009). Schizophrenia is a neurodevelopmental disorder with dysfunction of neuronal networks as a consequence of interaction of genetic and environmental factors (Murray and Lewis 1987). Psychotic symptoms, particularly delusions and hallucinations are related with sensitization and dysregulation of dopaminergic pathway in between limbic structures, such as the hippocampus and prefrontal cortex (van Os and Kapur 2009).

The septum pellucidum (SP), a part of the limbic system, is a thin, vertical membrane lining the inner walls of the lateral ventricles of the brain. During fetal development, SP consists
of two leaflets (laminae) separated by a space. The space disappears during the first 3-6 months of life (Shaw and Alvord 1969). In a small percentage of the society, laminae of SP stay disunited (partially or completely) with a space called cavum septum pellucidum (CSP) (Sarwar 1989). Cavum vergae (CV) is the most severe form of CSP anomaly where laminae stay completely detached (Shaw and Alvord 1969).

Structural anomaly of SP might be a sign of developmental disruption of other limbic system formations including hippocampus and corpus callosum (Flashman et al. 2007). CSP might be related to other structural malformations in the mid-brain and agenesis of the limbic system, which in turn might be associated with schizophrenia and other psychotic disorders (Nopoulos et al. 1998, Flashman et al. 2007, Yasaki et al. 2013). Alternatively, CSP may develop with different clinical presentations such as fetal alcohol syndrome, Apert syndrome, obsessive-compulsive disorder and Tourette syndrome (Renier et al. 1996, Swayze et al. 1997, Onur et al. 2007). Thus, CSP can be associated with various psychopathology.

In this case report, we present a patient with a 25-year history of untreated command auditory hallucinations and delusions. We discuss differential diagnosis, structural brain anomaly, probable association of symptoms with the anomaly, and treatment.

**CASE**

This case discusses a 60-year old male who was divorced, retired as a night guard, graduated from primary school, and living with one of his three children in a metropolitan district of Izmir. He presented to our institution with his daughter because of the increasing threats against him from the creatures whose voices he has been hearing for many years. In the first assessment, he stated that he has been arranging his daily life according to commands of the voices. He has been threatened with the death of a family member if he hasn’t carried out commands. He also pointed out that he lost his uncle and father after being unable to carry out the commands properly. Because of their death, he has been staying away from his family for years. Recently the voices started to threaten to kill his daughter and he decided to receive professional help because of his fear of losing her.

His complaints existed for over 15 years and 25 years according to him and his family (his wife, brother) respectively. In the meantime, he didn’t receive any regular treatment for his complaints. He used haloperidol and olanzapine once each at different times but he discontinued both of these medications. On the other hand he accomplished his work as a night guard at a public institution within this period without any complication. It was noted that he referred to our institution previously with physical complaints, but at that time he didn’t mention his auditory hallucinations or persecutive and mystic delusions. He was admitted to inpatient unit for medication arrangement, further examination and treatment.

In the psychiatric examination, slightly attenuated self-care, inappropriate affect, auditory (voices in the form of commentary/command/referral of mystic creatures) and visual (cats and dogs getting inside his body) hallucinations, circumstantial speech, persecutive and mystic delusions, and lack of insight were noted. He was wearing shirts with special colors allowed by mystic creatures. The patient was diagnosed as schizophrenia, paranoid type with the clinical evaluation according to Structural Clinical Interview for DSM-IV (First et al. 2002).

Magnetic resonance imaging (MRI) of the brain revealed cavum septum pellucidum (cavum vergae) (Figure 1). The size of CV was calculated as 43x20x10 millimeters. The other brain structures and laboratory examinations (liver function tests, kidney function tests, glucose level, lipid profile, thyroid function tests, hemogram, vitamin B12 and folic acid levels, serological tests, and electroencephalography) were normal.

As a treatment regimen, the patient was started on risperidone 2mg/day, which was tapered up to 4mg/day. Positive and Negative Symptom Scale (PANSS) (Kay et al. 1987) was used for monitoring the severity and the treatment response (Figure 2). Symptoms remitted in a short period of
time. Total PANSS scores of the patient were 98, 81 and 68 at the first assessment, the third week of treatment and after five weeks of inpatient care, respectively. Psychotic symptoms of commanding voices and persecuting thoughts remitted almost completely. After discharge, total PANSS scores of the patient were 61 and 64 on the 2nd and 6th weeks of follow-up. There was at least 30% decrease of the total PANSS scores, which was indicative of an adequate level of treatment response at the end of 12-week follow-up. During the last assessment with the patient and his relatives, there were no remaining psychotic symptoms. P1, P2, P3 and P6 items of PANSS, which assess the severity of the psychotic symptoms, were rated as 1 (none).

Neurocognitive assessment of the patient revealed mild impairment in the category fluency test (score: 6 and perseveration: 1) and in short-term verbal memory, and moderate impairment in long-term verbal memory. Basic and complex attention and ability to sustain attention were normal. Other cognitive tests, including Stroop Test (score= 45), verbal fluency test (score= 13 and perseveration= 0), and subsequent motor continuity test (score=1 failure/ 10) were normal. There was mild impairment in verbal memory. No impairment was detected on short and long term visual memory.

DISCUSSION

Incomplete closure of the space between leaflets of the SP might be associated with the developmental anomaly of the mid-brain structures (Sarwar 1989). Several morphological changes of the mid-brain, including corpus callosum agenesis and arachnoid cysts, have been associated with schizophrenia and other psychotic disorders (Alptekin et al. 1990, Shenton et al. 2001). Such malformations of the brain structures might be associated with the neurodevelopmental etiology of schizophrenia (Wood et al. 2008). Neurodevelopmental anomalies of the SP might be also associated with schizophrenia (Wolf et al. 1994, Nopoulos et al. 1998, Liao et al. 2012, Shrestha 2012).

In several case reports and surveys, the prevalence of CSP is reported higher in psychotic disorders, and particularly in schizophrenia, compared to controls (Degreef et al. 1992, DeLisi et al. 1993, Gewirtz et al. 1994, Galarza et al. 2004). However, more recently, the published prevalence rates of CSP in schizophrenia have been decreasing. According to recent studies, there is no increase in the prevalence of CSP in schizophrenia relative to general community (Takahashi et al. 2008). A meta-analysis of 15 brain imaging studies investigating the association of CSP and psychosis suggested that only a large CSP (> 6 mm) might be associated with psychotic disorders, whereas a small CSP might be considered a normal developmental variation (Trzesniak et al. 2011). A first-episode psychosis follow-up study suggested that CSP might be related to the progression of the disease rather than the onset of psychotic symptoms (Trzesniak et al. 2012). On the other hand, another study found associations between CSP length and cognitive functions such as intellectual functioning, verbal learning and memory (Flashman et al. 2007). In the light of this evidence, it is possible that a larger CSP may be a risk factor for psychotic disorders. Severe structural abnormalities like CV might play a role in the onset and progression of psychotic symptoms.

In our case, the size of CV is larger than the sizes indicated in scientific sources. This large structural abnormality may indicate the existence of disturbances and associated deficits in the other midline structures. Therefore, this abnormality may be linked to the psychotic symptoms of our case.

A distinctive feature of our case was the lack of treatment, which had been maintained for many years despite positive psychotic symptoms. There are many different factors affecting the treatment of people with psychiatric problems, and particularly those with psychotic disorders (van Os ve Kapur 2009). Treatment of psychotic patients is often associated with positive symptoms rather than negative symptoms and mood symptoms (Murphy et al. 2012). Even though negative and mood symptoms are associated with functionality, severe positive symptoms are the most decisive symptom clusters for social functionality (Ucok et al. 2004). In first episode psychosis patients, DUP usually lasts 1 or 2 years. However this duration may be longer depending on the social environment and the levels of functional disturbance (Ucok et al. 2004).
In our case, in spite of ongoing psychotic symptoms, the relatively well-preserved social and professional functionality might be a reason for the long delay in treatment admission.

**CONCLUSION**

CSP, a mid-brain anomaly, is reportedly more common in schizophrenia. Psychotic symptoms are considered to be associated with the size of abnormality. Therefore, in our case, the large size of the CSP abnormality might have led to psychotic symptoms. Since symptom clusters other than positive symptoms were not prominent in this case, it may be considered that CSP indicates disturbances in midline brain structures and preservation of prefrontal structures. Consequently, that negative symptoms and mood symptoms may have been overshadowed in this case.

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**REFERENCES**


