CASE REPORT

pISSN: 0126-074X | eISSN: 2338-6223
https://doi.org/10.15395/mkb.v56.3347
Majalah Kedokteran Bandung. 2024;56(2):153–156

Majalah Kedokteran Bandung (MKB)

Received: January 27, 2023
Accepted: April 11, 2023
Available online: June 30, 2024

Clinical Profiles of Obstructive Hydrocephalus in Patient with Von Hippel–Lindau

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Abstract

Von Hippel-Lindau (VHL) is an autosomal dominant disease that affects multiple systems that may result in benign and malignant multisystem tumors. The estimated incidence of VHL is 1 in 36,000 births. Disease incidence ranges from 10 to 40 years, with an average of 26 years, and it impacts diverse ethnic groups. VHL results from mutations in the germ line that have been mapped to chromosome 3p25. Currently, this is the only gene known to cause the syndrome. This study presented a case of obstructive hydrocephalus in a patient with VHL. A 19-year-old female was referred to the Eye Clinic for a diagnosis of papilledema. She began to experience vagal abdominal discomfort for no apparent reason. Per exam, the patient had 20/20 OD and 20/400 OS, with an intraocular pressure of 14 OU. The patient's MRI revealed a posterior fossa cranial cystic brain lesion that was obstructing the fourth ventricle and causing obstructive hydrocephalus. Early detection, management, and focal laser treatment of capillary hemangiomas in the retina's periphery led to favorable visual outcomes. Even after vitreoretinal surgery, the tumors may cause exudative retinal detachment and have an inferior visual prognosis if left untreated.

Keywords: Hemgioblastomas, hydrocephalus, von Hippel-Lindau disease

Introduction

Von Hippel-Lindau (VHL) disease is an inherited disorder that affects 1 in 36,000 newborns. Individuals with VHL develop benign and malignant tumors, such as hemangioblastomas of the retina and central nervous system, clear cell renal cell carcinomas (RCC), pheochromocytomas, pancreatic neuroendocrine tumors, and endolymphatic sac tumors (ELST).[1,2] The loss of function of the VHL gene on one allele at chromosome 3p25-26 causes VHL.[3] A somatic "second hit" results in the loss of the other allele and the development of a tumor. Loss of VHL function in cells increases HIF expression and stabilization. The VHL protein/HIF pathway has been linked to developing hemangioblastomas, renal cell carcinomas, and other VHL malignancies. VHL disease is confirmed by clinical examination, imaging, and genetic testing for VHL mutations.[2] Surgical resection of symptomatic tumors (hemangioblastomas), metastasis-prone tumors (RCC larger than 3cm), and tumors causing hormonal symptoms (pheochromocytomas) is the primary treatment for VHL disease.[1] There are several cancer surveillance strategies for VHL patients that have been created, all of which are based on professional judgment and the course of VHL disease.[4] This study reports the case of a female patient who presented to the emergency department with obstructive hydrocephalus with Von–Hippel–Lindau. Examining the clinical profile of obstructive hydrocephalus in patients with VHL is important for a targeted approach to diagnosis, treatment, and management. Besides, the process of distinguishing it from alternative etiologies of hydrocephalus is beneficial in the determination of suitable treatment approaches, such as the implantation of shunts or the utilization of endoscopic techniques, which can be customized to address the specific underlying pathology associated with VHL disease.

Case

The Neurology Department referred a 19-year-old female to the Eye Clinic to diagnose papilledema. The patient was in good health until

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six months ago, when she began to complain of vagal abdominal pain with no discernible cause. Two weeks before the presentation, her headache was worsening. The patient presented to emergency care and was referred to the Eye Clinic for evaluation of optic nerve edema. The vision was 20/20 OD and 20/400 OS per exam. Intraocular pressure is 14 OU. The pupil was equal and reactive, with an afferent pupillary defect. The anterior segment was unexceptional. A dilated eye exam revealed a normal retina on the right with a hyperemic disc and a similar hyperemic disc with peripheral capillary hemangioma and a normal macula on the left. The patient's MRI revealed a cystic brain lesion in the posterior fossa cranial area that was obstructing the fourth ventricle and causing obstructive hydrocephalus. The family tree revealed that the mother had previously undergone surgery for retinal detachment. A relative passed away due to an unidentified abdominal and cerebral tumor. An additional two relatives and her grandmother also passed away from abdominal tumors. The hospitalized patient underwent an emergency ventriculoperitoneal shunt to reduce elevated intraocular pressure. During her recuperation period, and because this is her excellent eye, the patient had a superficial orange lesion with minor blemishing on her capillary hemangioma. Two months later, during her follow-up, the lesion was unchanged. The research ethics committee of the affiliated institution of the authors reviewed and approved the study, which follows the rules of the National Committee of Bio-Ethics. The patient provided her consent to participate in this study.

Discussion

The investigation of the clinical characteristics of obstructive hydrocephalus in individuals diagnosed with VHL syndrome holds significance in facilitating a focused strategy for the identification, intervention, and control of this condition. Moreover, the act of differentiating it from other potential causes of hydrocephalus holds advantageous implications for identifying appropriate therapeutic strategies, such as the insertion of shunts or the application of endoscopic methods, which can be tailored to target the specific underlying pathology linked to VHL disease. In this case report, we present the case of a female patient who was diagnosed with obstructive hydrocephalus and VHL. This case highlights the importance of early detection and follow-up for young patients with VHL. Our patient presented with a cystic brain lesion in the posterior fossa cranial, which was blocking the fourth ventricle and producing obstructive hydrocephalus. To lower the increased intraocular pressure, the patient had an emergency ventriculoperitoneal shunt. Hydrocephalus is treated with a ventriculoperitoneal shunt, a cerebral shunt. The conduit eliminates surplus cerebrospinal fluid. Hydrocephalus, if left untreated, can result in numerous adverse effects, including chronic headaches and visual disturbances.[5]

According to the patient's family history, her mother had previously undergone surgery for retinal detachment. Unidentified abdominal and cerebral tumors led to the death of a relative. Additionally, two additional relatives and her grandmother died from abdominal malignancies. An alternative screening method for patients with VHL could be based on the specific mutation they possess. It has been demonstrated that missense mutations in VHL impart a higher risk for pheochromocytoma than deletions or truncating mutations.[6] Moreover, surface missense substitutions may impart a higher risk for pheochromocytoma than deep missense mutations.[4]

Von Hippel-Lindau is an autosomal dominant syndrome induced by a mutation in the germ line. The gene that has been mapped to chromosome 3P52 in VHL.[3,8] This is the only gene known to cause VHL at present. The prevalence in the Saudi population is unknown, but the population is identical to that of other nations. Since VHL is autosomal dominant, it occurs once in every 36,000 births.[2] Children of affected parents have a 50% chance of developing VHL, but approximately 20% of cases involve de novo mutations.[8] The disease is marked by bilateral multifocal capillary hemangioma, central nervous system hemangioblastoma, renal cell carcinoma, pancreatic islet cell tumor, endolymphatic sac tumor, and renal, pancreatic, and epididymal cyst.[2] The diagnosis of VHL is based on a family history or hemangioma's clinical presentation. If there is a family history, only one lesion is required for the diagnosis of retinal capillary hemangioblastomas (RCHs); otherwise, at least two hemangiomas or one hemangioma and a visceral lesion are required.[9] The differential diagnosis is extensive but may include isolated hemangioblastoma, retinal angioma, and renal cell carcinoma with clear cells.[2,9]

A diagnostic procedure is used to establish the diagnosis and assess the severity of

clinical manifestations.[10] CT scans or MRIs to diagnose CNS tumors, Pheochromocytoma, and Endolymphatic sac tumor.[11] MIBG labeled with radioiodine for the evaluation of extra-adrenal lesions. Sequence analysis or deletion/duplication analysis constitutes Molecular Genetic Testing.[11]

The treatment approach for obstructive hydrocephalus in individuals diagnosed with VHL disease commonly encompasses a blend of surgical and medicinal modalities. Von Hippel-Lindau disease is a hereditary condition characterized by the formation of tumors, particularly within the central nervous system, which can potentially result in the occurrence of hydrocephalus. The management of obstructive hydrocephalus in people with VHL syndrome is contingent upon various factors, including the underlying etiology, the severity of hydrocephalus, and the general health status of the affected individual. The treatment for VHL differs based on the location, size, and associated cyst of the tumor.[10] In general, the goal of treatment is to treat the growths when they are causing symptoms but are still minor, so that they do not cause permanent problems by placing pressure on the brain or vertebrae, obstructing the passage of cerebrospinal fluid in the nervous system, or impairing vision.[10] Most cases of VHL are treated with surgery to remove the lesions before they become dangerous. Certain malignancies can be treated with high-dose, focused radiation. Laser photocoagulation, cryotherapy, photodynamic therapy, and radiation, as well as surgical 7excision, are the traditional methods for destroying ocular VHL tumors.[10,12] Photodynamic therapy (PDT) with verteporfin is a sanctioned treatment for choroidal neovascular membranes. PDT has also been attempted with variable degrees of efficacy in cases of retinal angiomatosis.[9] The use of systemically or locally administered anti-angiogenic therapy (bevacizumab) has recently been associated with a sustained reduction in exudation, regression of the tumor, and improvement in visual acuity.[10,12] The Location of the RCH has a substantial impact on the efficacy and applicability of treatment.

Patients with VHL have a prognosis dependent on the location and severity of their lesions. VHL can cause blindness and/or permanent brain injury if left untreated.[10] The prognosis is significantly enhanced with early detection and treatment. Typically, complications from brain lesions or renal cancer result in death. A more frequent follow-up could increase the likelihood of early detection of pheochromocytoma, thereby increasing the viability of partial adrenalectomy.[4]

In conclusion, the identification of capillary hemangiomas in the peripheral region of the retina and subsequent treatment with focal laser therapy has yielded positive visual outcomes in to ocular VHL early detection. In the absence of appropriate medical intervention, the tumors have the potential to progress into exudative retinal detachment, leading to a less favorable visual prognosis, even following vitreoretinal surgery.

References

1. Chittiboina P, Lonser RR. Von Hippel-Lindau disease. Handb Clin Neurol. 2015;132:139–56. doi:10.1016/B978-0-444-62702-5.00010-X.
2. Chou A, Toon C, Pickett J, Gill AJ. von Hippel-Lindau syndrome. Front Horm Res. 2013;41:30–49. doi:10.1159/000345668.
3. Ben-Skowronek I, Kozaczuk S. Von Hippel-Lindau Syndrome. Horm Res Paediatr. 2015;84(3):145–52. doi:10.1159/000431323
4. Fugaru I, Goudie C, Capolicchio JP. Von Hippel-Lindau disease and rapidly progressing pheochromocytomas in siblings. Fam Cancer. 2022;21(2):229–33. doi:10.1007/s10689-021-00252-2.
5. Fowler JB, De Jesus O, Mesfin FB. Ventriculoperitoneal Shunt. In: StatPearls. Treasure Island (FL): StatPearls Publishing; August 23, 2023.
6. Fagundes GFC, Petenuci J, Lourenco DM Jr, Trarbach EB, Pereira MAA, Correa D'Eur JE, et al. New Insights Into Pheochromocytoma Surveillance of Young Patients With VHL Missense Mutations. J Endocr Soc. 2019;3(9):1682–92. doi:10.1210/js.2019-00225.
7. Faiyaz-Ul-Haque M JM, Aslam M, Abalkhail H, Al-Dayel F, Basit S, Nawaz Z, et al. Novel and recurrent germline mutations in the VHL gene in 5 Arab patients with Von Hippel-Lindau disease. Cancer Genet. 2020;243:1–6. doi:10.1016/j.cancergen.2020.02.006
8. Wittström E, Nordling M, Andréasson S. Genotype-phenotype correlations, and retinal function and structure in von Hippel-Lindau disease. Ophthalmic Genet. 2014;35(2):91–106. doi:10.3109/13816810.2014.886265
9. Wiley HE KV, Gaudric A, Gorin MB, Shields

C, Shields J, Aronow ME, et al. Management of retinal hemangioblastoma in von hippel-lindau disease. Retina (Philadelphia, Pa). 2019;39(12):2254–63.
10. Xu N, Duan W, Zhang R, Yang B. Imaging diagnosis of von hippel-lindau syndrome. J Craniofac Surg. 2019;30(7):e674–7. doi:10.1097/SCS.0000000000005760.
11. Fairbanks AM, Hoyek S, Patel NA. Systemic treatment reduces von-hippel-lindau-associated retinal capillary hemangioblastoma. Ophthalmology. 2023;130(5):524. doi:10.1016/j.ophtha.2022.07.007