Schizophrenia and empty sella – casual or correlated?

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Summary

A male patient, 44 years old, with schizophrenia which started at the age of 18. At his last follow-up visit, laboratory tests and brain magnetic resonance imaging (MRI) were performed, revealing the presence of a sellar arachnoidocele. To our knowledge, there is only one similar case report of a set of male monozygotic triplets with schizophrenia and empty sella syndrome. High-resolution chromosome analysis found an extra band at chromosome 15p in all the triplets and their father. We performed a similar evaluation in our patient and his family to compare the results and identify new information on neuroanatomical abnormalities, hormonal alterations or genetic origins of schizophrenia.

Key words: schizophrenia • empty sella • hypothyroidism • genetic disease

Background

Schizophrenia is a complex genetic disorder. Its expression is an interplay between multiple susceptibility genes, epigenetic factors, and environmental influences [1]. In the case report by Christer Härnryd et al., a set of male monozygotic triplets with schizophrenia which developed at the age of 20, simultaneously showed an empty sella syndrome, found on brain MRI in all of them [2]. Coincidentally, a detailed chromosomal analysis by means of polymerase chain reaction (PCR) found extra strands of DNA on chromosome 15p in all 3 brothers and their father [3]. Actually, it is well known that chromosome 15q, but not 15p, is strongly linked to schizophrenia [http://www.schizophreniaforum.org]. A positive genetic linkage to the 15q13-q14 region has been found in 11 studies, which supports the idea that this region [4] and various clinical features, such as periodic catatonia, are associated with chromosome 15q15 in schizophrenic patients [5,6]. Our case report presents a patient with schizophrenia and empty sella sign without hormonal alterations or abnormalities in the karyotype. This may be a fortuitous finding, but we decided to study the association between the two entities. Morphological alterations in the central nervous system of schizophrenic patients remain unknown. As there exists a correlation between comorbidities, both the morphological and the functional alterations of the brain could provide us with new information necessary for identifying the etiology and implementing effective therapies of schizophrenia.

Case Report

A male patient, 44 years old, with a history of mental illness since the age of 18 years, manifesting itself with social withdrawal, affective flattening, and visual and auditory hallucinations present for 6 months. He was taken by his relatives for a psychiatric evaluation where he was diagnosed with schizophrenia and started on a treatment with trifluoperazine (Stelazine®) 10 mg daily. Three years ago it was changed to olanzapine (Ziprexa®) 20 mg daily. He was brought to the emergency room of Psychiatric Hospital by his brother, due to abandonment of treatment 6 months earlier, insomnia, aggressiveness, irritability, and visual hallucinations. Disorganized thoughts with delusional ideas of reference, affective flattening without awareness of mental illness, and altered view of reality were found. Routine laboratory tests showed: HB of 11.3 mg/dl, WBC of 11,350×mm³. Complete blood count, liver and kidney functions, level of glucose, cholesterol, and triglycerides were within normal limits. HIV and VDRL test were nonreactive.
Growth hormone was evaluated at 0.10 ng/ml, gonadotropic hormone at 25.6 mUI/ml, thyroid-stimulating hormone at 2.26 UI/ml, triiodothyronine (T3) at 3.7 pg/ml, thyroxine (T4) at 1.26 ng/dl, and prolactin at 16.05 ng/ml. An MRI showed a slight accentuation of the parietal fissures and a sellar arachnoidocele (empty sella). Taking into account the study of the triplets, we decided to study the karyotype of the patient and his parents; it was found normal. The EEG showed a slow baseline activity. He had not history of any other illness and was considered physically healthy. The patient showed terminal bilateral horizontal nystagmus, dysarthria, and blunted speech. There was a chronic neuroleptic-induced dystonia in the right arm, especially in the middle and annular fingers (flexion), and also in the left arm and left hand with flexion of all fingers (hand hook). Moreover, the extension of the fingers was voluntary and could be controlled by over 2 minutes. Tendon reflexes were present, with a less pronounced biceps reflex on the right arm. The neurological evaluation was normal otherwise. Psychological assessment showed different scores (rates) for the patient and his parents, which was related to age but there were no significant qualitative differences in their cognitive and judgment abilities. However, the intelligence test (Raven’s test) showed significant differences between the patient and his parents (ANOVA, F = 7.91, P < 0.05), due to differences in subjects’ age. The patient’s intelligence was mid-level. Karyotypes were obtained from 20 metaphases with the G-banding technique. The patient and his father had a normal male karyotype 46 XY. Patient’s mother had a normal female karyotype 46 XX.

On the first day of hospitalization, the treatment consisted of intramuscular haloperidol 5 mg twice a day, which was changed on the next day for risperidone at an initial oral dose of 4 mg per day, increased to 6 mg daily. Levomepromazine, intramuscular injection, was administered for the first 5 days at a dose of 25 mg daily, and then switched to oral form, administered at a dose of 20 mg daily. Carbamazepine 600 mg orally, biperiden 2 mg daily and clonazepam 1 mg orally were given until discharge. The outpatient treatment consisted of 30 mg of aripiprazole daily and it was introduced after one month of hospitalization which led to the diagnosis of paranoid schizophrenia (DSM IV).

**Discussion**

The heritability of schizophrenia is substantial, but the etiology of the disorder is poorly understood. Empty sella is a radiographic term denoting region from the subarachnoid space to the sella turcica filled with cerebrospinal fluid. There are two types of empty sella: primary empty sella (i.e. the absence of pathologies that produce it) and the secondary empty sella, which arises as a consequence of a pathological process of the pituitary gland [7]. In a study of the most frequent clinical presentations, mental disorders such as anxiety and behavioral disturbances were found very frequently (in 80.2% of a total of 71 cases studied) [8]. Some reviews showed progressive brain changes in schizophrenia [9,10] but there was no evidence of any relationship between schizophrenia and empty sella in the literature; only the case report of male monozygotic triplets with schizophrenia who developed the disease at 20 and showed empty sella on brain MRI with extra DNA strands on chromosome 15p. It is possible that both conditions could result from this chromosomal alteration. However, the same group of authors reported later on that an extra band on chromosome 15p in the Swedish triplet is not related to the development of schizophrenia among multiple monozygotic births [11]. We found in our patient schizophrenia and empty sella but his parents did not have schizophrenia or empty sella and none of them showed an extra band on chromosome 15p or any alterations in the karyotype.

Another possibility is that empty sella and schizophrenia in our case are not correlated whatsoever, and this is rather an accidental phenomenon.

The karyotype in our patient and his parents did not show abnormalities like the one in the case report of male
monozygotic triplets with schizophrenia. However, the possibility that such alterations arise from epigenetic mechanisms, such as DNA methylation, cannot be ruled out; actually, they are widely linked with schizophrenia. The correlation between schizophrenia, empty sella and genetic alterations needs to be verified by more evidence-based studies, further research is needed to resolve these questions and to improve the life quality, one day the cure or even the ultimate aim prevention of schizophrenia that cause great suffering on patients and their environment.

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Conflict of interests

The authors declare no conflicts of interests.

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