
Letter to the editor

Dandy-Walker variant and refractory psychosis

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Dear Editor,

The Dandy-Walker Complex corresponds to a group of disorders believed to represent a continuum spectrum of posterior fossa malformations (including the Dandy-Walker malformation, the Dandy-Walker variant and the mega-cisterna magna). The Dandy-Walker malformation is characterized by a cystic dilatation of the fourth ventricle, an abnormally high tentorium and the agenesis of the cerebellar vermis¹. The Dandy-Walker variant (cerebellar hypoplasia without an enlarged posterior fossa) and the mega-cisterna magna (an enlarged posterior fossa with a slighter cerebellar hypoplasia) are considered lesser forms of the Dandy-Walker malformation².

In scientific literature, some cases of mega-cisterna magna have been associated to mania or schizophrenia^{1,3}, and many cases of Dandy-Walker variant have been linked to psychosis^{2,4-8} and other psychiatric conditions, such as the obsessive-compulsive disorder⁹.

Psychosis associated to the Dandy-Walker complex are characterized by an early onset, a family history of psychosis, atypical symptoms, a high prevalence of cognitive deficit and borderline intelligence, refractoriness to antipsychotic treatments^{4,6,8,9} or a greater sensitivity to its side effects².

We report the case of a patient with a history of physical abuse and diagnosed as suffering from a schizophrenic disorder in which auditory hallucinations are prevalent. She has not responded well to a series of antipsychotic treatments, including clozapine. Imaging tests reveal a significant loss of cerebellar volume, which fits in well with a Dandy-Walker variant.

Clinical Case

It involves a 34-year-old woman who first came to the Mental Health Center three years ago. She had been referred from Primary Care after showing symptoms of anxiety triggered by the abuse she suffered during childhood. Days before the first doctor visit, she overdosed on benzodiazepines and was discharged by the ER Service. Following her first visit, she was diagnosed as suffering from a generalized anxiety disorder and was prescribed a serotonin reuptake inhibitor. During the second visit, she still showed symptoms of severe distress. She seemed distrustful and kept claiming someone would harm her children without offering any specific details. Consequently, she was put into antipsychotic treatment. In the next visit, she mentioned she had been hearing voices since she was a child and that, recently, those voices had warned her children were in danger.

As for her personal history, the only thing that stands out is a cardiological study carried out in 2011 because of vasovagal syncope thought to be triggered by low blood pressure.

She is the eldest of four siblings and has little contact with her parents. She recently got in touch with two half-siblings by her father: one of them is a drug user and the other has a history of admissions in psychiatric hospitals. She lives with her husband, who is her third couple, and four children: the first one from her first couple, the second (suffering from attention-deficit hyperactivity disorder, ADHD) and third ones from her second couple and the fourth one from her current husband. When it comes to her children, she seems to be overly-protective and is currently checking the news for any incidents to do with minors. She also surfs the web to learn more about infancy and maternity-related topics.

She says she was twelve years old when her mother left the family home and took her to another city where, allegedly, she was abused by a man. She says it was then when she started hearing voices, and that these have been recently causing her much more distress than years ago. They call her a "bad mother" and urge her to end her life so that her kids do not suffer. She believes her condition has worsened after undergoing an abortion due to acute fetal malformations, for which she feels very guilty. Hallucinations grow more intense when she sets foot in the street, warning her of the proximity of rapists and pedophiles. This, in turn, has made her become more isolated. She has requested to be declared permanent incapable to work.

At the doctor's office, she displays signs of paranoia. She suffered a car accident and misconstrued it for a murder attempt. She is afraid of being diagnosed as schizophrenic and

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being interned in the psychiatric ward, away from her children.

In the Positive and Negative Syndrome Scale for Schizophrenia, she scored 27 points in the positive scale, 25 in the negative scale and 56 for general psychopathology.

A computed tomography scan of the brain was requested and it showed a significant cerebellar atrophy given the patient's age. No other pathologic alterations regarding density or mass were found. An MRI of the brain was also carried out, showing an enlargement of the suprasellar cistern associated to a hemispheric and cerebellar vermis volume loss. The patient was diagnosed as suffering from the Dandy-Walker variant.

A video-electroencephalography was also performed, showing no signs of diffuse or focal brain injuries, asymmetries or paroxysmal episodes.

The only thing that stood out in the neurological examination was a minor incoordination of limb movement.

From a pharmacological point of view, several antipsychotics have been used. The patient did not respond to olanzapine (a daily dose of up to 20 mgs) when administered as a single agent or in combination with haloperidol (up to 10 mg). Later on, the olanzapine was replaced with paliperidone (up to 12 mg), but the response was equally insufficient. Right now, the patient is being administered 5 mg of haloperidol daily and clozapine is being gradually brought in (up until a daily dose of 600 mg). Blood tests have not shown any alterations or side-effects linked to the medication. After several months of treatment with clozapine, symptoms remain constant and equally intense. Adding lamotrigine or amisulpride to the treatment is currently being considered¹⁰.

The therapeutic relationship with the patient is difficult given her mistrust. She has refused to enter a mental institution but has agreed to return for intensive outpatient treatment when necessary. She is only half aware of her disorder.

The psychiatric diagnosis issued, according to the DSM-5, corresponds to an unspecified schizophrenia spectrum disorder (F29), since other criteria belonging to schizophrenia spectrum disorder are not met¹¹.

Discussion

There are plenty of scientific papers that link the Dandy-Walker complex to psychotic symptomatology. In this case, the diagnosis was of a Dandy-Walker variant and psychosis. The early onset of the psychosis, the patient's resistance to treatment and the atypical symptoms were key in making this association.

As for the role the cerebellum plays in psychoses, it has been suggested that it regulates the cognitive and emotional processing (hence concepts such as "limbic cerebellum", "cerebellar cognitive-affective syndrome" or "cognitive dissonance")¹²⁻¹⁴.

Postmortem examinations and neuroimaging studies support the idea that anomalies in the cerebellum or in its connections with the brain can help positive symptoms linked to schizophrenia and cognitive deficit emerge¹³⁻¹⁵.

Some go as far as to suggest anomalies in the cerebellar function or their manifestation through minor neurological symptoms can be used as a biomarker for an increased risk of psychosis¹⁶⁻¹⁹.

Perhaps, the simultaneous presence of psychosis and a Dandy-Walker variant is the manifestation of a single developmental disorder concerning the central nervous system of this patient. If we consider schizophrenia to be a neurodevelopmental disorder, genetic or environmental factors would have caused (between the seventh and tenth week of pregnancy) the cerebellar malformation that resulted in the Dandy-Walker variant⁴. Once the maturity of the central nervous system is reached, the patient starts using circuits in which the anomalous cerebellum is involved, thereby triggering the psychotic symptoms²⁰.

It is also possible that the Dandy-Walker variant is a necessary, but not sufficient, factor to make the patient vulnerable to psychotic breaks. Another factor that could have acted as a "second stroke" in the central nervous system is the child abuse²¹. This is believed to play a crucial role in cases of psychosis where hallucinations are prevalent^{22,23}.

Admittedly, the association can be purely fortuitous in this and other cases.

Nevertheless, we need to learn more on this matter to better understand this and other similar cases.

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Radiosurgery in Obsessive-compulsive disorder, a case report

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Dear Editor,

Obsessive-compulsive disorder (OCD) affects 2-3% of the general population¹. Twenty percent of these patients have chronic, very disabling forms of the disease², resistant to current pharmacological and psychotherapeutic therapies, leading to an important suffering and a significant deterioration in their quality of life. For these patients, there are alternative solutions that can be effective such as Gamma Knife Radiosurgery (RCGK). After initial experiences by

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Prof. Leksell's group, few neurosurgeons have treated psychiatric patients using radiosurgical techniques³⁻⁶. Although in the last decades there has been an increase in psychiatric disorders treated by radiosurgery due to the demonstration of the safety of these treatments that partially overcame the social and cultural repairs associated with these therapies⁷.

The purpose of the present case is to reflect on the used prescription dose, the posttradiosurgery time that elapses between its application and the improvement of the patient, as well as the characteristics of this improvement and its repercussion on the quality of life.

Clinical Case

A 64-year-old woman living alone, without a partner or children, previously married for years. She worked in the domestic service until the age of 30. She is the second of a family of six siblings. One sister was diagnosed of depressive disorder and a second cousin of OCD.

She was first evaluated in psychiatry when she was 24, where she was diagnosed as "neurosis", without requiring any pharmacological treatment. From the age of 28, she started to receive treatments for recurrent depressive symptoms, obsessive ideas of doubt and compulsions consisting of repetition of checking behaviors. She was given venlafaxine (75-150 mg/day) and olanzapine (5 mg/day). She presented orofacial dyskinesias but the patient was difficult to be followed in a specialized follow up with psychiatry in the last ten years.

In February 2009, she consulted with the mental health team for exacerbation of obsessive-compulsive symptomatology with anxiety, depressive symptoms and orofacial dyskinetic movements. The obsessive-compulsive symptoms consisted of repeated and repetitive ideas, irrational, that intensively assaulted the patient's conscience and which implied doubts about social and neighborhood situations that forced her to ask in a compulsive and socially indiscreet way. These symptoms were associated with significant suffering and deterioration of family and social relationships, so that the patient became socially isolated.

The use of first-line drugs for OCD such as serotonin reuptake inhibitors (SSRIs), despite improving obsessive-compulsive symptomatology, were associated with a worsening of oral dyskinesias, which led to a treatment incomplete with escitalopram and sertraline. It was decided to add mirtazapine, an antidepressant with noradrenergic effect (30-45 mg/day) to the SSRI treatment. With this treatment she remained partially stable between October 2009 and October 2010.

Since 2011, the evolution was unfavorable due to the intensification of obsessive-compulsive symptoms. She was offered the possibility of initiating treatment with clomipramine or initiating strategies of potentiation with antipsychotic drugs. The patient rejected them and did not contemplate areas of more intensive treatments in a Brief Hospitalization Unit.

The patient was evaluated using the Y-BOCS, HDRS and GAF scales, with a score of 37, 17 and 19, respectively. Due to the resistance of the TOC⁸ with an important dysfunction in the personal, familiar, social life and the worsening of the dyskinesias with the SSRIs, the possibility of performing a bilateral capsulotomy by Gamma Knife Radiosurgery (RCGK) was offered. The protocol included assessment by a second independent psychiatrist, confirming that she met selection criteria for neurosurgical treatment (Table 1).

In December 2012, this procedure was carried out, which consisted of the placement under local anesthesia, a stereotaxic frame and the performance of a magnetic resonance brain (NMR). A fusion was performed with the tractography that had been performed on the patient the previous days using a 3-tesla functional MRI and planning was carried out, locating the anterior part of the internal capsule at the "knee" level of said tract, located next to the head of the caudate nucleus. In this zone and bilaterally two

Table 1 | **Criteria for the selection of neurosurgical treatment in patients with OCD**

Diagnosis of Obsessive-Compulsive Disorder (OCD) as well as invalidating symptoms
Chronic disease lasting at least 5 years
Failure of all specific psychiatric treatments applied having reached a reasonable limit on the drugs applied and the corresponding doses
Impossibility for the patient of having a normal life according to their cognitive and emotional faculties, blocked by the symptoms of their illness
Consent of the patient and his legal representatives. In writing and raised with a certain time
Reports from two independent psychiatrists indicating that the above mentioned criteria are met
Structural and functional magnetic resonance before the beginning of the neurosurgical treatment showing no evidence of anatomical abnormalities and the functional profile of the patient

Modified by Perez Sola I, et al.; 2012⁹

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shots were fired, or irradiation positions, using 4 millimeters collimator and administering a maximum dose of 120 Gy. The entire procedure was uneventful and the patient was discharged the same day of treatment.

Follow-up was performed at 2, 6, 8, 12 and 17 months after the intervention, and no side effects were observed, although there was no significant improvement in obsessive-compulsive phenomena or involuntary movements. During this time the patient was treated with mirtazapine between 30-45 mg and tetrabenazine 75-100 mg/day.

Twenty-two months after surgery, a significant decrease in obsessive-compulsive and depressive symptoms was observed, and an improvement at the functional level (Y-BOCS 10, HDRS 6 and GAF 70-61), having doubts about neighbors and relatives that caused impulsive / compulsive acts that compromised in their social relations disappeared. She showed no interference from obsessive phenomena with the activities of her daily life. At last follow-up at 44 months, the patient remained clinically stable and obsessive-compulsive phenomenology remained attenuated, with a significant improvement in her quality of life.

Discussion

Current studies support the etiological model of dysfunction in the cortico-striatum-thalamus-cortical circuits in OCD¹⁰. Dysfunction of these circuits are the pathophysiological basis of existing neurosurgical treatments.

One of the neurosurgical techniques with the best evidence and experience is the anterior capsulotomy, which consists of injuring the anterior arm of the internal capsule. The interruption or blockage of the fibers connecting the prefrontal cortex to the dorsomedial thalamus nuclei has proved to be very useful for the treatment of obsessions and compulsions⁵.

Since the 1960s, there have been reports of cases of OCD treated by anterior capsulotomy bilateral, performed using RCGK^{5,11}. The initial results, applied to patients with correct indications, were similar to those obtained with open ablative procedures (70% of cases with significant improvement), although adverse effects were observed with affection in cognitive functions, apathy and disinhibition. The authors related the appearance of these effects with the extension of the lesions made and with their somewhat later location in the thalamus.

In recent years, the introduction of functional MRI studies, specifically tractography and cortical activation systems, have greatly increased the effectiveness and safety of these lesions^{12,13}.

It is necessary to point out that changes in the patients' situation appear between six months and one year after radiosurgery¹³, although in our case the most notable symptoms improvement was detected at the 22nd months. In addition, the maximum dose applied (120 Gy) in this case is lower than the previous series¹⁴.

Another advantage with this maximum dose and the planning based on the functional studies centered on the tract of the internal capsule, is that it is unlikely that peripheral structures will be damaged, which could avoid the side effects mentioned in previous studies¹⁴.

Unlike the surgical interventions in which electrodes are implanted for stimulation, the RCGK is a procedure without surgical risks and with a significantly lower cost, where a "neuromodulation" effect has been evidenced: for example, the white matter appears to recover after 2-4 years post treatment¹⁵, although the tracts are blocked when the functional control MRI is performed. The concept of "reversibility" of the electrodes is therefore in full discussion today.

In summary, medical treatment resistant TOC is a significant health and social problem, and requires safe and effective alternatives. In light of the evolution of neuroimaging and neurosurgical techniques in recent years and the degree of safety with which they are performed, these techniques should be more accessible. The creation of multidisciplinary working groups between neurosurgeons, psychiatrists, neurologists, psychologists and radiologists would facilitate a better coordination, information and application of these techniques to be able to continue advancing in this promising field.

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