Bergaoui *et al.*
Journal of Medical Case Reports (2025) 19:159
https://doi.org/10.1186/s13256-025-05196-0

Journal of
Medical Case Reports

CASE REPORT

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Bilateral papillary cystadenoma of the broad ligament: a manifestation of Von Hippel–Lindau disease: a case report

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Abstract

Background While papillary cystadenomas of the epididymis are relatively common, the occurrence of papillary cystadenomas in female individuals, particularly in the ovaries, remains exceedingly rare.

Case presentation A 62-year-old white North African woman diagnosed with Von Hippel–Lindau disease in 2021 presented with multiple manifestations, including a left petrous bone tumor, left pheochromocytoma, left renal cell carcinoma, multi-cystic right kidney, and pancreatic masses. She underwent various treatments, including radiotherapy, adrenalectomy, nephrectomy, and cephalic duodenopancreatectomy. Ultrasonographic and magnetic resonance imaging examinations revealed a solid cystic mass in the left adnexal region. Laparoscopy identified cystic tumors in the right and left mesosalpinx. Following a hysterectomy with bilateral adnexectomy, histological examination revealed bilateral clear-cell papillary cystadenomas of the mesosalpinx and broad ligament, consistent with Von Hippel–Lindau disease.

Conclusion This case highlights the rare occurrence of bilateral clear-cell papillary cystadenomas of the mesosalpinx and broad ligament in a woman with Von Hippel–Lindau disease, a condition typically associated with men. The comprehensive diagnostic and therapeutic approach, including imaging studies, laparoscopy, and histological examination, underscores the importance of vigilant monitoring and tailored management in patients with this complex, multisystem disorder.

Keywords Von Hippel–Lindau disease, Papillary cystadenoma, Fallopian tube diseases/surgery, Diagnosis, Female, Pathology, Case report

Background

Von Hippel–Lindau disease (VHL) was first described in 1926 as an inherited disease, characterized by tumors of the retina, brain, kidney, adrenal gland, and pancreas. Recently the *VHL* gene was identified as a tumor suppressor gene on the short arm of chromosome 3 (*3p25-26*). VHL disease is an autosomal, dominantly inherited, multisystemic tumor syndrome due to a gene mutation with an incidence of 1 in 36,000 live births [1]. In 20% of cases *de novo* mutations occur [2]. The mutations cause a situation analogous to hypoxia with an increase in various growth and angiogenic factors [3].

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Affected individuals are at high risk for developing various benign and malignant tumors. Lesions in VHL disease tend to be multiple and bilateral in paired organs [1, 4, 5]. Though rarely described in the literature, a benign adnexal papillary tumor of probable mesonephric origin (APMO) is highly significantly associated with VHL disease. The World Health Organization (WHO) classification differentiates between two main clinical types, on the basis of the risk for developing a pheochromocytoma and/or renal cell carcinoma, and is related to the type of mutation [1, 6].

Most tumors develop at younger age, between 20 and 40 years. The penetrance of the disease is about 96% by the age of 60 years, with renal cell cancer in 69%, retinal tumor in 70%, and cerebellar hemangioblastoma in 85% [1, 6].

Metastases determine the prognosis, and intracerebral hemorrhages due to bleeding from carcinomas or hemangioblastomas of the brain are the main cause of death [4].

Improved surveillance, earlier diagnosis of the lesions with modern imaging (magnetic resonance imaging [MRI]), improvements in treatment, and increased knowledge of this disease have resulted in an improved prognosis and reduced rates of complications. An interdisciplinary team is beneficial for optimal assessment, treatment, and follow-up. It is also recommended that the family of the index patient is examined because individuals with a predisposition for an inherited tumor syndrome, such as VHL disease, benefit from early screening at around 11 years of age, ophthalmologic examination, catecholamine testing, and magnetic resonance imaging [4].

This case report contributes to the medical literature by emphasizing the clinical manifestations and surgical management of Von Hippel–Lindau disease, particularly the rare occurrence of adnexal papillary tumors associated with this condition. While VHL is primarily known for its impact on the kidneys and central nervous system, the identification of adnexal lesions can offer new insights into the spectrum of VHL-related tumors. The case underscores the importance of awareness among healthcare professionals regarding the potential for atypical presentations of VHL disease, which may be overlooked in routine evaluations. Furthermore, it highlights the necessity for interdisciplinary collaboration in managing complex cases, ensuring that both the benign and malignant potentials of VHL manifestations are effectively addressed.

Case presentation

A 62-year-old Tunisian Arab postmenopausal female diagnosed with Von Hippel–Lindau disease in 2021 presented with various manifestations related to the disease. She had a history of multiple surgeries, primarily for renal, adrenal, and pancreatic tumors, with incidental findings of ovarian masses.

The patient was asymptomatic from a gynecological standpoint, but primarily complained of headaches before undergoing brain surgery. She had no significant family or psychosocial history.

Her surgical history included

- 2021: A non-operable tumor (6 cm) of the left petrous bone endolymphatic sac, managed with radiotherapy.
- 2021: Left adrenalectomy for a 6 cm pheochromocytoma. Pathological examination revealed pheochromocytoma.
- 2021: Left nephrectomy for a ruptured left renal tumor. Microscopy showed multifocal clear-cell renal carcinoma of nuclear grade 2.
- 2022: Cephalic duodenopancreatectomy for a mass in the pancreas. Histological examination confirmed three serous cystadenomas and two well-differentiated neuroendocrine tumors.

In January 2021, during postoperative surveillance with an abdominal–pelvic computed tomography (CT) scan, a 4 cm solid cystic left adnexal mass was incidentally discovered, which raised suspicion of malignancy. The mass was confirmed by transvaginal ultrasound and pelvic MRI, classified as Ovarian-Adnexal Reporting and Data System (O-RADS) 5 (high suspicion for malignancy) (Fig. 1).

Gynecological examination and surgical history

Physical examination: No abdominal–pelvic mass detected.

Speculum examination: Healthy cervix observed.

Surgical scars from previous left nephrectomy and cephalic duodenopancreatectomy were noted.

A multidisciplinary staff meeting concluded that surgery was necessary. A laparotomy was performed via a midline incision below the umbilicus, revealing a well-defined solid cystic mass in the left adnexa. No ascites or signs of peritoneal carcinomatosis were present, and the right adnexa appeared normal, with no macroscopic signs of malignancy observed intraoperatively, including the absence of exocystic vegetations.

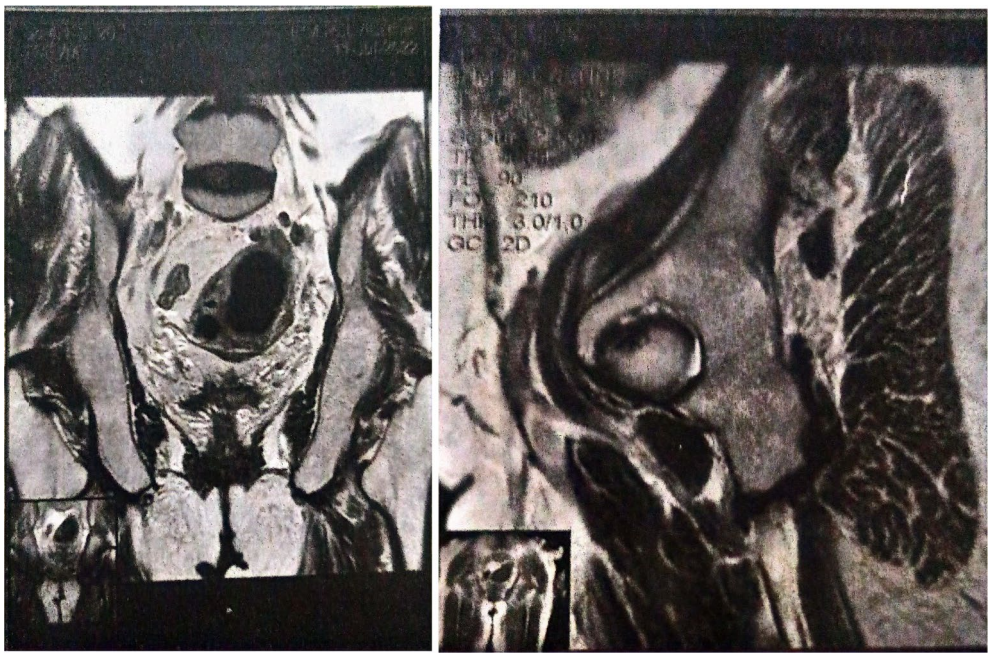

Fig. 1 Abdominal–pelvic magnetic resonance imaging showed a solid cystic left ovarian mass classified as Ovarian-Adnexal Reporting and Data System 5

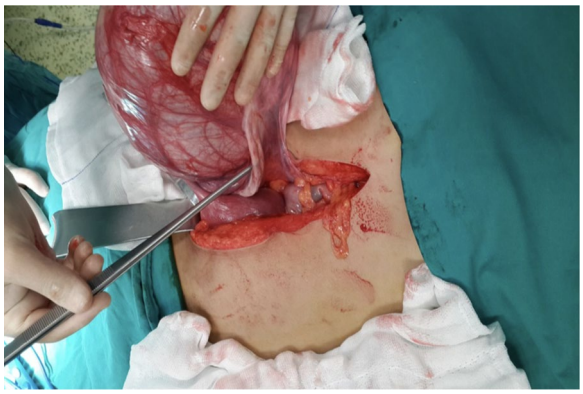

Fig. 2 The smooth-surfaced cystic mass, originating from the right mesosalpinx

Cytology was performed along with left adnexectomy, and the specimen was sent for frozen section examination. The results were inconclusive, raising the possibility of borderline tumors or tumors specific to Von Hippel–Lindau syndrome. Considering the patient's postmenopausal status, a right adnexectomy and total hysterectomy were performed (Fig. 2).

Histological examination later revealed bilateral clear-cell papillary cystadenomas of the Fallopian Tubes and broad ligament, characteristic of Von Hippel–Lindau disease (0.5 cm on the right side and 4 cm on the left side).The tumors consisted of tightly packed papillae with fibrous cores, covered by monolayered epithelium (Fig. 3).

The immediate postoperative period was uneventful, and at the 1-month follow-up, no abnormalities were detected. The patient has since been followed up with every 4 months with normal pelvic ultrasounds. During these 2 years of follow-up, no complications have arisen, but the patient was recently readmitted to the neurosurgery department for recurrence of a brain tumor.

Discussion

Papillary cystadenomas of the mesosalpinx are rare benign lesions. Bilaterality can be a diagnostic hint of VHL disease [1].

The mean age of women at presentation as well as frequency of cystadenomas in this disease is unknown. The earliest age at which this tumor has been diagnosed is 16 years, but in other reports, the age of onset is between 22 and 46 years [7, 8].

These lesions can be diagnosed by CT imaging or ultrasonography. The tumors are grossly and histologically similar to epididymal cystadenomas.

Surgery is necessary if symptoms occur. The APMO is histologically identical to the papillary cystadenoma of the epididymis in male individuals, where it is usually diagnosed easier [8, 9]. With regard to long-term consequences proper follow-up concerning renal cell

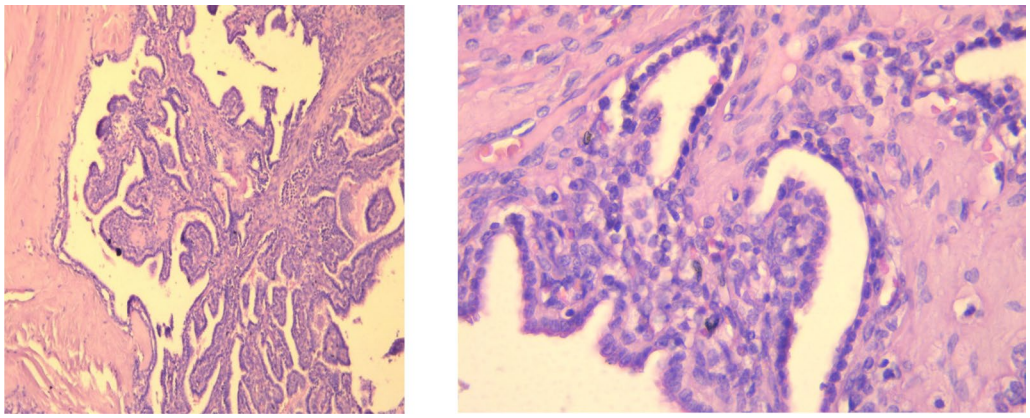

Fig. 3 Microscopy revealed a cystic tumor with papillary excrescences. Tumor papillae are lined by a monolayer of cuboid to columnar epithelial cells with monomorphic oval nuclei and a rim clear cytoplasm

carcinoma is mandatory because the risk of metastatic disease increases with tumor size [4]. Vice versa, proper surveillance of the gonadal region in VHL patients is necessary since metastasis of renal cell carcinomas to the adnexae and epididymes are described. These metastases might even develop within existing VHL lesions, such as in hemangioblastoma of the brain or in cystadenomas of the epididymis, the adrenal gland, and the gall bladder [6].

The histological similarity between papillary cystadenoma and renal cell carcinoma can be explained by the similar phylogenetic origin of renal tubules, ductules efferentes, and mesonephric remnants [10]. Thus, papillary cystadenomas can be found intra- and extraperitoneally in remnant parts of the mesonephric duct, including the broad ligament, the mesosalpinx, along the lateral wall of the uterus, and in the wall of the vagina [11, 12]. There are reports on VHL tumors of both Mullerian and Wolffian origin containing numerous glands (characterized by tall columnar cells) [9, 13]. Interestingly, these lesions might be associated with a histological identical papillary middle ear/temporal bone tumor definitive genetic tests [11].

Considering the surgical approaches available for managing adnexal masses in patients with Von Hippel–Lindau disease, laparoscopic surgery offers several advantages over traditional open surgery. The minimally invasive nature of laparoscopy typically results in reduced postoperative pain, shorter recovery times, and less scarring. Additionally, laparoscopic techniques allow for a clearer visualization of the pelvic anatomy, which is particularly beneficial when evaluating for possible malignancy. However, it is essential to recognize that laparoscopic surgery may not be appropriate in all cases, especially if there are concerns regarding the extent of the disease or if a larger tumor is present that requires more extensive resection. Surgeons must carefully evaluate each patient's condition to determine the best surgical approach while considering the potential benefits and drawbacks of laparoscopic surgery [14, 15].

Furthermore, it is important to acknowledge that not all malignancies benefit from adequate screening and management methods. In light of the findings from this study regarding pelvic masses, recent evidence suggests that many patients, particularly those with complex medical histories such as VHL disease, may experience delays in diagnosis or may not undergo recommended screening protocols. This highlights the necessity for ongoing research and the implementation of improved screening strategies that can enhance early detection and treatment of malignancies in these at-risk populations. Implementing a structured follow-up regimen, including imaging and laboratory assessments, could help mitigate these challenges and ensure better outcomes for patients [16, 17].

Our case report intends to make gynecologists aware that APMO could be manifestation of VHL disease. Since early diagnosis is relevant for long-term prognosis of the patient and its family, the gynecologist should trigger genetic tests and imaging studies to prove or rule out VHL disease [14].

Conclusion

The new insights into the underlying mechanisms of tumor formation, greater knowledge of the natural history of the various lesions associated with von Hippel–Lindau disease, and more precise diagnostic studies should lead to an improved quality of life and extend the life expectancy of affected individuals. The diverse multisystem effects of this disease need careful, selective, and coordinated planning to determine the treatment

of individual lesions that will provide the best long-term management of these patients.

Acknowledgements
We would like to acknowledge the entire team of Gynecology and Anesthesia at the Maternal and Neonatal Center in Monastir for their invaluable support.

Author contributions
Each author has contributed to the writing of the original draft, data curation, and conceptualization.

Funding
No funding was received for this article.

Data availability
The data and materials are available upon request.

Declarations

Ethics approval and consent to participate
Ethical approval for the case report was obtained from the institutional review board, and written informed consent was acquired from the patient for publication.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare no competing interests.

Received: 9 August 2024 Accepted: 27 December 2024
Published online: 05 April 2025

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