WebLog Journal of Endocrinology and Diabetes

Research Article
Published: 10 Feb, 2026

Clinical and Biological Features of Primary Hyperparathyroidism in Multiple Endocrine Neoplasia Type 2A: A Retrospective Study of Five Cases

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

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

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

Abstract

Introduction: Multiple Endocrine Neoplasia type 2A (MEN2A) is a rare genetic disorder primarily characterized by Medullary Thyroid Carcinoma (MTC) and Primary Hyperparathyroidism (PHPT) in 20 to 30% of cases. PHPT is rarely the initial presenting symptom. This study aims to describe the clinical and biological features of PHPT in MEN2A to improve understanding and management of this condition.

Patients and Methods: This is a retrospective descriptive study over seven years, including five patients harboring RET gene mutations diagnosed with MEN2A and PHPT, followed at the Endocrinology Department of Ibn Sina University Hospital, Rabat.

Results: The mean age at PHPT diagnosis was 26.8 years. One case of renal lithiasis and one case of bone fracture were reported. The mean Parathyroid Hormone (PTH) level was elevated at 182.2 pg/mL, with a normal mean serum calcium of 101.2 mg/L. Parathyroid ultrasound revealed lesions in all cases, leading to parathyroid surgery involving excision of one to three glands.

Discussion and Conclusion: PHPT associated with MEN2A presents specific clinical features, including a high frequency of normocalcemic forms possibly related to prevalent vitamin D deficiency. Systematic screening is essential for early diagnosis and appropriate management. This study highlights the importance of rigorous monitoring protocols in this at-risk population.

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Correspondence:

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

Received Date: *08 Jan 2026*

Accepted Date: *09 Feb 2026*

Published Date: *10 Feb 2026*

Citation:

Gorgi K, Chaouche M, Rifai K, Iraqi H, Gharbi MH. Clinical and Biological Features of Primary Hyperparathyroidism in Multiple Endocrine Neoplasia Type 2A: A Retrospective Study of Five Cases. WebLog J Endocrinol Diabetes. wjed.2026.b1002. https://doi.org/10.5281/zenodo.18794677

Introduction

Multiple Endocrine Neoplasia type 2A (MEN2A) is an autosomal dominant hereditary disorder caused by activating mutations in the RET proto-oncogene. It is primarily characterized by the development of Medullary Thyroid Carcinoma (MTC), pheochromocytoma, and in 20 to 30% of cases, Primary Hyperparathyroidism (PHPT) [1, 2].

PHPT in MEN2A is often discovered incidentally during evaluation for other manifestations or during genetic follow-up, and rarely presents as an initial symptom. Its clinical presentation may differ from sporadic PHPT, notably with a tendency towards normocalcemic or minimally symptomatic forms [3].

This study aims to analyze the clinical, biological, and radiological features of PHPT in a cohort of MEN2A patients to improve diagnostic and therapeutic strategies.

Patients and Methods

Study Design and Population

A retrospective descriptive study conducted from January 2015 to December 2022 at the Endocrinology Department of Ibn Sina University Hospital, Rabat.

Five patients with confirmed RET gene mutations and concomitant diagnoses of MEN2A and PHPT were included.

Data Collected

- Demographic data: age, sex
- Clinical data: medical history, symptoms, complications (renal lithiasis, fractures)

- Biological data: total serum calcium, PTH, phosphocalcic profile, vitamin D levels
- Imaging: cervical ultrasound, parathyroid scintigraphy
- Surgical data: number of parathyroid glands excised

Results

In this series of five MEN2A patients with PHPT:

- The mean age at diagnosis was 26.8 years (range 18-34 years).
- Three patients were female.
- One patient had renal lithiasis.
- One patient suffered a bone fracture related to metabolic bone disease.
- Two patients were asymptomatic regarding PHPT at diagnosis, detected during genetic screening or routine evaluation.
- The mean serum calcium level was 101.2 mg/L, within the upper normal range.
- The mean PTH level was markedly elevated at 182.2 pg/mL (normal range 8-76 pg/mL), indicating active hyperparathyroidism.
- The mean vitamin D level was low at 18.5 ng/mL, suggesting frequent deficiency in this population.
- Parathyroid ultrasound identified lesions in all cases, leading to surgery with excision ranging from one to three glands (Table 1, Figure 1).

Discussion

PHPT in MEN2A is characterized by an earlier onset compared to sporadic PHPT, as confirmed in our series with a mean age below 30 years [4, 5]. This early onset emphasizes the need for targeted screening in RET mutation carriers.

Most patients in our study presented with normal or high-normal serum calcium levels despite markedly elevated PTH, suggestive of normocalcemic or minimally symptomatic PHPT, a phenomenon documented in the literature and potentially linked to prevalent vitamin D deficiency in this population [6, 7].

Clinical complications such as renal lithiasis or fractures were infrequent, likely due to regular surveillance and early diagnosis [8]. This supports the value of genetic and biochemical monitoring protocols to prevent major complications.

Parathyroid surgery remains the treatment of choice, tailored to the number and localization of lesions. In our series, excision ranged from one to three glands, consistent with current recommendations [9].

Vitamin D deficiency in this context may mask disease severity and complicate management. Careful supplementation is advised with close monitoring of serum calcium to avoid complications [10, 11].

Table 1: Demographic, clinical, and biological data of included patients.

Parameter	Mean (min–max) / N
Number of patients	5
Mean age at diagnosis (years)	26.8 (18–34)
Female sex	3
Renal lithiasis	1
Bone fracture	1
Serum calcium (mg/L)	101.2 (98–105)
PTH (pg/mL)	182.2 (120–250)
Vitamin D (ng/mL)	18.5 (12–25)
Number of parathyroids excised	1 to 3

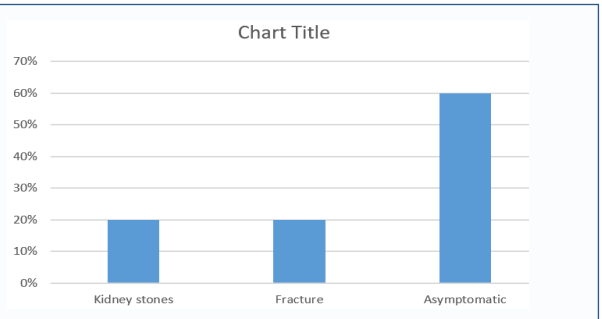

Figure 1: Distribution of clinical manifestations in MEN2A patients with primary hyperparathyroidism (n=5).

Conclusion

PHPT associated with MEN2A presents distinct clinical features, including early onset and frequent normocalcemic forms. Systematic screening of RET mutation carriers is crucial for early diagnosis and appropriate management. Careful monitoring of biochemical parameters, including vitamin D status, optimizes therapeutic outcomes and complication prevention.

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