Dandy-Walker Malformation Presenting with Affective Symptoms

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ABSTRACT

Dandy-Walker malformation is defined by enlarged posterior fossa, cystic dilatation of the fourth ventricle, and cerebellar hypoplasia. Although developmental delay and mental retardation are common in Dandy-Walker malformation cases, other comorbid psychiatric conditions have been rarely reported. There are limited numbers of case reports about comorbidity of bipolar disorder with Dandy-Walker malformation in the literature. Herein, a Dandy-Walker malformation case presenting affective symptoms is reported, and psychiatric symptoms which might be seen in this rare malformation are discussed along with diagnosis, treatment, and follow-up processes. A 27-year-old male patient, hospitalized for compulsory treatment, had been diagnosed with Dandy-Walker malformation in childhood. First complaints were attention deficiency, behavioral problems, learning difficulties; and manic and depressive episodes have occurred during follow-ups. He recently complained of decreased need for sleep, irritability, and increased speed of thought, and psychiatric examination was consistent with manic episode. Cranial computed tomography (CT) revealed bilateral ventriculomegaly, enlarged third and fourth ventricles with posterior fossa cyst, and cerebellar hypoplasia. His

treatment included 30 mg/day aripiprazole, 1000 mg/day valproic acid, 200 mg/day quetiapine, 4 mg/day biperiden, and 100 mg/month paliperidone palmitate. Beside its traditional role in the regulation of coordination and motor functions, cerebellum is increasingly emphasized for its involvement in the mood regulation. Thus, as seen in Dandy-Walker malformation, cerebellar anomalies are suggested to play a role in the pathophysiology of mood disorders. Further studies are needed to better understand the relationship between mood disorders and cerebellum. Moreover, treatment options should be considered carefully in terms of resistance to treatment and potential side effects, for psychiatric disorders occurring in these cases; and detailed examinations, including cranial imaging, would be beneficial in bipolar cases with early onset, unresponsiveness to treatment, presenting atypical symptoms, mental retardation, and developmental delay as well as neurological symptoms and signs.

Keywords: Dandy-Walker syndrome, cerebellum, mood disorders, bipolar disorder

Cite this article as: Batmaz M, Balçık ZE, Özer Ü, Hamurışçi Yalçın B, Özen Ş. Dandy-Walker Malformation Presenting with Affective Symptoms. Arch Neuropsychiatry 2017; 54:277-281.

INTRODUCTION

Dandy-Walker complex (DWC), also known as the Dandy-Walker syndrome (DWS), defines a group of developmental anomalies of posterior fossa and includes Dandy-Walker malformation (DWM), Dandy-Walker variant (DWV), mega cisterna magna, and posterior fossa arachnoid cyst (1,2,3). DWM was first defined by Dandy and Blackfan (4) in 1914 and was named as Dandy-Walker by Benda (5) in 1954. Although it is known with the classical triad of hypoplasia of cerebellar vermis, cystic dilatation of the fourth ventricle and hydrocephalus, different definitions were also suggested as a result of studies till date (6) (Table 1). Although Hirsch et al. (7) mentioned hydrocephalus as a frequent complication of DWM, they suggested that it is not necessary for the diagnosis.

The incidence of DWM is approximately 1 in 25,000 to 35,000 live births (7). Hydrocephalus is present in 91%, and objective neurologic signs are observed in 73% of patients with DWM. Among the most frequent symptoms and signs are macrocrania, eye anomalies, spasticity, developmental delay, ataxia-walking difficulties, headache, nausea, lethargy, seizures, cranial nerve palsy, and quadriplegia (8). Although the symptoms and signs occur in early childhood in the majority of cases, some cases are diagnosed in adult life (8,9).

Psychomotor developmental delay and mental retardation have been mentioned frequently in DWM patients in the literature (7,8,9,10). Other psychiatric disorders accompanying this malformation have been rarely reported. In these case reports, generally paranoid delusions and schizophrenia-like psychotic symptoms have been defined in the DWK and DWV cases (11,12,13,14). There are also a few case reports indicating comorbidity of DWS with bipolar disorder (15,16,17,18,19).

In the literature, it is highlighted that the relationship between DWM and psychiatric symptoms is complex and much more studies are required in this field. In this article, a forensic case of DWM suffering from affective symptoms is presented, and psychiatric symptoms as well

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Received: 03.05.2016 **Accepted:** 29.06.2016

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as diagnosis, treatment, and follow-up processes are discussed in this rare malformation.

CASE PRESENTATION

A 27-year-old male patient was hospitalized for compulsory treatment. He was single, graduated from primary school, exempted from military service, and was living with his family. Chief complaints were decreased need for sleep, irritability, and recently increased speed of thoughts.

In the first psychiatric examination, he was observed to have a normal level of consciousness, full cooperation, and normal orientation. His speech was loud, with an increased rate and speed. His associations were fast but goal-directed. He had a grandiose attitude, his mood was irritable with an elevated effect, and he was prone to anger. No delusions or hallucinations were observed. He had no insight about his condition. The rating on the Young Mania Rating Scale (YMRS) (range 0-44) score, which was applied on the first day, was found to be 33 (20).

According to family history and that obtained from the medical records, he had psychomotor developmental delay (speaking at the age of 3, walking at the age of 4) and primary enuresis nocturnal until the age of 8. Therefore, he had been seen by a child psychiatrist and then referred to a neurologist and a neurosurgeon. DWM had been diagnosed because of his first cranial MRI (defining hydrocephalus, posterior fossa cyst, and cerebellar hypoplasia). Because of the potential risks caused by the location of the cyst, operation has not been suggested, but a regular follow-up in 6-month intervals was started. In the follow-ups, attention deficiency, behavioral problems, and learning disability were observed; his IQ was rated as 85 by WISC-R at the age of 14; and he had been diagnosed with borderline intellectual functioning. A dose of 100 mg/day quetiapine had been prescribed 5 years by a psychiatrist because of sleep problems; he also mentioned that he did not use it regularly and he applied to the outpatient clinic only for 4 times. He had applied again 2 years ago to the psychiatrist complaining of anger pangs, damaging goods, decreased self-care, thoughts of persecution, increased libido, and overspending. Owing to this, he had been prescribed 30 mg/day aripiprazole and 3 mg/day haloperidol, and later 100 mg/day sertraline had been added due to headaches, sleep disturbance, and depressive symptoms. It was found out from the medical records that he was found "legally irresponsible" due to "organic mental disorder" diagnosis for "the official document forgery" crime that he committed 5 years ago. He was not consuming alcohol or drugs, but he was smoking a pack a day. He had no psychiatric disease in the family history. He was born with normal

spontaneous vaginal delivery, and prenatal and postpartum periods were unremarkable.

Mild macrocephaly was detected in physical examination, and neurological examination was unremarkable except truncal ataxia. Biochemistry tests, complete blood count, sedimentation rate, thyroid function tests, vitamin B12 and folic acid levels, ECG, and EEG were reported normal. VDRL-RPR was negative. No drug metabolite was found with urinalysis. Cranial CT showed bilateral ventriculomegaly (Figure 1), enlarged third ventricle, enlarged fourth ventricle with posterior fossa cyst (Figure 2), and cerebellar hypoplasia (Figure 3), which was consistent with his previous cranial MRI. Verbal IQ score was rated 92; performance IQ score was rated 86 in WAIS; and the results were evaluated as in normal intelligence range.

At the beginning of treatment, 400 mg/day quetiapine was added to 30 mg/day aripiprazole that had already been used by the patient. On the fifth day of the treatment, 1000 mg/day valproic acid and 6 mg/day Paliperidone were added. On the eighth day of the treatment, 150 mg paliperidone palmitate intramuscularly was prescribed because of lack of insight and noncompliance to oral treatment. Biperiden (4 mg/day) was added because of acute dystonia. After the tenth day of the treatment, improvement in the symptoms was observed, and grandiose attitude and irritable mood regressed. Speed and rate of speech and associations were in normal range, as well as the need for sleep was increased. On the 15th day, YMRS was rated as 1.

Compulsory treatment process ended with the report from the board of health. The final treatment was determined as 30 mg/day aripiprazole, 1000 mg/day valproic acid, 200 mg/day quetiapine, 4 mg/day biperiden, and 100 mg/month paliperidone palmitate intramuscularly, and the patient was discharged from the hospital with a control appointment 1 week later. He was diagnosed with DWM and bipolar disorder. Informed consent was obtained during discharge.

DISCUSSION

Cerebellum is traditionally known as the regulator of coordination and motor functions. Nowadays, it is also thought that cerebellum is connected to many brain areas that affects cognition and behavior, such as dorsolateral prefrontal cortex, medial frontal cortex, anterior cingulate, and posterior hypothalamus, especially via thalamus and gets noradrenergic, serotonergic, and dopaminergic inputs from nuclei of brainstem. It is also thought that it might have a role in the regulation of sensory, procedural, linguistic, and emotional activities via its connections with limbic and cortical association areas. Therefore, it is suggested that cerebellum plays an important role on the regulation of mood,

Table 1. Features of Dandy-Walker malformation

Klein et al. 2003 (10)	Burton 2008 (27)
1. Large median posterior fossa cyst widely communicating with the fourth ventricle	1. Absence of cerebellar vermis or hypoplasia of cerebellar vermis with upward rotation
2. Small, rotated, raised cerebellar vermis in touch with tentorium	2. Enlarged posterior fossa with the upward displacement of falx, lateral sinuses and torcula
3. Upwardly displaced tentorium and lateral sinuses	3. Cystic dilatation of the fourth ventricle connected to the retrocerebellar cyst with thin walls which generated by the roof of the fourth ventricle
4. Emergence backward of posterior fossa contributing its dilatation	
5. Antero-laterally displaced but apparently normal cerebellar hemispheres

Figure 1. Enlarged lateral ventricles in DWM

Figure 2. Enlarged third ventricle (thick arrows) and enlarged fourth ventricle with posterior fossa cyst (thin arrow) in DWM

Figure 3. Cerebellar hypoplasia in DWM

and cerebellum anomalies might contribute to the pathophysiology of mood disorders (21,22,23). For example, Schmahmann described "cerebellar cognitive affective syndrome," which includes impairments in executive functions, visuospatial, and linguistic abilities, along with a large spectrum of affective symptoms ranging from depression and affective blunting to disinhibition and psychotic symptoms, in patients having cerebellar lesions (24).

In some neuroimaging studies, decreased cerebellar volumes have been reported in bipolar patients (25). Although enlargement of third and lateral ventricles has been reported in bipolar patients in some studies, other studies showed no significant difference in the sizes of brain ventricles and posterior fossa structures, when bipolar patients were compared with healthy controls (22,26). In some other studies, the total cerebellar volume of bipolar patients was not found to be lesser than healthy controls, but it was found out that patients with multiple mood episodes had decreased size of cerebellar vermis. This situation was tried to be explained as a late neurodegenerative phenomenon or a neuroanatomic sequel of bipolar disorder (23,25). Affective and behavioral changes have been especially reported in cerebellar vermis lesions in the literature, emphasizing the possible effects of cerebellar vermis neurons in mood regulation (27).

Hypoplasia of cerebellar vermis is observed in both DWM and DWV (14,28). DWC, also known as DWS, is used as a general definition that contains those two situations (1,2,3). There are a few case reports in the literature about bipolar disorder comorbid with DWS and DWV (15,17,18,19). Hypoplasia of cerebellar vermis is remarkable in all those cases, consistently with the pathophysiology mentioned above. Bakhla et al. (16) have reported an adult case with DWM who experienced two manic episodes. Baliyan et al. (28) have described treatment-resistant mania in an 8-year-old DWM case. As far as we know, our case is one of the few cases in the literature having bipolar disorder comorbid with DWM and differently from those cases, manic episodes are accompanied with depressive episodes in our case. It is also striking that our case is a forensic case, and he was found "legally irresponsible" due to "organic mental disorder."

Hydrocephalus comes first among DWM's typical clinical symptoms and because of it, macrocephaly, eye findings such as horizontal and lateral gaze palsy, nystagmus, strabismus, and irritability and vomiting due to increased intracranial pressure might be observed in childhood. Cerebellar findings such as ataxia-walking difficulties, which are rare in childhood may occur in later life (29,30). Spasticity, developmental delay, headache, nausea, lethargy, seizures, cranial nerve palsy, and quadriplegia are among other frequent symptoms (8,14). Those findings occur in a large spectrum in the cases in the literature (15,17); neurologically asymptomatic cases also might be seen (18). Truncal ataxia was observed in neurological examination of our case. Variable IQ scores ranging from mild mental retardation to normal intelligence have been reported in the literature, behavioral symptoms secondary to mental retardation might complicate differential diagnosis with mood disorders (15,17,18). Even psychomotor developmental delay and learning disability were found out in the history of our patient, IQ level measured in the adulthood was considered normal.

It is reported in the literature that central nervous system (CNS) anomalies accompany DWM frequently (corpus callosum agenesis is the most common). Extracranial malformations such as facial hemangiomas, car-

diovascular defects, finger anomalies, cleft lip, and cleft palate have been also reported frequently (29,30). Neuronal migration anomalies seen in DWS are also important for increased tendency of bipolar disorder and psychosis (31). Additional CNS anomalies were not detected in our case, any systemic complaints were defined, physical examination findings were normal, and ECG and laboratory tests were within normal range.

It is highlighted in the literature that difficulties are experienced in the treatment and follow-up of comorbid mood disorder in cases with DWS and DWV. It is suggested not to choose lithium in the treatment of these cases because of increased sensitivity to lithium which is well-known for its toxicity to cerebellum and increased rate of side effects (16). DWS has been also associated with frequently repeated manic episodes, atypical symptoms, and poor response for treatment (15-17,28). Aimua et al. (17) reported a DWV case that failed to respond to the treatment, despite an efficient dosage of mood stabilizer and antipsychotic was used. No response to lithium was observed in the case of Can et al. (19). Our patient's treatment was continued with multiple antipsychotics and valproic acid as mood stabilizer; it was decided to add an anticholinergic due to acute dystonia that occurred with paliperidone. A significant improvement in mood symptoms was obtained with this combination treatment.

Although DWM and mood symptoms might be observed together coincidentally in our case, cerebellar dysfunction due to DWM might be effective in the emergence of mood symptoms. Considering studies connecting cerebellum and mood symptoms, it is likely to find a causal relationship between DWM accompanied with cerebellar hypoplasia and the pathophysiology of mood symptoms.

Despite these findings, it is obvious that comprehensive studies are required to better understand the relationship between mood disorders and cerebellum. It is crucial to be aware of psychiatric symptoms, including mood symptoms, in cases having congenital cerebellar pathologies, and it would be helpful to follow these cases with psychiatry and to review carefully the treatment options considering resistance to treatment and potential side effects.

These cases also remind us the importance of detailed examinations including cranial imaging, in bipolar disorder that occurs in early age, going on with atypical symptoms, having poor response to treatment, demonstrating neurological findings in addition to psychomotor developmental delay and mental retardation.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.B., Ü.Ö.; Design - M.B., Ü.Ö.; Supervision - Ş.Ö.; Resource - M.B., Z.E.B.; Materials - M.B., Z.E.B.; Data Collection and/or Processing - M.B., Z.E.B., B.H.Y.; Analysis and/or Interpretation - M.B., Ü.Ö.; Literature Search - M.B., Z.E.B.; Writing - M.B., Ü.Ö.; Critical Reviews - Ş.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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