Situs Inversus Totalis and Schizophrenia Comorbidity

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SUMMARY

The comorbidity of structural or genetic diseases with schizophrenia is seen as an opportunity to understand the formation of schizophrenia. This case report presents a patient with comorbidity of schizophrenia, tetralogy of fallot (TOF) and total situs inversus. TOF is a cyanotic heart disease, which can be linked to 22q11 deletion and trisomy 21. Situs inversus totalis (SIT) is a congenital condition in which the major visceral organs, including the heart, are positioned in a mirror image from normal conditions. The comorbidity of TOF and SIT is quite rare. In our case report, schizophrenia is added to this rare comorbidity.

This case report discussed the comorbidity and probable causal relationships. Furthermore, the research method of how transposition in internal organs is reflected in brain lateralization is also presented.

Keywords: schizophrenia, tetralogy of fallot, situs inversus

INTRODUCTION

High incidence of comorbidity of schizophrenia with other medical conditions has led to the investigation of these diseases in order to understand better the etiology of schizophrenia (Mitchell and Malone, 2006). Comorbidity of cardiac diseases with schizophrenia showed (Karayiorgou et al., 1995) significant correlations with velocardiofacial syndrome (VCFS), a common congenital genetic disorder characterized with conotruncal anomalies. Bipolor disorder is also linked to VCFS, with a 25 fold increase of psychosis risk (Kates et al., 2006).

Tetralogy of Fallot (TOF) has been observed in 16% of patients with VCFS (Ferencz et al., 1989). TOF is a common cyanotic congenital cardiac disease characterized with ventricular septal defect (VSD), dextroposition of the aorta (or the overriding aorta), pulmonary stenosis and narrowing of the exit from the right ventricle and right ventricular hypertrophy (Hoffman,1995). Situs inversus totalis (SIT), is a congenital condition in which the major visceral organs, including the heart, are positioned in a mirror image from normal conditions (Brown, 1950). Despite the very rare comorbidity of TOF and SIT, psychiatric disorders have been observed to be comorbid with both of these congenital diseases (Piran et al., 2011).

This case reported discusses the comorbidity of TOF, SIT and schizophrenia and the probable causative relationships together with our research findings on the effects of the internal organ transposition on lateralization of brain function.

CASE

The 36-year old single, unemployed, university graduate male patient consulted the emergency service with the complaints of a conspiracy to poison him. He avoided eating

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CASE

The 36-year old single, unemployed, university graduate male patient consulted the emergency service with the complaints of a conspiracy to poison him. He avoided eating any cooked meals, exhibiting aggressive behavior and lack of compliance with any treatment protocol. The patient did not have any previous psychiatric consultation and related drug use. However during the last year, he developed internalizing symptoms, decreased socializing and sensitivity to sounds in his surrounds. Medical examination revealed that he started eating packaged foods, suspected of being poisoned by the people around him and believed he was followed by police for the software he developed. He had no family history of psychiatric disorder. However, his medical history revealed episodes of hypoxia and cardiac surgery at the age of five. There were no signs of primary ciliary dyskinesias (Kartagener syndrome) such as bronchiectasis, pneumonia, chronic sinusitis or otitis media and no history of substance or alcohol use. Smoking history was 15 packs/years. He was admitted to the psychiatry service as an inpatient.

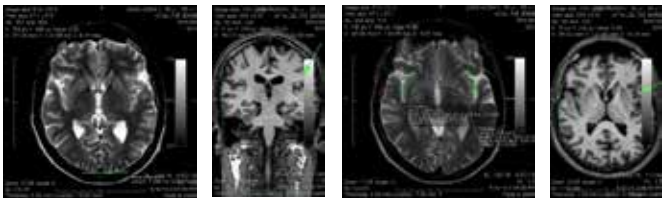

Figure 1. Anatomical brain MRI, from left to right 1) Left occipital petalia (left hemisphere protrudes posteriorly.) 2) Left temporal planum size is bigger than right temporal planum. 3) Left insular cortex length is longer than the right side. 4) Left silvian fissure is longer than the right side.

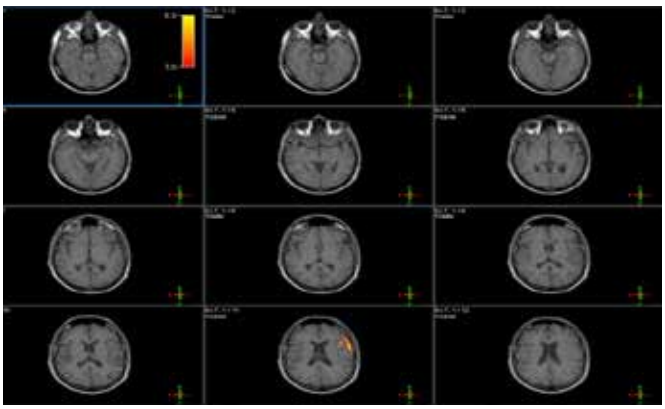

Figure 2. Functional MRI (fMRI) shows that motor speech center is located on left posterior sylvian cortex.

His physical examination did not indicate neurological or sytemic pathology only a S1 and S2 heart sounds revealed dextrocardia. His psychiatric examination revealed that he was conscious and displayed a defensive attitude, anxiety, anxious, irritable, psychomotor aggression and uneasiness. His judgment of reality was impaired and he had persecutory delusions about getting harmed and being controlled, He complained of lack of appetite and insomnia. His routine blood test and electroencephalogram (EEG) was within normal limits. However, cranial magnetic resonance imaging (MRI) indicated an approximately 2-cm long gliosis in the right frontocortical area, with atrophy and sulcal widening. His initial psychiatric assessment showed a score of 35 on the Brief Psychiatric Rating Scale (BPRS), 28 on the Scale for the Assessment of Positive Symptoms (SAPS), 29 on the Scale for the Assessment of Negative Symptoms (SANS) and 0 on the Simpson-Angus Extrapyramidal Symptoms (EPS) Scale. The patient was started on risperidone (2 mg/day) with the preliminary diagnosis of psychotic disorder.

Further brain imaging were planned to investigate any reflection in the brain tissue on the transposition of his internal organs on the y-axis.

Anatomically, the structural cerebral asymmetry consists of (1) a larger grey matter volume of the left versus the right planum temporale, (2) a longer course of the left sylvian fissure than compared to the right hemisphere, (3) posterior protrusion of

the left hemisphere on the right hemisphere (occipital petalia), and (4) a longer right insular cortex as compared to the left. Structural MRI showed that all these anatomic particulars were preserved in the patient (Figure 1). Functional MRI (fMRI) was used to investigate the areas activated during verbal generation. Activity was observed in the left posterior sylvian area, indicating preservation of the cerebral asymmetry (Figure 2). The patient preferred to use the right hand on the basis of the Chapman&Chapman questionnaire on handedness.

The patient was discharged with the diagnosis of schizophrenia on the basis of DSM-V criteria, after the clinical observations on the recession of his positive psychotic symptoms and of his psychomotor agitation, and improvement of his appetite and sleep hygiene. A 2-year follow up showed no positive symptoms on an outpatient basis. However, his level of social and work-related functionality was still low, which was probably due to his educational level, sociocultural background and his premorbid characteristics.

DISCUSSION

Known genetic mutations that are causes TOF are 22q11 deletion and trisomy 21 or Down syndrome (Apitz et al., 2009). TOF may result in hypoxic neuronal damage due to hypoxic episodes at an early age, which is included in the etiology of psychotic disorders (Rees et al., 2008). Depressive disorder, anxiety disorder, early onset of schizophrenia, hyperactivity, attention deficit disorder and learning disabilities are being observed in patients with TOF (Piran et al., 2011).

Situs inversus is the congenital transposition on the y-axis of major visceral organs from their normal positions. If the heart is displaced to the right thorax, the condition is described as 'situs inversus and dextrocardia comorbidity' or simply as 'situs inversus totalis (SIT)' (Brown 1950). TOF is a frequently seen congenital anomaly with a reported prevalence of 0.02%. Its comorbidity with SIT, however, is very rare. The study from Abraham et al. showed that only 1.4 % (2 out of 147) of the people with TOF had dextrocardia (Abraham et al., 1979). A pubmed searched only revealed 3 case reports of SIT with schizophrenia (Dixit and Khanna 1993; Mohan et al., 2013; Ponzano et al., 1978). Mohan et al. investigated the clinical ciliary dyskinesia (CD) symptoms in schizophrenia patient and reported the lack of CD comorbidity with schizophrenia. Given the observed comorbidity of SIT and Kartagener's syndrome, this finding has been emphasized in the literature, and the cases with comorbid psychotic disorders have been included (Ermis et al., 2009). Also, considering hemispheric dominance to be an important sign, handedness has also been evaluated and right hand preference has been determined (Mohan et al., 2013) as observed with the case reported here.

Brain hemispheres have anatomical and functional asymmetry. There is some contradiction in the literature regarding the lateralization of the cognitive processes and motor functions such as handedness and language. Hutsler and Galuske, 2003 state that language was lateralized whereas others reported that the retention of this function is based in the left hemisphere (Everett, 1963; Kennedy et al., 1999; Tanaka et al., 1999). However, this asymmetry has not been evaluated in the literature on cases of comorbidity with psychosis.

Anatomically investigation of the brain revealed that a greater volume of the left planum temporale as compared to the right planum temporale (Geschwind, 1974). Another feature of anatomical asymmetry is the petalia, with right frontal lobe protruding forward (frontal petalia), and left occipital lobe protruding backwards (occipital petalia) (Toga and Thompson, 2003). The greater upward angle of the Sylvian fissure in the right hemisphere is accepted as the most consistent asymmetry in the brain (Lofrus et al., 1993). The petalia aymmetry in the brain has been reported to follow the asymmetry of the visceral organ. In situs inversus, an asymmetry is obsevered between the left frontal petalia and a right occipital petalia aymmmetry as contrast to normal cases. On the other hand, no difference was observed with respect to planum temporale and inferior frontal gyrus asymmetry (Ihara et al., 2010). Many studies have discussed the hemispheric asymmetry and lateralization (Sommer et al., 2001). Although studies have indicated a trend in the loss of cerebral asymmetry in schizophrenia patients, in our case, the patient natural functional and structural asymmetry of brain has been preserved.

One of the limitations in this case reported is the lack of genetic testing, given that 22q11 deletion is one of the cardinal causes of TOF, and underlies VCFS, which is linked to a high risk of schizophrenia. The microdeletions in q11 band of chromosome 22 probably plays a role in the high risk of psychosis since this region contains critical factors such as COMT, ZDHHC8, PRODH and GNB1L that can play a role in schizophrenia. (Bray et al., 2008).

To our knowledge this is the first case report of a comorbidity of TOF, situs inversus totalis and schizophrenia. Even if the comorbidity was coincidental, it may provide information on the neurodevelopmental roots in the etiology of schizophrenia.

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