CASE REPORT

Psychiatry and Clinical Psychopharmacology 2024;34(2):197-200
DOI:10.5152/pcp.2024.23765

A Von Hippel-Lindau Syndrome Case Diagnosed While Hospitalized for Major Depression

Furkan Bahadır Alptekin

Department of Psychiatry, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

ABSTRACT

Von Hippel-Lindau syndrome (VHL) is a rare genetic disorder inherited in an autosomal dominant manner. It progresses with the presence of cranial and visceral organ tumors. Psychiatric symptoms may be accompanied by tumor location and hormonal changes. However, it is rare for the disease to first appear with psychiatric symptoms, which may delay the diagnosis of the disease. In this article, a case of VHL, first presenting with major depression, is discussed. The diagnosis and treatment of major depression may obscure the diagnosis of VHL due to the similar mean age at diagnosis and the confounding effect of neurovegetative symptoms accompanying depression.

ARTICLE HISTORY

Received: September 06, 2023
Revision requested: October 11, 2023
Last revision received: October 26, 2023
Accepted: November 5, 2023
Publication Date: February 2, 2024

INTRODUCTION

Von Hippel-Lindau syndrome (VHL) is a rare genetic disorder characterized by autosomal dominant inheritance. It manifests as a familial neoplastic syndrome affecting multiple organs due to genetic mutations in the VHL tumor suppressor gene. These patients are more susceptible to benign and malignant tumors in various systems, including the central nervous system (CNS) and visceral organs.[1] The prevalence of VHL syndrome is about 1 in 36 000 live births. Clinical signs of VHL usually appear during the second decade of life, and approximately half of the patients experience symptoms at diagnosis. Among VHL patients, the most common type of lesion is CNS hemangioblastomas, often found as multiple infratentorial growths.[2] Diagnosis of VHL involves the identification of at least 2 tumor foci that fit the disease definition in persons with familial factors or identifying a pathogenic germline variant (usually a loss-of-function mutation) in the VHL gene that accompanies the tumor focus.[1]

Depression is one of the most common psychiatric disorders. The first onset of the major depressive episode is most likely between mid-adolescence and mid-40s. Approximately 40% of individuals experience their first episode of depression before age 20, with an average onset age in the mid-20s (mean age 25). Depression is almost twice as common in women as in men, and depression in both sexes peaks in the second and third decades of life.[3,4]

Depressive disorder is marked by specific symptoms, including anhedonia, exacerbation of depressive symptoms at particular times of the day, and heightened feelings of guilt related to the illness. On the other hand, certain symptoms, such as neurovegetative symptoms consisting of fatigue, loss of appetite or weight, and insomnia, are also common in various other medical conditions.[3,5] As observed, VHL and major depression share common features, including age of onset, age of diagnosis, and neurovegetative symptoms.

This study aims to present and discuss a case who received long-term outpatient and inpatient treatment for major depression and was diagnosed with VHL after cerebellar tumor detection. For this case study, an informed consent was obtained.

CASE PRESENTATION

A 19-year-old female patient, a high school graduate living with her father, lost her mother to cancer 3 years ago. A month or two after her mother's passing, she started experiencing symptoms such as low mood, decreased interest, lack of energy, loss of appetite, and weight loss. She did not seek treatment for the first year. A psychiatrist consulted neurology as a routine practice to exclude organic pathologies when she applied a year later. A neurologist evaluated the patient through physical examination and was referred back to psychiatry as no evidence of organic pathology was detected. Symptoms of depressive mood, decreased interest, lack of energy

Corresponding author: Furkan Bahadır Alptekin e-mail: furkanbahadir0155@gmail.com

Cite this article as: Alptekin FB. A Von Hippel-Lindau syndrome case diagnosed while hospitalized for major depression. *Psychiatry Clin Psychopharmacol*. 2024;34(2):197-200.

and weight loss, and decreased psychomotor activity were suggestive of major depressive disorder. The patient had no history of substance use, and the absence of past psychotic symptoms and manic episodes ruled out diagnoses such as substance-induced depressive disorder, psychotic disorders, and bipolar disorder. Although the depressive symptoms were related to the mother's death, the patient did not associate the depressive mood with the mother's loss. Therefore, the diagnosis of pathological grief was excluded. Since the neurological examination was routine, neurological pathologies were excluded, and a diagnosis of major depressive disorder was made. She was prescribed sertraline 50 mg and olanzapine 2.5 mg. The patient initially partially benefited from the treatment. She was infected with coronavirus disease 2019 (COVID-19) during treatment, and her complaints increased. She dropped from 56 kg to 45 kg. She was vomiting. Her worsening was linked to the infection. She became partially immobile. Despite recovering from the COVID-19 infection, unhappiness, loss of interest, appetite, energy, and weight loss continued. The symptoms were thought to be related to major depressive disorder, and she was referred to psychiatry. Due to her limited oral intake and poor general condition, it was decided that she receive inpatient treatment in the psychiatric ward.

She was conscious, cooperative, and oriented on our first mental status examination. Her self-care was not good, and she was partially immobile. Her affect and mood were depressive, and her speech was dysarthric. There were no hallucination or delusions. In the interviews, she stated that her appetite loss was unrelated to body image. Therefore, a diagnosis of the eating disorder was also excluded. On physical examination, there was a 2 cm pressure sore in the sacral region. Neurological examination revealed bilateral pupil dilation and loss of muscle strength in the right upper extremity. Dysmetria was positive in both hands in the cerebellar test. The laboratory assessments showed normal values.

Diffusion magnetic resonance imaging (MRI) with susceptibi lity-weighted imaging (SWI) section was performed with the recommendation of the neurologist. A space-occupying lesion was detected in the cerebellum. Thereupon, the patient was consulted by the neurosurgery department. She was transferred to the neurosurgery department for detailed examinations and planned operations. In the cranial MRI of the patient, a 45 × 32 mm mass lesion was detected in the cerebellar hemisphere with a contrasting mural nodule on its wall (Figure 1A and 1B).

In the SWI section, brain diffusion MRI identified the space-occupying lesion. In addition, contrast mass lesions in the opposite cerebellar hemisphere and lesions with multiple drop metastases were detected in the spinal canal. Lumbar MRI revealed a spinal metastatic nodular lesion at the T12 level in the posterior section. A cervical spinal MRI revealed diffuse metastatic masses in the cervical spinal cord and brainstem (Figure 2).

The pathology report of the excised tumor showed that the mass was hemangioblastoma (hemangioblastoma—WHO grade 1, 2021). Ophthalmology, endocrinology, ear, nose, and throat departments were consulted to evaluate other possible tumors suspected of VHL due to multiple tumors accompanying the CNS. It was genetically tested, and the test result was consistent with VHL, showing a mutation [p.Asn78Ser (c.233A>G) HETEROZYGOT]. The patient underwent 3 cranial operations for tumor excision 12 months after the diagnosis, during which she regained some of her neurological functions. Psychiatric outpatient follow-ups continued, and her final neurological examination was routine. Appetite and sleep were normal under psychiatric control, and she was starting to gain weight. Although she had a depressive mood, she partially recovered with sertraline 50 mg and mirtazapine 15 mg treatment.

DISCUSSION

Von Hippel–Lindau syndrome could cause several psychiatric symptoms because of disease burdens, hormonal disorders, and pressure effects in particular brain parts.[6,7] However, a few VHL patients were encountered with psychiatric complaints. One was a 39-year-old male who had experienced long-standing depressive and psychotic disturbances. His VHL diagnosis was verified with the autopsy, revealing cerebellar hemangioblastoma, multiple renal bilateral carcinomas, pancreatic cyst papillary, and solid neuroendocrine carcinoma.[8]

Another case was a 19-year-old woman who was consulted by psychiatry because of loss of appetite and suspected anorexia nervosa. After 3 weeks of psychiatric hospitalization, she developed progressive gait abnormality and bilateral dysmetria, which was worse on the left side. A brain MRI examination revealed a massive lesion. This lesion, together with the pancreatic cysts, was diagnosed with VHL.[7] As seen in the example cases and our case, depressive and eating disorder symptoms could overshadow the organic state. Patients might be prescribed psychiatric medications, potentially delaying the diagnosis and surgical treatment. In our case, the onset of depressive symptoms after her mother's death and partial recovery with medicines led her to focus on psychiatric treatment. The fact that the neurological examination was normal

MAIN POINTS

- The coexistence of psychiatric and organic disorders is a common occurrence.
- Organic pathologies, especially cranial cases with psychiatric symptoms, can be overlooked without care.
- In particular, neurovegetative symptoms and other common features of diseases may play a role in evaluating organic pathologies, primarily in psychiatric cases.

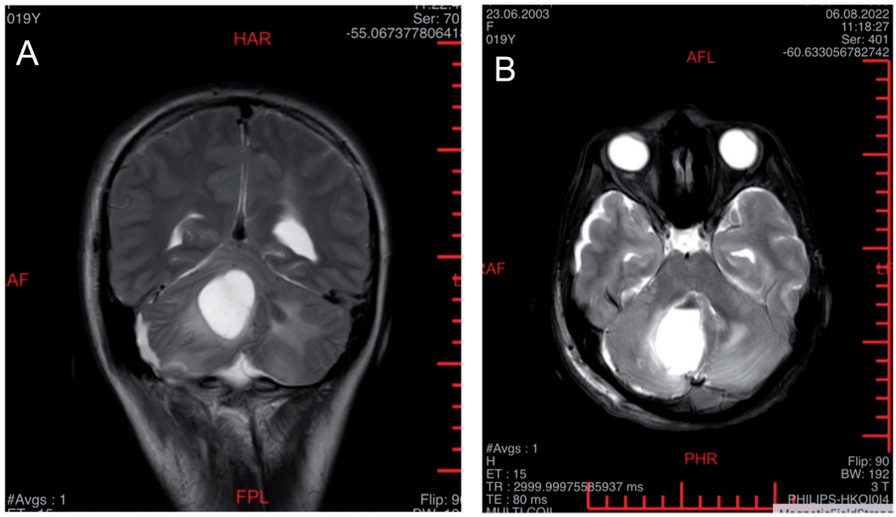

Figure 1. Initial cranial magnetic resonance imaging, axial (A) and coronal (B) T2-weighted turbo spin echo sequence. A massive lesion in the right cerebellar hemisphere with a 45 × 32 mm wall with a contrasting mural nodule.

when psychiatric symptoms occurred prevented further examinations and contributed to this situation. That is probably because the space-occupying mass was small initially; it did not cause neurological findings. Therefore, internal and neurological symptoms accompanying psychiatric symptoms should be taken seriously, and evaluations should be reviewed when necessary.

Actually, it is not uncommon for organic diseases to progress with psychiatric symptoms. A retrospective study of patients aged 18-65 revealed that 2.8% of patients admitted to psychiatric units had psychiatric symptoms attributable to a medical disorder. The results of a comparative study of patients 65 years of age and older were more significant and concerning. This study detected a situation requiring emergency medical intervention within 12 hours in 2.3% of the patients admitted to psychiatry services.[9] Moreover, the research findings indicated that individuals inappropriately placed in psychiatric units experienced reduced instances of comprehensive medical history assessments, physical examinations, cognitive evaluations, laboratory tests, and the management of abnormal vital signs compared to those admitted to medical units.[10]

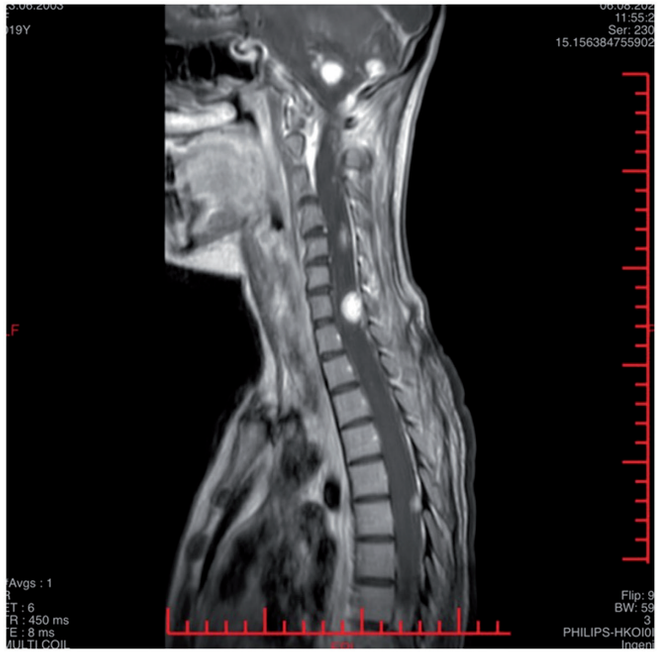

Figure 2. Multiple lesions on sagittal T2-weighted cervical and thoracic magnetic resonance imaging.

On the other hand, the need for psychiatric support in organic diseases is also an important issue. Neglecting psychiatric symptoms during treatment may worsen the disease's progression and negatively impact the patient's quality of life. Our case still needed antidepressant treatment after 3 cranial operations. She had partially benefited from sertraline and mirtazapine. Depressive symptoms were related to the restrictions of VHL and the disease's burden.

The diagnosis of VHL in our case was made after cerebellar hemangioblastoma was seen. Vomiting, weight loss, and restriction of mobilization were probably due to the space-occupying lesion. When examining existing literature, instances of hemangioblastoma, glioneuronal tumor, meningioma, and metastatic tumors have been reported to present with psychiatric symptoms. These cases presented with depression, psychosomatic symptoms, visual and auditory hallucinations, speech disorders, sleep disturbances, and persecution delusions.[11] According to a systematic review, 13.3% of posterior fossa tumors involving the cerebellum are accompanied by psychiatric symptoms, as in our case.[12]

The depressive complaints of our patient before and after the diagnosis of VHL were not evaluated with objective

questionnaires. This constitutes a limitation of the study. However, the diagnosis of depression was confirmed by many psychiatrists who made evaluations at different times.

In conclusion, organic pathologies, especially brain tumors, may present with psychiatric symptoms. VHL is one of them. When a psychiatric disorder is diagnosed, it is important to exclude organic pathologies in order not to delay the treatment. The presence of stressor factors that explain the presence of psychiatric symptoms should not mislead us in this regard.

Informed Consent: Informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The author has no conflicts of interest to declare.

Funding: The author declared that this study has received no financial support.

REFERENCES

1. Chittiboina P, Lonser RR. Von Hippel-Lindau disease. In: *Handb Clin Neurol*. Amsterdam: Elsevier; 2015;132:139-156. [CrossRef]
2. Varshney N, Kebede AA, Owusu-Dapaah H, Lather J, Kaushik M, Bhullar JS. A review of von Hippel-Lindau syndrome. *J Kidney Cancer VHL*. 2017;4(3):20-29. [CrossRef]
3. Malhi GS, Mann JJ. Depression. *Lancet*. 2018;392(10161):2299-2312. [CrossRef]
4. Smith MV, Mazure CM. Mental health and wealth: depression, gender, poverty, and parenting. *Annu Rev Clin Psychol*. 2021;17(1):181-205. [CrossRef]
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Association; 2013. [CrossRef]
6. Lammens CR, Bleiker EM, Verhoef S, et al. Psychosocial impact of von Hippel-Lindau disease: levels and sources of distress. *Clin Genet*. 2010;77(5):483-491. [CrossRef]
7. Marques J, Batista R, De Moraes M, et al. Anorexia as the first clinical manifestation of von HippelLindau syndrome. *Mol Clin Oncol*. 2020;13(5):1-1. [CrossRef]
8. Suck MLT, Bojórquez DR, Lara CS. Depression and psychotic disturbances as unique manifestation of Von Hippel Lindau disease. *Patol Rev Latinoam*. 2011;49(suppl1):5-10.
9. Yeager-Cordial E, Ison J, Becker R, Boyd C, Weinstock M. Psychiatric manifestations of organic disease: don't get fooled! *J urgent care Med*. 2022;16(11):11-15.
10. Reeves RR, Parker JD, Loveless P, Burke RS, Hart RH. Unrecognized physical illness prompting psychiatric admission. *Ann Clin Psychiatry*. 2010;22(3):180-185.
11. Madhusoodanan S, Ting MB, Farah T, Ugur U. Psychiatric aspects of brain tumors: a review. *World J Psychiatry*. 2015;5(3):273-285. [CrossRef]
12. Ghandour F, Squassina A, Karaky R, Diab-Assaf M, Fadda P, Pisanu C. Presenting psychiatric and neurological symptoms and signs of brain tumors before diagnosis: A systematic review. *Brain Sci*. 2021;11(3):301. [CrossRef]