WebLog Journal of Endocrinology and Diabetes

Case Series
Published: 22 Jan, 2026

Von Hippel–Lindau Disease Revealed by Bilateral Pheochromocytomas: A Series of 4 Cases and Literature Review

K. Gorgi[1], M. Chaouche[2], K. Rifai[1], H. Iraqi[1] and M.H. Gharbi[1]*

[1]*Department of Endocrinology, Ibn Sina University Hospital, Rabat, Morocco*

[2]*Department of Dermatology, Mohammed VI University Hospital, Agadir, Morocco*

Abstract

Introduction: Von Hippel–Lindau (VHL) disease is an autosomal dominant genetic disorder predisposing to the development of benign and malignant tumors, notably pheochromocytomas, which are often bilateral and of early onset.

Objective: To describe the clinical, biological, radiological, and evolutionary characteristics of patients with bilateral pheochromocytomas associated with VHL disease and to compare our results with the literature data.

Methods: A retrospective descriptive study of four patients managed for bilateral pheochromocytoma with genetic confirmation of a VHL gene mutation.

Results: Age at diagnosis ranged from 12 to 44 years. All patients had bilateral pheochromocytomas with predominant noradrenergic secretion. Total bilateral adrenalectomywas performed in all patients. One patient experienced a local recurrence after the first surgery. Clinical and biological outcomes were overall favorable under substitution therapy and regular follow-up.

Conclusion: Bilateral pheochromocytomas are a common mode of presentation of VHL disease, especially in young subjects. Genetic screening, appropriate surgical management, and prolonged surveillance are essential to improve prognosis.

Keywords: Von Hippel–Lindau; Pheochromocytoma; Bilateral; Adrenalectomy; Genetics

OPEN ACCESS

Correspondence:
Dr. Gorgi Khaoula, Department of Endocrinology and Metabolic Diseases, Ibn Sina University Hospital, Rabat, Morocco; Tel: 0615591874; E-mail: khaoulagorgi@gmail.com

Received Date: *31 Dec 2025*
Accepted Date: *20 Jan 2026*
Published Date: *22 Jan 2026*

Citation:
K. Gorgi, M. Chaouche, K. Rifai, H. Iraqi, M.H. Gharbi. Von Hippel–Lindau Disease Revealed by Bilateral Pheochromocytomas: A Series of 4 Cases and Literature Review. WebLog J Endocrinol Diabetes. wjed.2026.a2203. https://doi.org/10.5281/zenodo.18447867

Introduction

Von Hippel–Lindau (VHL) disease is a rare autosomal dominant genetic disorder caused by mutations in the VHL gene located on chromosome 3p25–26 [1]. It is characterized by a predisposition to develop multiple and recurrent tumors affecting various organs, including the central nervous system, kidneys, pancreas, and adrenal glands [2]. Pheochromocytoma is a major endocrine manifestation of VHL disease. It generally occurs at an earlier age than sporadic forms and is frequently bilateral with preferential noradrenaline secretion [3].

Through this series of four cases, we illustrate the clinical and evolutionary features of pheochromocytomas associated with VHL and discuss diagnostic, therapeutic, and surveillance strategies in light of current literature data.

Patients and Methods

Study type

Retrospective descriptive study conducted in the Endocrinology Department of Ibn Sina University Hospital, Rabat.

Inclusion criteria

- Biologically and histologicallyconfirmedpheochromocytoma
- Bilateraladrenalinvolvement
- Genetic confirmation of a VHL gene mutation

Table 1:

Patient	Age (years)	Initial Symptoms	Biology (UMN)	Imaging	Surgery	Genetics	Outcome
1	44	Resistant hypertension, headache	Very high normetanephrine	Bilateral adrenal lesions	Bilateral adrenalectomy	VHL +	Local recurrence, then good evolution
2	13	Headaches, dizziness	Elevated normetanephrine	Bilateral adrenal lesions	Bilateral adrenalectomy	VHL +	Good
3	12	Abdominal pain	Elevated normetanephrine	Bilateral adrenal lesions	Bilateral adrenalectomy	VHL +	Good
4	20	Hypertensive crises, sweating	Elevated normetanephrine	Bilateral adrenal lesions	Bilateral adrenalectomy	VHL +	Good

Data collected

- Clinical data (symptoms, age at diagnosis)
- Biologicalassessment (urinarymetanephrines)
- Imaging (CT scan)
- Therapeutic management
- Genetic data
- Clinical and biologicalevolution

Clinical Observations

Case 1

A 44-year-old female patient, type I diabetic since age 16, complicated by diabetic retinopathy treated with three laser sessions. She presented to the emergency department for resistant hypertension under dual therapy, accompanied by refractory frontal headaches, palpitations, and sweating. Urinary metanephrine assay showed a marked elevation of normetanephrine at 66,000 nmol/24 h (normal values: 400–2100 nmol/24 h) and metanephrine<100 nmol/24 h (normal: 200–1500 nmol/24 h). Abdominal CT scan revealed bilateral adrenal lesions measuring 50x45 mm on the right and 38x50 mm on the left. After medical preparation with antihypertensives, total bilateral laparoscopic adrenalectomywas performed. Histological examination confirmed bilateral pheochromocytoma. A local recurrence was later detected, requiring a second surgery. The patient is under hydrocortisone replacement therapy and shows good clinical and biological evolution. Genetic testing confirmed the VHL gene mutation.

Case 2

A 13-year-old female admitted to the emergency department for headaches and dizziness. Urinary metanephrines showed elevated normetanephrine at 1224 nmol/24 h (normal: 44–213 nmol/24 h). Abdominopelvic CT scan showed bilateral adrenal lesions measuring 25 mm on the left and 13 mm on the right, suggestive of bilateral pheochromocytoma. After medical preparation, total bilateral laparoscopic adrenalectomywas performed. Postoperative course was uneventful. Histopathology confirmed bilateral pheochromocytoma. The patient receives lifelong hydrocortisone and mineralocorticoid replacement. Genetic testing confirmed a heterozygous VHL gene mutation. Her growth and pubertal development are normal.

Case 3

A 12-year-old female admitted for diffuse abdominal pain. Abdominal CT showed bilateral adrenal lesions measuring 22 mm on the right and 26 mm on the left. Biological assessment revealed elevated normetanephrine at 1500 nmol/24 h (normal: 44–213 nmol/24 h) and normal metanephrine at 59 nmol/24 h (normal: 40–228 nmol/24 h). After medical preparation, total bilateral laparoscopic adrenalectomywas performed. Histology confirmed bilateral pheochromocytoma. Genetic testing confirmed a heterozygous VHL gene mutation. Growth and pubertal development are normal.

Case 4

A 20-year-old male consulted for chronic headaches, paroxysmal hypertensive crises, and sweating. Urinary metanephrines showed elevated normetanephrine at 12,405 nmol/24 h (normal: 400–2500 nmol/24 h) and normal metanephrine at 500 nmol/24 h (normal: 200–1500 nmol/24 h). Thoraco-abdominal CT revealed bilateral adrenal lesions measuring 30 mm on the right and 26 mm on the left. After medical preparation, total bilateral laparoscopic adrenalectomywas performed. Histology confirmed bilateral pheochromocytoma. Genetic testing confirmed the VHL gene mutation. The patient is under hydrocortisone replacement therapy.

In summary, all four patients presented symptoms suggestive of catecholamine secretion (headaches, paroxysmal hypertension, sweating, palpitations). Biological diagnosis was based on marked elevation of urinary normetanephrine with normal or mildly elevated metanephrine levels, reflecting a noradrenergic phenotype typical of VHL. CT imaging revealed bilateral adrenal lesions in all patients. Total bilateral laparoscopic adrenalectomywas performed after adequate medical preparation.

Results

See Table 1.

Discussion

Our series illustrates several classical yet essential features of pheochromocytomas associated with VHL disease.

The mean age at diagnosis in our cohort was 22 years, consistent with literature reporting early onset, often before 30 years of age, in contrast to sporadic forms diagnosed later [4]. Bilateral involvement was observed in 100% of our patients, a rate higher than some series (50–70%) but consistent with genetic forms of VHL [5]. This particularity calls for specific therapeutic considerations to limit long-term endocrine consequences.

Biologically, all patients had a predominant noradrenergic secretion profile, characterized by marked elevation of urinary normetanephrine with normal metanephrine levels. This profile is considered typical of pheochromocytomas associated with VHL mutation, related to the lack of phenylethanolamine N-methyltransferase expression [6].

Regarding surgical management, total bilateral adrenalectomywas performed in all patients. Although partial adrenalectomycan be discussed to preserve residual adrenal cortical function, the risk of local recurrence remains high in VHL [7]. In our series, one patient had a recurrence requiring reoperation, supporting the choice of complete excision in evolving bilateral forms. Long-term surveillance is a key element in managing patients with

VHL. It should include annual clinical, biological, and radiological follow-up to detect early recurrences and other tumor manifestations associated with the disease [8].

Conclusion

Bilateral pheochromocytomas represent a frequent and sometimes inaugural manifestation of Von Hippel–Lindau disease. Their occurrence at a young age, bilaterality, and noradrenergic profile should suggest a genetic etiology. Management relies on a multidisciplinary approach integrating surgery, genetics, and lifelong follow-up.

References

1. Maher ER et al. Von Hippel–Lindau disease. Lancet. 2011.
2. Lonser RR et al. vonHippel–Lindau disease. Lancet. 2003.
3. Neumann HPH et al. Pheochromocytoma in VHL. N Engl J Med. 2002.
4. Lenders JWM et al. Pheochromocytoma and paraganglioma. Lancet. 2020.
5. Fishbein L et al. Pheochromocytoma genetics. Endocr Rev. 2021.
6. Eisenhofer G et al. Catecholamine phenotype in VHL. J Clin Endocrinol Metab. 2012.
7. Castinetti F et al. Adrenal-sparing surgery in hereditary pheochromocytoma. J Clin Endocrinol Metab. 2014.
8. Rednam SP et al. Von Hippel–Lindau surveillance guidelines. Clin Cancer Res. 2017.