A Case of Simultaneous Mania and Idiopathic Normal Pressure Hydrocephalus: Etiology or Comorbidity?

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SUMMARY

Normal pressure hydrocephalus (NPH), typically associated with the triad of gait disturbance, dementia and urinary incontinence, rarely presents with symptoms of mania, depression or psychosis and psychiatric disorders may complicate the diagnosis. Few cases of NPH and psychiatric disease comorbidity have been reported so far. In most of these cases, NPH was associated with depression and psychotic symptoms. Mania symptoms were also reported in a few cases those of which were associated with a history of bipolar disorder (BPD) or subthreshold BPD symptoms. In this paper, we present a case of late-onset mania symptoms simultaneously presenting with NPH in a healthy individual without a history of psychiatric disorder.

Keywords: Normal pressure hydrocephalus, ventriculomegaly, late-onset, secondary mania

INTRODUCTION

Normal pressure hydrocephalus (NPH) is a syndrome characterized with dilatation of the ventricular system resulting from impaired CSF circulation with normal cerebrospinal fluid (CSF) pressure, and presents with the typical clinical symptoms of walking difficulties, mild dementia and urinary incontinance (Ishikawa et al. 2008, Oliveira et al. 2013). No motor or sensory dysfunction accompanies these symptoms. Patients generally complain of imbalance and difficulty in walking, especially when ascending or descending a staircase. Their steps are short and staggered; they often fall and have to stop frequently during walking.

The NPH syndrome was first described by Hakim and Adams in 1965 and has been called "Hakim-Adams" or "Adams-Hakim" syndrome. NPH is either primary or idiopathic (iNPH), with an unknown etiology, or secondary (sNPH) to pathologies such as head trauma, subarachnoid hemorrhage, meningitis, and tumours (Ishikawa et al. 2008, Oliveira et al. 2013, Hebb and Cusimano 2001).

The annual incidence of iNPH is reported to be 1.8 per 100.000 (Hamlat et al. 2006). Symptoms typically develop insidiously and appear at the 6-8th decades of life (Oomen et al. 1996). Gait disturbance occurs in 21.1%, dementia occurs in 9.4%, and urinary incontinence occurs in 14.7% of iNPH patients (Brown et al. 1999). All of the symptoms of the classic triad are not required for iNPH diagnosis.

The main methods of NPH diagnosis consist of radiological and metabolic investigations, research on CSF dynamics and neuropsychological evaluations. The most frequent method used to determine whether shunt treatment is appropriate is to decrease CSF pressure by lumbar puncture (LP) and to observe whether improvement occurs in the patient's clinic.

Investigations have shown that normal pressure hydrocephalus may present with very variable psychiatric and behavioural

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symptoms (Kito et al. 2009). There is a close relationship between the anatomic location of brain damage and the neuropsychiatric symptoms (Mendez 2000). Normal pressure hydrocephalus may present with a clinical picture resembling mania, depression, and psychosis in addition to the classical triad of dementia, imbalance, and urinary incontinance (Ishikawa et al. 2008). In literature, there is a limited number of studies in which normal pressure hydrocephalus is comorbid with bipolar disorder (Kwentus and Hart 1987, Oliveira et al. 2014). In this article, a case with late-onset mania symptoms simultaneous with normal pressure hydrocephalus is presented.

CASE

The 57-year old, high school graduate employed male patient came to psychiatry clinic accompanied by his wife with complaints of insomnia, hyperactivity, excessive talking, gait disorder, and increased psychomotor energy. It was learned by history taking that his gait disturbance, noticed not by him but by his relatives, had started 6 months previoulsy, becoming more prominent within the previous 1 month such that he had started falling while walking. When further queried, he reported increased frequency of urination and occasional urinary incontinance were included in his complaints when symptoms of imbalance and walking difficulty had started. Hydrocephalus had been detected at another healthcare centre by brain magnetic resonance imaging (MRI), when CSF pressure was found to be 130-140 mm H_2O. Evacuation LP was performed; and when gait disturbance had persisted with increases in his complaints, he was referred to the Neurosurgery Clinic of Adana Başkent University. Cranial MRI repeated at Başkent University Hospital revealed enlargement in the ventricles, narrowing in the callosal angle, and disproportionality between ventricular enlargement and sulcal enlargement. The Evans index was determined to be 0.36, and increased periventricular signal was not observed (Figure 1A-1B).

Investigation of CSF flow showed hyperdynamic CFS flow throught the aquaduct. It was concluded that brain MR findings supported NPH. The case was diagnosed as NPH by the Neurosurgery Clinic of Adana Başkent University. Further surgical intervention was not required after LP repetition when clinical improvement was not observed, medical treatment with acetazolamide (750 mg/day) was arranged and the patient was discharged from hospital with the planning of a control brain MRI 3 months later. This case was also evaluated by the Neurology and the Infectious Diseases Clinic of Adana Başkent University. Neurological deficits or cognitive disturbances, other than staggered, wide-based and unsafe gait with small and slow steps when unsupported, were not observed. Anomalies of infection parameters and results of laboratory tests including endocrine investigations were not detected. Consultation was seeked with the psychiatry clinic on grounds of behavioural disturbances.

The patient's relatives reported that during the previous 10 days the patient had slept very little, talked continuously, behaved abnormally, and experienced emotional fluctuations without an obvious reason. The patient personally stated during his examination that he perceived himself as a 16-year old, that his brain was recreated by God, that he would pave the roads for the benefit of the people, and that a divine power was assisting him. He did not have a personal or family history of any psychiatric disorder or a history of alcohol or substance use.

In his mental examination, he was conscious and cooperative. Perception and memory were normal. Orientation to place, time and person were normal. He was distractable. He stood up frequently and handled and examined the objects on the table during the interview. He had fast associations, flighty ideas and poor judgment. His thought content included grandiose delusions on being very strong, being chosen by divine power and having a recreated brain. His mood was euphoric. In his memory examination, the Mini-Mental Status Examination score was 28/30. The Young Mania Rating Scale (YMRS) score was 39. Increased psychomotor activity was detected in extroverted behaviours.

The patient had not used within the previous 1 month any drug other than acetazolamide prescribed for NPH. Results of thyroid function tests and vitamin B12 level were within normal limits. He did not have a history of head trauma. Diagnosis of dementia was excluded after neurological and cognitive evaluations and the history taken from the relatives. LP outcome, physical, neurological examinations, imaging results, infection parameters and laboratory results did not reveal a secondary cause other than NPH that could explain the manic episode.

On the basis of elevated mood, reduced need for sleep, increased talking, raised self esteem, grandiose delusions with a severity to disrupt social functionality and lasting longer than one week, the patient was diagnosed with manic attack according to DSM-5 criteria and treatment was started with risperidone (4 mg/day) to control mania and quetiapine (200 mg/day) for sedation.

Since insomnia and hyperactivity continued 3 days later, quetiapine dose was increased to 400 mg/day and risperidone dose was increased to 6 mg/day. After testing on the Extrapyramidal Symptom Evaluation Scale (ESES), moderate levels of akathisia and bradykinesia due to antipsychotic use, and extrapyramidal parkinsonism symptoms in the form of mild level of tremor and dystonia were detected; and biperiden (4 mg/day) was added to his treatment. In his control visit 15 days later, his euphoria had subsided, and the

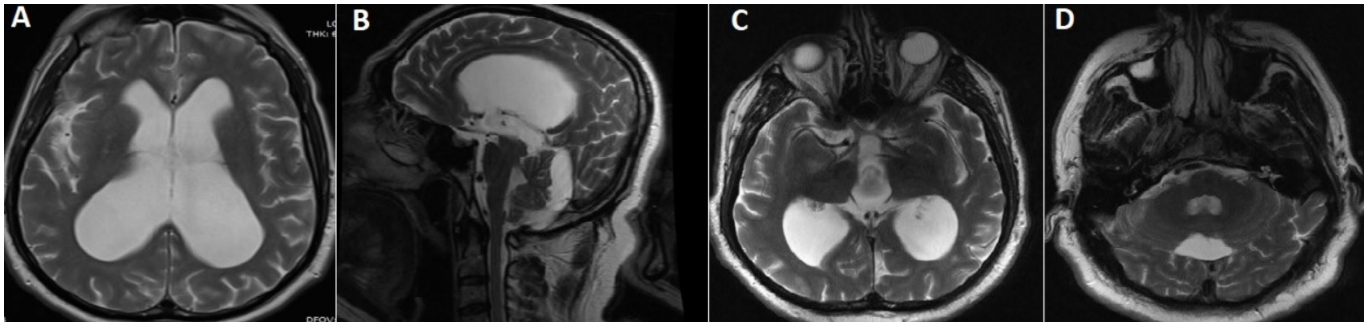

Figure 1A-B. T2W axial and sagittal images showing the dilatation of the lateral ventricles, narrowing of the callosal angle, disproportion between ventricular expansion and sulcal expansion, and absence of periventricular ischemia **1C-D.** T2X axial images showing the dilatation of the third and fourth ventricles.

score on the YMRS had decreased to 14. In his control visit a month later, the patient was euthymic, his YMRS score was 3. His gait problem continued with short, slow, and staggered steps, and imbalance. Follow up of the patient was continued with risperidone (2 mg/day) and quetiapine (200 mg/day). At his 3rd month control, quetiapine and biperiden were discontinued and risperidone was continued at a maintenance dose of 1 mg/day. Signs of dementia were not detected (MMTE= 28/30). However, his gait disturbance with short steps, slow and staggered walking was found to continue with the same severity. After 6 months he was admitted to Çukurova University Neurology Clinic because of continuing gait disorder. At his consultation neurological deficit other than determination of a walking pattern with short steps, slow and staggering movements with a wide-based gait, could not be detected. Cranial MRI demonstrated dilatations in lateral ventricles (Figure 1A), enlargement in the third and the fourth ventricles (Figure 1C-1D). CSF flow MRI revealed hyperdynamic flow signal at the aqueducts (9.3 cm/sec) (Figure 1B) which was considered as hydrocephalus sequela and follow up without medication was recommended. The patient did not attend his follow up control, and he and his family were contacted by telephone when it was learned that neither improvement nor deterioration had occurred in the symptoms due to NPH; that manic or depressive symptoms had not been seen during this period and that 2 months previously he had stopped taking risperidone without the advice of a physician.

DISCUSSION

The diagnosis on the case was "Bipolar and Associated disorders, with manic features due to another health condition (NPH)" based on the clinically predominant euphoria, grandiose delusions, increased psychomotor energy, and also absence of a psychiatric history, normal results of physical examination and laboratory tests. The term 'secondary mania' is used if the mood disorder is related to an antecedent medical condition. Krauthammer and Klerman (1978) proposed this term for describing a case of clinical mania that presented after brain damage, stating that "secondary mania" may develop in association with organic dysfunction -medical and pharmacological- in patients without a history of affective disorder. Features of secondary mania include onset following a somatic illness, absence of family and personal history of psychiatric disease, and late age of onset. In the case discussed here, demonstration of ventricular dilatation in cranial MRI, determination of normal pressure hydrocephalus after LP, the onset of mood symptoms just after the exacerbated gait disturbance, lack of a family history, the absence of a history of depression, and late onset of manic attack are features that met secondary mania criteria.

Cerebrovascular disease, dementia, epilepsy, brain tumors, and encephalitis are the main neurological causes of mania. Mania symptoms were exhibited by 10% of the patients within 1 year of experiencing closed-head injury (Shprecher et al. 2008). Vascular dementia, Huntington's disease, normal pressure hydrocephalus, and prion diseases have also been associated with mania (Broadhead and Jacoby 1990). Systemic causes of mania include Cushing's syndrome, hyperthyroidism, and vitamin B12 deficiency. In the literature, mania and hypomania have been reported in 3% of hospitalised patients with Cushing's syndrome; and some studies have shown that hyperthyroidism was seen in one third of the cases hospitalized for mania (Oomen et al. 1996). Antidepressants, psychostimulants, and corticosteroids are also agents that most frequently cause mood swings; and a quarter of the patients treated with high doses of steroids present with hypomania and mania (Brown et al. 1999). In the case presented here, these causes were excluded by examination, neuroimaging, laboratory investigations and history taking.

Personality changes, anxiety, depression, psychotic symptoms, obsessive-compulsive disorder (Kaufman et al. 2003, Acar et al. 2018), delusions of jealousy (Yusim et al. 2008) and mania-like symptoms (Kwentus and Hart 1987) were reported in NPH patients. The most common neuropsychiatric symptoms observed in NPH were apathy, depression, and aggression (Kito et al. 2009). In the case

discussed here, aggression was attributed to mania, but symptoms of apathy or depression were not detected. After evaluating 35 NPH cases, Oliveira et al. (2014) reported one patient with bipolar disorder who had been regularly followed up by a psychiatry clinic before diagnosis of NPH. Callari et al. (2014) described the case of a patient with a history of subthreshold manic symptoms, who developed NPH 2.5 years after surgery and radiotherapy for thalamic glioblastoma and presented with mania symptoms following the peritoneal shunt procedure. The manic symptoms were thought to be associated with increased dopaminergic tonus after the peritoneal shunt. Tretament with haloperidol (3 mg/day) and quetiapine (600 mg/day) achieved full remission in manic symptoms after 7 days. The differentiating features of the presented case from the previously reported cases of NPH comorbid with mania, are absence of a psychiatric history and lack of a shunt procedure; which we believe make this case the first to be reported in the literature. Our literature screening yielded only three case reports of mania associated with NHP, amongst others about depression, psychosis, obsessive-compulsive disorder, and delusional disorders comorbid with NPH. However, these mania cases had history of depressive attacks and subthreshold bipolar spectrum symptoms before the development of NPH. In contrast to the case of manic attack developed after peritoneal shunt to relieve NPH, which was completely reversed in a week after combined treatment with a typical and an atypical antipsychotic agents (Callari et al. 2014), it took 1 month by dual atypical antipsychotic therapy for full remission in the case reported here when high sensitivity to extrapyramidal side effect was observed. Although these results are not enough for generalization, they suggest that antipsychotic treatment response in these cases is good and the lack of prior antipsychotic use might have contributed to high antipsychotic efficiency at the receptor level.

Manic symptoms are believed to present with the disinhibition of limbic mechanisms resulting from impairment in frontotemporal pathways (Shulman 1997). Although it is not possible to exclude the incidental coexistence of NPH and mania, the manic symptoms observed in the case discussed here have been attributed to a rare clinical condition associated with NPH, resulting from the mass effect of the enlarged ventricular system on the neighbouring structures with outcomes of ischaemic and degenerative changes that lead to development of mania.

Treatment of primary and secondary manias are similarly based on the use of mood stabilisers lithium, valproic acid and carbamazepine and the antipsychotics risperidone, quetiapine, olanzapine, and aripiprazole as recommended in the guidelines for treating acute and chronic mood disorders (Gafoor and O'Keane 2003). However, unlike with the primary manias, the necessity of using these agents for the maintenance treatment of secondary manias remains as a subject of debate. Hence, with the diagnosis of secondary mania, symptomatic treatment was started in the case presented here without planning a long term treatment with mood stabilisers. A positive response was obtained with quetiapine and risperidone. Low dose antipsychotic treatment (risperidone 1 mg/day) was continued during the 1.5 years follow up of the case, and no affective attack was observed. Maintenance of remission with low dose antipsychotic treatment (he didn't use any medication for last 2 months) during the long follow up period without requiring an additional mood stabilizer supports the NPH associated mania claim for this case. These results support the decision for mania associated with hydrocephalus pathophysiology in this case with evidence based on radiological imaging and clinical summary of neurological symptoms of gait disturbance, late-onset mania in the absence of any personal or family history of psychiatric disorder, and lack of any significance in the laboratory test results.

Hence, late-onset mood disorders should be evaluated carefully as secondary clinical pictures of underlying organic pathologies. Medical causes should be considered in the evaluation of mania symptoms appearing at advanced age and brain imaging should be performed. In addition to detailed physical and neurological examination

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