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Subependymal Heterotopia With Psychosis and Imperforate Anus in a Female Patient

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ABSTRACT

In the last couple of years, with the advancement of imaging methods, the diagnosis of gray matter heterotopia has been more promising. Gray matter heterotopia is a rare disorder in the general population, but recent attention to its psychiatric aspects encouraged us to introduce a patient with a form of gray matter heterotopia, who suffers from the anatomical abnormalities with a variety of psychiatric disorders. Our patient is a 25-year-old woman, who presented a variety of organogenesis disorders such as imperforate anus and rectovaginal fistula with the presence of gray matter heterotopia and history of refractory mood and psychotic disorders during 9 past years. Because of the various clinical manifestations of the disease, syndromic attention to this disease seems to be helpful in diagnosing and treating its various aspects.

Introduction

There are some cases in which the association between brain anatomical alteration, along with the manifestations of some psychiatric symptoms, has led to different clinical judgments about the etiology of psychiatric disorders. Gray matter heterotopia is an anatomical disorder of the central nervous system, which is formed by the disruption of the migration of the neuroblasts during the fetal period [1].

In the last few years, with the advancement of imaging methods, the diagnosis of gray matter heterotopia has

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been more promising [2]. Gray matter heterotopia is a rare disorder in the general population [3]. In the past, the emphasis was on the seizure demonstrations and neuronal development problems of this disease. Now the researchers' attention has turned on the psychiatric aspects associated with this disorder [4, 5]. Thus, we introduce a patient with a form of gray matter heterotopia (subependymal), who suffers from the anatomical abnormalities and a variety of psychiatric disorders.

We emphasize on the synchronization aspect of these disorders, which calls for a syndromic approach to these abnormalities. We recently had a patient with subependymal cortical heterotopia that in addition to this disorder, suffered from problems such as imperforate anus, rectovaginal fistula, and persistent fecal incontinence with a variety of neuropsychiatric symptoms.

Case Presentation

Our patient was a 25-year-old woman, presented with the history of sadness, frustration, reduced verbal communication skills, low self-esteem and loss of appetite, three months before admitting to a psychiatric hospital, following her cousin's death.

The patient experienced a weight loss of 16 kg over a period of 3 months and became a tiny girl with a weight of 39 kg (height: 150 cm, body mass index: 17.3 kg/m^2). Because of her hallucinatory behavior and permanent inclination of leaving home, she admitted to a psychiatric hospital. There, the patient had a labile mood. Sometimes she was happy, and sometimes was crying over and over. She had self-talking and was permanently calling her last candidate for marriage, while writing a storybook, with a love affair. Various parts of this book were carefully drawn and parallel to the image.

The first psychiatric problems of the patient began at the age of 16. At that time, she fell in love with his cousin and shortly after being banned from a romantic relationship, she suffered from depression, loss of academic education, and low self-care. She experienced auditory hallucination and heard the voice of her neighbor's son who was permanently talking to her. When referring to a psychiatrist, with the diagnosis of psychotic disorder N.O.S (according to the criteria of DSM IV), she took an outpatient's treatment with risperidone and imipramine. Partial improvement occurred and shortly afterward, severe obsessional thought and repetitive behaviors appeared as she was asking for repetition of the sentences she heard and watching a movie or hearing a sound more and more in a day.

Because of the aggravation of her symptoms and suddenly leaving the house with inappropriate clothing, she was admitted again with the previous diagnosis and comorbidity of obsessive-compulsive disorder and treated with risperidone and sertraline and improved partially. She was on outpatient treatment for three years on risperidone and the therapeutic process continued with partial amelioration. She always experienced auditory hallucinations, and some of her hallucinatory behaviors were manifested.

At the age of 19 and three years after the onset of symptoms, the resurgence of symptoms by severe obsessive-compulsive behaviors, high sexual activity, decreased sleep need, increased energy, and restless-

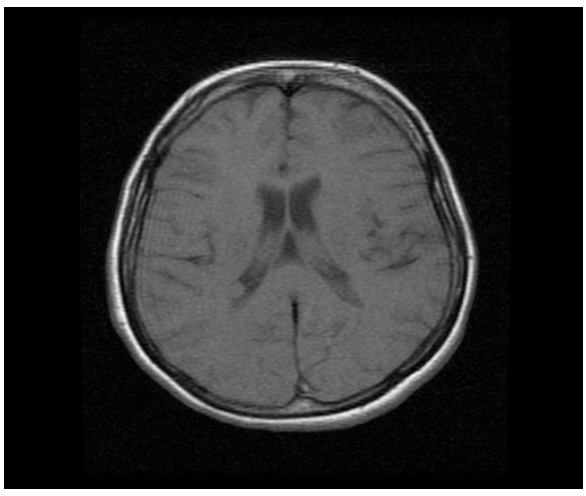

Figure 1. Brain MRI of the patient;T1(subependymal heterotopia)

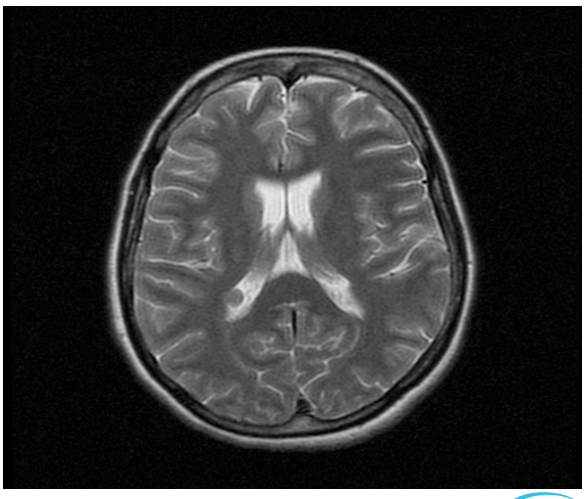

Figure 2. Brain MRI of the patient; T2; axial view (subependymal heterotopia)

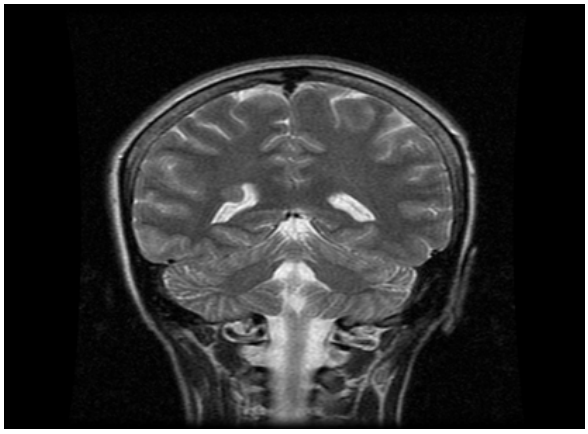

Figure 3. Brain MRI of the patient; T2; coronal view (subependymal heterotopia)

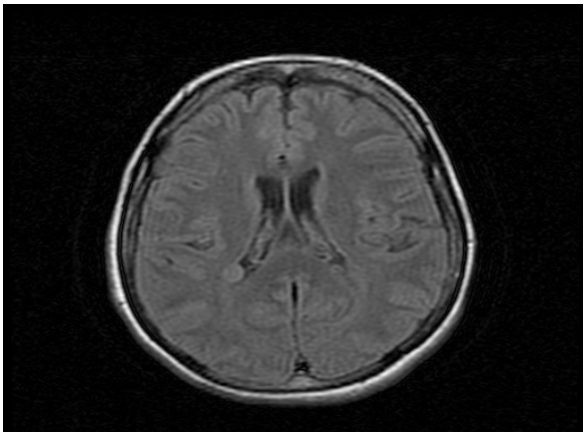

Figure 4. Brain MRI of the patient; flair (subependymal heterotopia)

ness appeared and she was admitted again with the diagnosis of obsessive-compulsive disease and BMD and treated with lithium and risperidone. After the control of symptoms and partial remission, she discharged and went on outpatient's care and showed good drug compliance. At that time, she went to the conservatory of sewing for one year when once again at age of 21 she developed the symptoms of acute hallucinations and elevated mood. Then, she was admitted and medicated with olanzapine and valproate sodium with the diagnosis of bipolar disorder (Lithium discontinued because of intolerance).

Also, the level of patient's intelligence was examined and reported as borderline IQ. At that year, another two admissions happened and she went on 6 sessions of the electroconvulsive therapy and showed partial remission. At the age of 22 and after a few months of partial symptom relief, she was engaged to a man for marriage that lasted 10 months but after two times of relapse of the symptoms, the patient's relationship with her candidate went on divorce. Shortly thereafter, following a reduction of drug compliance with exacerbation of auditory hallucinations, she admitted again for treatment.

At the age of 24, after a period of sadness, low self-care, and highlighting the symptoms of psychosis in the form of delusions (food poisoning and so on), the patient was admitted again in the hospital with the diagnosis of schizoaffective disorder. During admission, following the occurrence of two delirious conditions, she underwent CT-scan brain imaging that revealed a subependymal solid nodule. So, the diagnosis of subependymal heterotopia was made based on the results of the brain MRI (Figures 1, 2, 3, and 4). Also, her EEG was reported as normal. The patient was discharged with medication of clozapine, biperiden, and depakin and was advised to pursue outpatient treatment. The above mentioned history comprised the major part of the patient's psychiatric experiences, which led to her 14 times admissions to the psychiatric hospital during the last 9 years. Also, the patient's chromosomal karyotype was reported normal.

Other details related to this patient in addition to various disturbances of the psychiatric disorders and subependymal cortical heterotopia were congenital anomalies such as imperforate anus with rectovaginal fistula and neuromuscular disorders related to them at birth. In this regard and after birth, she was implicated in colostomy and went under the diagnostic procedures to define other constructional and anatomical abnormalities and, finally, the patient underwent surgery (anorectoplasty) in her first and second month of life and the other related surgeries when she was 4 and then 8 years old. Because of the patient 's fecal incontinence, she underwent third surgery at the age of 22 and neuronal transplantation was done, with no success in treatment. Still, the patient has some degree of fecal incontinence.

Significant points related to the history of the patient's embryonic time is one episode of severe vaginal bleeding reported in the second trimester of mother's pregnancy due to the placental development, which results in a 4-day maternal admission to the hospital. Finally, after treatment, improvement in symptoms occurred and in a full term pregnancy, the patient was born with a cesarean section due to Breich's condition.

Discussion

Two etiologies have been so far proposed for grey matter heterotopia; genetic and epigenetic causes. Genetic mutations can be mentioned, including those related to genetic causes. These factors can form syndromic disorders. Some associations between gray matter heterotopia with ectodermal dysplasia disorders are examples of these conditions [3]. From the epigenetic point of view, hypoxic-ischemic events during migration period of neuroblasts (at 7 to 16 weeks of fetal development) is an example that is related to our case due to vaginal bleeding of the patient's mother during pregnancy [1].

An important group of heterotopic subsets of gray matter is subependymal nodular heterotopia which has different clinical manifestations and prognosis in males and females that is related to genetic patterns and other factors [6]. Also, the differences in the location of nodules and their spread are related to different clinical manifestations and suggest the possibility of different etiopathologies [7]. Various reports have been released on the association of this disorder with varying degrees of mental disability among a range of patients [5] with disorders such as Chiari malformation [8] and Ehlers-Danlos syndromes [9].

In females, the typical epileptic episodes in the second decade of life are a common manifestation of the disease [6]. Various studies on the presence of epilepsy in periventricular nodular heterotopia [4] and drug-resistant epilepsy in patients with cortical heterotopy have been reported [7]. The clinical improvements in some cases of drug-resistant epilepsy have reported after surgery [10].

There have been reports of accompanying psychotic and mood disorders with subependymal nodular heterotopy [11] and the presence of neuropsychiatric symptoms has become a prominent manifestation of this disease, especially in recent years [2]. The existence of functional and structural relationships between different components of the heterotopia and other parts of the brain can be the source of secondary disorders in patients with subependymal nodular heterotopy [12].

Another important point is the possibility of minor clinical manifestations, or even the absence of any clinical signs or symptoms, in conjunction with subependymal cortical heterotopia [13], which may have a chance finding in diagnostic studies in some rare cases.

Because of the increased use of MRI in recent years and the identification of more cases of this disorder, it is now advisable to use this diagnostic tool, more than ever, in cases of multiple neuropsychiatric symptoms, initiation of psychotic manifestations for the first time, or in the resistant cases of mood or psychiatric disorders [14].

These recommendations have sometimes led to early use of diagnostic tools, such as fatal MRI in suspected cases, to detect this disorder earlier and rendering more effective diagnostic management and treatment [8].

In our patient, a variety of organogenesis disorders such as imperforate anus and rectovaginal fistula with the presence of gray matter heterotopia in the form of subependymal heterotopia were detected, also she had refractory mood and psychotic disorders during the past 9 years. In addition, the existence of borderline IQ is one of the other complications mentioned by our patient.

In this patient, as seen in most cases, imperforate anus disorder and rectovaginal fistula were associated with a number of neuromuscular disorders in the area [15]. The coincidence of maternal vaginal bleeding during pregnancy following the development of placenta with neuronal migration, during the second trimester of pregnancy and the possible impact of epigenetic factors on the formation of heterotopic disorder due to this ischemic-hypoxic condition, are the other clues in our patient's disease etiology. Reporting no history of seizure in our patient with normal EEG is uncommon in women with this disorder, which makes it an important point.

There are different opinions about the primary or secondary nature of the psychiatric problems in these people. It is a controversial point of view that these neuropsychiatric manifestations can be justified in the context of subependymal of heterotopic disorder or we are faced with a distinctly twofold disorder. Many recent multiyear studies have failed to provide reliable criteria for linking these processes.

According to our information, this is the only reported case of the association between subependymal cortical heterotopia, imperforate anus, and the other complications. Regarding the very low prevalence of this disorder in the general population, the association between these two disorders can reveal a syndromic complex feature of this disorder.

We believe that, pending the more precise determination of this situation, one has to think of the syndromic view of these manifestations and its associations with

other disorders. In the case of encountering this situation, other related syndromic comorbidities are also subject to diagnosis and treatment. This is particularly important with the wide range of comorbidities associated with this disorder.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article. The participant was informed about the purpose of the research and its implementation stages.

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Conflict of interest

The authors declared no conflict of interest.

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