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Tillmann Supprian · Dietmar Bengel · Erich Hofmann
Andreas J. Fallgatter · Ernst Franzek

Cavum veli interpositi and psychotic disorder in a monocygotic twin

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Abstract The case of monocygotic twins discordant for a psychotic disorder is presented. An anomaly of the septum pellucidum, a so-called cavum veli interpositi was found in the psychotic twin while his brother showed no such anomaly. Previous studies have shown a higher prevalence of septum pellucidum anomalies in schizophrenic patients. Abnormalities of the septum pellucidum may be associated with disturbed neuronal development in distinct limbic brain areas which cannot yet be visualized yet by brain imaging techniques. The finding of the cavum veli interpositi in the psychotic twin could be incidental; however, it may indicate a dysgenic process in early brain development and, thus, play a significant role in the etiology of psychosis.

Key words Septum pellucidum · Developmental disorder · Schizophrenia · Magnetic resonance imaging · Cavum veli interpositi · Cavum septi pellucidi

Introduction

Neurodevelopmental disturbances in the etiology of schizophrenic psychoses are currently in the focus of research. The concept is based on the assumption that abnormal brain development can be compensated in early childhood and youth before, in adulthood, an unknown factor triggers the disintegration of cognitive and emotional performance and psychotic symptoms occur.

Disturbed neuronal migration has been proposed as pathogenetic mechanism [1, 23] which may subsequently cause imbalance in neurotransmitter systems. There is a growing body of evidence that septum pellucidum (SP) anomalies may indicate developmental disorders and that they are associated with significant psychiatric and neurological symptoms. Anomalies of the SP appear as absence of the SP (ASP), cavum septi pellucidi (CSP), cavum vergae (CV), and cavum veli interpositi (CVI). Early pneumencephalography studies already indicated a higher prevalence of epilepsy as well as cognitive and behavioral alterations in subjects with CSP [6]. Cognitive dysfunction, learning disabilities and neurological abnormalities have shown to be associated with developmental anomalies of the SP [13, 18]. Modern brain imaging studies reported a higher prevalence of SP anomalies in schizophrenic patients [4, 5, 12, 14, 15, 19, 21]. Prevalence rates vary from 12–15 % in schizophrenic subjects which may be caused by different criteria for the definition of a CSP. Only one investigation found no difference of prevalence compared to normal controls [10]. Even the rare anomaly of the ASP has been described in schizophrenic patients [8, 22]. Currently, it is presumed that SP anomalies belong to a spectrum of neurodevelopmental alterations associated with schizophrenic psychosis. The following case report is well in line with this hypothesis.

T. Supprian (✉)
Department of Psychiatry, The Saarland University Hospital,
D-66421 Homburg (Saar), Germany
e-mail: netsup@med-rz.uni-sb.de
Tel.: ++49 6841 164100, Fax: ++49 6841 164147

D. Bengel · A. J. Fallgatter · E. Franzek
Department of Psychiatry, University of Würzburg,
Füchsleinstr. 15, D-97080 Würzburg, Germany

E. Hofmann
Department of Neuroradiology, University of Würzburg,
Josef Schneider Str. 11, D-97080 Würzburg, Germany

Case report

The twins were delivered via sectio cesarea at the expected delivery date. Their mother reported normal pregnancy and no perinatal complications. Birth weight for the first delivered twin was 3100 grams and for the second twin (index twin) 3000 grams. Early childhood and statomotoric development was normal in both twins. Both graduated from high school. However, the index twin showed learning difficulties and repeated one class before graduation. At the time of admission (aged 25 years) the index twin complained of sub-depressive mood, loss of interest in recreation activities and his job. He suffered from psychomotor restlessness and his ability to concentrate was poor. Vegetative symptoms included

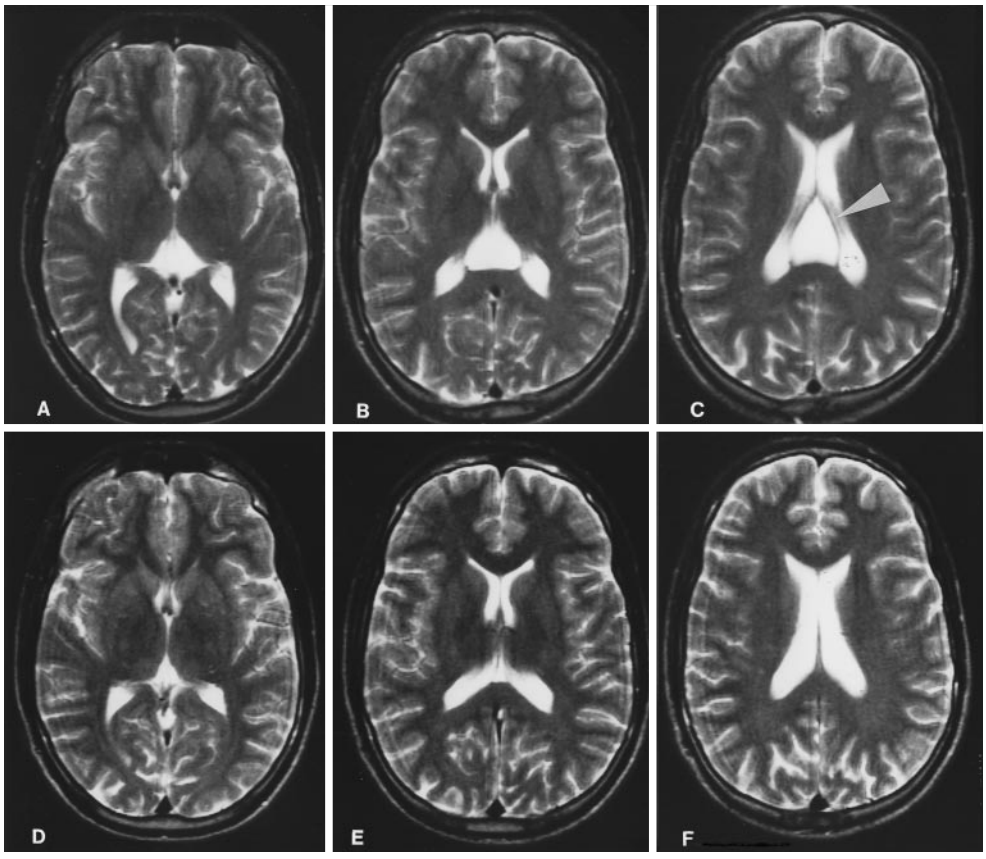

Fig. 1 Axial T2-weighted MRI (TR 1957 msec, TE 80 msec, matrix 192 * 256) showing a large cavum veli interpositi (arrow) in the psychotic twin (**A–C**) at the age of 25 years. Normal MRI scan of the healthy twin (**D–F**)

loss of appetite, weight loss, and sleep disturbances. Mental status was marked by a looseness of association; the patient often changed the subject when reporting and was unable to describe the meaning of abstract proverbs. He complained of "many thoughts in his head". There were no signs of hallucinations or paranoid ideas. The patient responded well to mild neuroleptic treatment with perazine and the observed formal thought disorder resolved completely within a few weeks. Based on the predominant formal thought disturbance, a brief psychotic episode (DSM-IV 298.8) was diagnosed. Physical examination, including a neurological status, was normal and clinical findings (EEG, laboratory tests) were also unremarkable. There was no family history for psychiatric diseases. MRI yielded a CVI without further pathological findings. The brother of the index twin agreed to a psychiatric examination and also to a MRI-investigation and was found to be completely inconspicuous. Monozygosity of the twins has been genetically confirmed by highly polymorphous microsatellites.

Discussion

The SP is a thin lamina which separates the lateral ventricles and is formed by two fused lamellae. The septum region can be differentiated into two parts, the SP, which is a translucent membrane (septum gliosum), and a nerve-cell containing part, the septum verum (septum gangliosum), which is related to the limbic system [2]. In the fetal period, the two leaflets of the SP are not yet fused. Fusion of the laminae of the SP begins around 36 weeks of gestation and is normally completed at the age of two [18]. As the fusion of the SP progresses from caudal to rostral, a CVI results from incomplete adhesion in the posterior portion of the SP. It is a leptomeningeal cistern located between the commissura fornicis and bounded rostrally by the interventricular foraminae (Monroe), dorsally by the corpus callosum, and ventrally by the roof of the third ventricle. Caudally it opens into the cisterna venae magnae (Galeni). Small CSP (1-3 mm) in the anterior portion of the SP, where the SP is attached to the corpus callosum, are frequently found in brain autopsies and have no clinical significance. A wide CSP is defined by some authors [18] by a separation of the leaves by more than 10 mm. Others have defined abnormal enlargement by the length of the CSP on consecutive coronal MRI scans [15]. For decades it has been controversial whether CSP, CV, and CVI are genuine developmental malformations. Since they are normal during fetal development it has been suggested to call these phenomena "persistent primitive structures" [2]. Sarwar [17] reviews the anatomical and developmental aspects of the SP and points out that the septum region is linked to the limbic system. The septum verum contains the septal nuclei and is connected via the fornices to the hippocampal formation, the amygdala, and other limbic brain areas. Furthermore, it may act as a relay station between the limbic system and diencephalic brain areas [2]. Dysgenetic alterations of the septal region may well account for cognitive, emotional, and behavioral symptoms seen in schizophrenic patients [24]. In contrast to previous reports [16, 19], in our opinion a large CVI may well have clinical significance. Just like large CSP, CV, and ASP, this anomaly may represent a

significant midline malformation. Yet, little is known about the association of this malformation with subtle disturbances in neuronal migration of limbic brain areas. However, clinical features are very broad in subjects with symptomatic CVI, CSP, CV, or ASP and are by no means pathognomonic [20]. In a recent study, Nopoulos et al. [15] found a higher incidence of CSP in early-onset forms of schizophrenic psychosis compared to normal controls. The authors suggest that extremely early-onset psychosis might have more severe developmental brain anomalies than those with adult onset. However, previous studies have shown that more severely ill psychotic individuals also seem to have a higher genetic load than less affected subjects [11]. Thus, the genetic contribution to the pathogenetic process in schizophrenia has not yet been elucidated. One possibility is that individuals with developmental anomalies are more prone to psychosis if they also carry additional genetic risk factors. If this is the case, both genetic components and developmental alterations may contribute to the manifestation of the psychotic disorder. On the other hand, developmental abnormalities may be independent factors in the etiology of psychotic disorders which is supported by the case presented here. The psychotic twin yielded a subtle developmental anomaly of the SP while his brother did not show such a finding. They both have the same genetic inventory, and similar environment can be assumed. Thus, it is unclear which event caused the development of the CVI in one of the twins. Maternal infections during pregnancy would probably affect both twins the same way. However, infectious and other toxic influences do not necessarily always affect both twins [3, 9]. Finally, it remains unclear why the dysgenic event in early brain development affected only one of the twins. With regard to the genetic influence, there is a growing body of evidence that genetic heterogeneity is related to different subtypes of schizophrenic psychoses [7]. Only limited conclusions can be drawn from this single case report. It cannot be excluded that the unaffected twin could develop psychotic symptoms in later life. However, further studies on the incidence of developmental anomalies and genetic risk factors are needed to clarify the relation between these factors and their contribution to the etiology of schizophrenic spectrum disorders.

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