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Acromegaly as the Initial Presentation of Multiple Endocrine Neoplasia Type 1: A Case Report

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Female, 34-year-old
Final Diagnosis: Acromegaly • hyperparathyroidism • multiple endocrine neoplasia type 1
Symptoms: Coarse facial features • enlarged hands • frontal bossing • hypercalcemia • kidney stones • visual impairment
Clinical Procedure: Trans-sphenoidal resection of the pituitary adenoma
Specialty: Endocrinology and Metabolic

Objective: Unusual clinical course

Background: Multiple endocrine neoplasia syndrome type 1 (MEN-1) is a rare autosomal-dominant disorder, caused by MEN-1 gene mutations, leading to tumors in multiple endocrine organs, classically the parathyroid glands, the anterior pituitary, and the pancreatic islet cells. Although primary hyperparathyroidism is usually the earliest manifestation, growth hormone-secreting pituitary adenomas rarely present as the initial clinical feature, potentially delaying recognition of the syndrome.

Case Report: A 34-year-old woman presented with acromegalic features and hypercalcemia. Laboratory testing and magnetic resonance imaging confirmed a recurrent growth hormone-secreting pituitary macroadenoma, and neck imaging identified a parathyroid adenoma. Genetic analysis demonstrated a rare pathogenic variant. After she underwent repeat transsphenoidal surgery, growth hormone and insulin-like growth factor-1 normalized following complete radiological tumor resection. Parathyroid surgery was planned, and the patient was enrolled in multidisciplinary MEN-1 surveillance.

Conclusions: The coexistence of a pituitary adenoma and hypercalcemia should prompt evaluation for MEN-1, even in the absence of a family history of the disorder. Early clinical suspicion and recognition enable timely surgical management and structured long-term surveillance, reducing the risk of delayed diagnosis and complications of additional MEN-1–associated tumors. Although MEN-1–associated pituitary adenomas are managed according to the same principles as sporadic tumors, affected patients benefit from multidisciplinary care and lifelong follow-up. Furthermore, reporting rare pathogenic MEN-1 variants contributes to the expanding understanding of genotype-phenotype correlations and the clinical spectrum of this hereditary syndrome. This case highlights that acromegaly may, rarely, represent the first clinical manifestation of MEN-1.

Keywords: Acromegaly • Endocrine Gland Neoplasms • Endocrine System Diseases • Hyperparathyroidism, Primary • Pituitary Neoplasms

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Introduction

Multiple endocrine neoplasia type 1 (MEN-1) is a rare autosomal dominant disorder caused by pathogenic germline variants in the MEN-1 gene, resulting in an endocrine tumor syndrome characterized by tumors involving multiple endocrine organs, particularly the parathyroid glands, anterior pituitary, and pancreatic islet cells [1-4].

Furthermore, beyond the classic endocrine neoplasms involving the adrenal cortex and neuroendocrine tissues of the bronchi and thymus, MEN-1 may also be associated with non-endocrine lesions, including lipomas, angiofibromas, collagenomas, and other benign tumors [3,5-7]. Primary hyperparathyroidism is usually the earliest manifestation, while pituitary tumors, most commonly prolactinomas, are also frequent [5,8]. Growth hormone-secreting adenomas causing acromegaly are less common, and acromegaly as the initial clinical presentation of MEN-1 is rare, reported in only 6.6% of acromegaly patients, with pituitary tumors being the first manifestation in 10-25% of MEN-1 cases [3,6,8,9].

We report a case of acromegaly preceding hyperparathyroidism, highlighting an uncommon initial presentation of MEN-1. The objective of this study is to present a case of acromegaly caused by a growth hormone-secreting pituitary adenoma that ultimately led to the diagnosis of MEN-1, emphasizing the importance of considering MEN-1 in patients with pituitary adenomas who later develop hypercalcemia or primary hyperparathyroidism.

Case Report

A 34-year-old female patient was admitted to the endocrinology outpatient clinic due to persistent hypercalcemia. She was a non-smoker, without any significant family history of endocrine tumors. Initial tests performed at an external center revealed total serum calcium of 11.3 mg/dL (reference range: 8.5-10.5), phosphorus of 3.2 mg/dL (reference range: 2.5-4.5), and elevated parathyroid hormone at 120 ng/L (reference range: 11-67).

On clinical examination, coarse facial features, frontal bone protrusion, and enlargement of the hands were noted. Upon further history, it was discovered that the patient had previously undergone surgery in 2021 for a pituitary macroadenoma after presenting with visual disturbances.

At that time, imaging revealed a 3 × 2-cm pituitary mass compressing the optic chiasm. Laboratory tests demonstrated growth hormone of 26 mcg/L and insulin-like growth factor-1 (IGF-1) of 950 mcg/L, confirming the diagnosis of acromegaly. She underwent transnasal transsphenoidal resection, after which her visual impairment resolved.

Postoperatively, she was started on octreotide long-acting release (LAR), a somatostatin analog.

Four months later, treatment was discontinued due to spontaneous pregnancy. At that time, her calcium was 9.6 mg/dL and

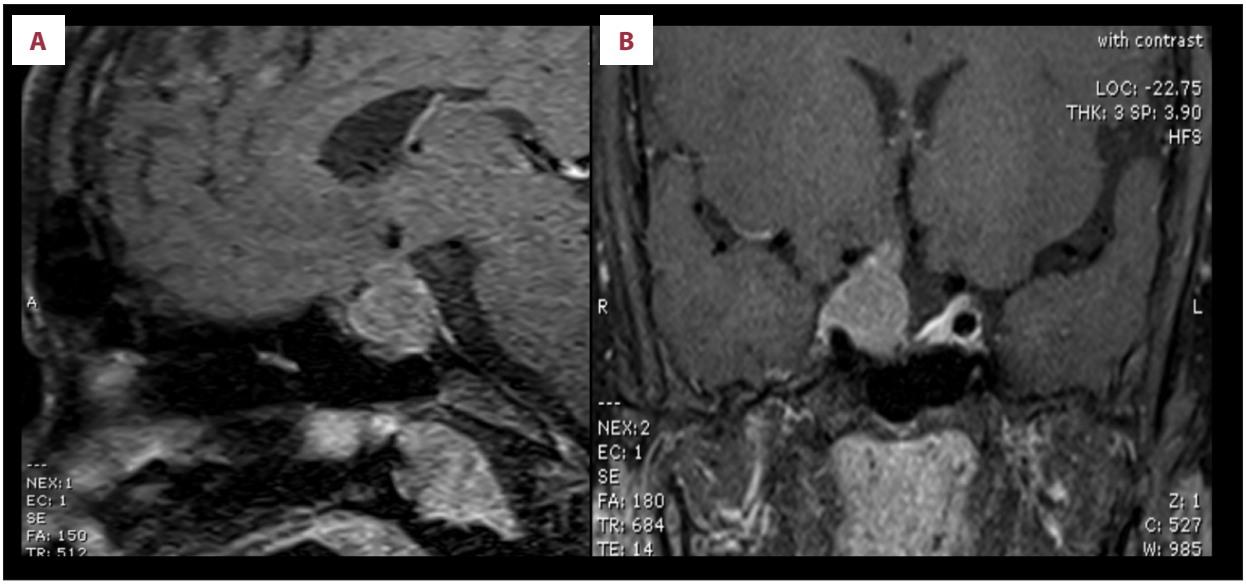

Figure 1. (**A**) Pre-operative contrast-enhanced sagittal T1-weighted magnetic resonance imaging (MRI) of the sellar region demonstrating a pituitary macroadenoma arising from the pituitary gland with suprasellar extension, consistent with recurrent growth hormone-secreting adenoma. (**B**) Pre-operative contrast-enhanced coronal T1-weighted MRI of the sellar region showing a recurrent pituitary macroadenoma measuring approximately 15 × 10 mm in the right pituitary hemisphere, with lateral extension and encasement of the right internal carotid artery.

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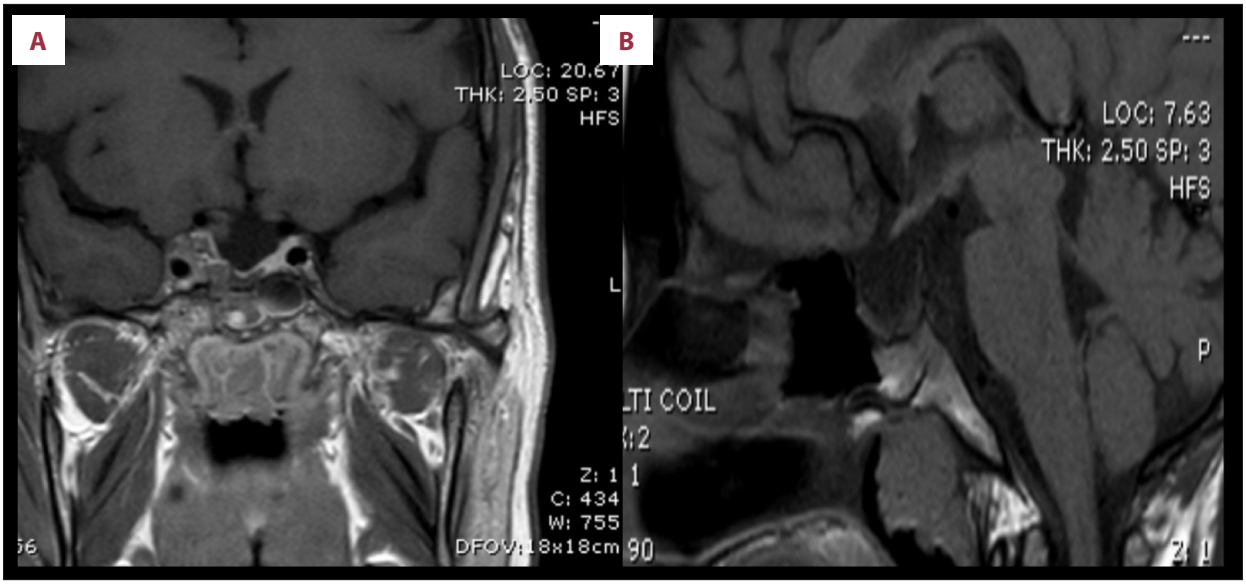

Figure 2. (**A**) Post-operative contrast-enhanced coronal T1-weighted magnetic resonance imaging (MRI) of the sellar region demonstrating complete resection of the pituitary macroadenoma following repeat transsphenoidal surgery. The sellar cavity appears decompressed with no evidence of residual enhancing tumor and with preserved suprasellar structures and cavernous sinuses. (**B**) Post-operative sagittal T1-weighted pituitary MRI obtained after repeat transsphenoidal resection demonstrating complete removal of the pituitary tumor with restoration of normal sellar anatomy.

her phosphorus 3.6 mg/dL. She did not receive any treatment during pregnancy or the subsequent 2-year lactation period. On later follow-up, biochemical investigations demonstrated growth hormone of 4 mcg/L, IGF-1 of 560 mcg/L, calcium of 11.2 mg/dL, phosphorus of 3.2 mg/dL, and 24-hour urinary calcium of 560 mg/24 h. Renal ultrasonography revealed a calculus in the left kidney. Pituitary magnetic resonance imaging (MRI) showed a recurrent macroadenoma measuring 15 × 10 mm, located in the right pituitary hemisphere and encasing the internal carotid artery (**Figure 1**). Neck ultrasonography identified a 9 × 6-mm hypoechoic lesion in the left lower pole of the thyroid gland, consistent with a parathyroid adenoma. Parathyroid methoxy-isobutyl-isonitrile (MIBI) scintigraphy confirmed focal uptake in the same region.

Given the coexistence of acromegaly and primary hyperparathyroidism, a genetic evaluation was performed, which demonstrated a heterozygous MEN-1 c.1087_1089delAGG, p.E363del (rs869025185) mutation, confirming the diagnosis of "Multiple Endocrine Neoplasia type 1".

The patient subsequently underwent a second pituitary operation. One month postoperatively, her basal growth hormone level had decreased to 0.84 mcg/L and IGF-1 to 147 mcg/L. Follow-up MRI (**Figure 2**) confirmed resection of the pituitary adenoma. Surgical intervention for hyperparathyroidism was scheduled. Pancreatic MRI did not reveal any additional lesions. The patient was enrolled in a multidisciplinary evaluation involving endocrinology, surgery, nephrology, and genetic counseling. Long-term follow-up with periodic screening for tumors associated with MEN-1 (parathyroid, pituitary, pancreatic, and thoracic neuroendocrine tumors) was recommended. The chronological progression of clinical manifestations, interventions, and outcomes is summarized in **Table 1**.

Discussion

Multiple endocrine neoplasia type 1 (MEN-1) is an inherited neoplastic syndrome transmitted in an autosomal dominant manner, conferring a lifelong predisposition to the development of tumors affecting multiple endocrine organs [8,10]. MEN-1-associated tumors arise from the loss of function of the MEN-1 gene on chromosome 11q13, which encodes menin, a nuclear tumor-suppressor protein that regulates endocrine cell growth through chromatin remodeling and cell-cycle gene control [8,10]. Tumor formation in MEN-1 follows the classic 2-hit tumor-suppressor model: a heterozygous germline MEN-1 mutation, whether inherited (familial) or arising during early embryogenesis (de novo germline), constitutes the first hit. The second hit is a somatic mutation that results in loss of heterozygosity in the remaining allele of the predisposed endocrine cell, initiating clonal expansion. Loss of heterozygosity at 11q13 drives the development of MEN-1-associated tumors in more than 90% of cases [8,10,11].

MEN-1 syndrome can be diagnosed when any of the following criteria are fulfilled: (i) identification of a germline MEN-1 mutation,

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Table 1. Chronological timeline of clinical findings, diagnostic investigations, therapeutic interventions, and outcomes in a patient with MEN-1 initially presenting with acromegaly due to a growth hormone-secreting pituitary macroadenoma.

Year / age	Clinical findings	Intervention / management	Outcome
2021 / 32 y	Visual disturbances; 3 × 2-cm pituitary macroadenoma	Transsphenoidal resection	Visual symptoms resolved
4 months later	Pregnancy	Medical therapy	Discontinued
2021-2023 / 31-33 y	No treatment during pregnancy and lactation	Observation; GH and calcium not regularly monitored	Patient remained clinically stable
2023 / 34 y	Routine follow-up: – Serum calcium: 11.3 mg/dL – 24-hour urinary calcium: 560 mg/ 24 h – GH: 4 mcg/L – IGF-1: 560 mcg/L – Phosphorus: 3.2 mg/dL	– Pituitary MRI – Neck USG – Kidney USG – MIBI scintigraphy	– Renal USG: calculus in the left kidney – Pituitary MRI: 15 × 10-mm recurrent macroadenoma – Neck USG: 9 × 6-mm parathyroid adenoma – Parathyroid MIBI scintigraphy: focal uptake in parathyroid adenoma
2023 / 34 y	Coexistence of pituitary macroadenoma and parathyroid adenoma	Genetic testing	Heterozygous MEN-1 c.1087_1089delAGG, p.E363del (rs869025185) mutation
2023 / 34 y	– Pituitary macroadenoma – Parathyroid adenoma	– Second transsphenoidal surgery – Surgery for hyperparathyroidism	1-month post-operative follow-up: GH 0.84 mcg/L IGF-1 147 mcg/L MRI: complete tumor resection
Ongoing	Long-term monitoring	Periodic biochemical and imaging surveillance	Early detection of MEN-1-associated tumors; patient enrolled in multidisciplinary care

MEN-1, multiple endocrine neoplasia type 1; GH, growth hormone; IGF-1, insulin-like growth factor 1; MRI, magnetic resonance imaging; USG, ultrasonography; MIBI, technetium-99m methoxyisobutylisonitrile (sestamibi; scintigraphy used for localization of parathyroid adenomas).

even in the absence of symptoms; (ii) the presence of two or more MEN1-associated endocrine tumors; or (iii) the presence of at least one MEN-1-associated endocrine tumor in an individual who has a first-degree relative with confirmed MEN syndrome [8,10-12].

MEN-1 syndrome exhibits variability in age of onset, clinical presentation, and tumor aggressiveness. The type of glandular disorder that develops largely determines the clinical presentation. This inherited endocrine tumor syndrome is characterized predominantly by neoplastic involvement of the parathyroid glands, anterior pituitary, and pancreatic islet cells [8,10-12]. Hyperparathyroidism is the first endocrinopathy in most patients, typically between 20-25 years of age and occurring in the majority of affected individuals by 40 years of age. Unlike sporadic hyperparathyroidism, MEN-1 hyperparathyroidism usually involves all parathyroid glands, leading to manifestations seen with hypercalcemia [8,10]. Pituitary adenomas occur as the first manifestation in 25% of MEN-1 cases, as observed in this patient.

The symptoms depend on both the secreted pituitary hormone and/or compressive effects of tumor size. Only 25% of MEN-1-associated pituitary tumors secrete growth hormone, as in our case, whereas 60% are prolactin-secreting adenomas (prolactinomas) [8,10].

Generally, MEN-1 syndrome is uncommon and occurs in approximately 1 in 30 000 individuals [10,13]. This patient illustrates a rare syndrome and an uncommon clinical presentation, with acromegaly from growth hormone-secreting pituitary macroadenoma as the first clinical sign of MEN-1 preceding primary hyperparathyroidism. This presentation may be overlooked if clinical attention remains focused on an apparently isolated pituitary lesion [1,8].

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Most mutations are inactivating. Frameshift deletions or insertions (≈40-45%) and nonsense mutations (≈25%) are the most common, while small in-frame deletions or insertions (≈5%) and large or whole-gene deletions (<1%) are rare [8,10]. In the case of our 34-year-old female patient, she was diagnosed with MEN-1 syndrome after confirmation of a heterozygous in-frame deletion in the MEN-1 gene (c.1087_1089delAGG, p.E363del), an extremely uncommon variant. This deletion results in the loss of a glutamic acid at position 363, a functionally important region of the menin protein. This mutation has been previously reported in the literature and has been classified as pathogenic in the ClinVar database (accession: RCV000018165.14), with 4 independent submissions supporting this classification [13]. Although in-frame deletions are relatively uncommon among MEN-1 mutations, this case underscores that even small in-frame deletions can disrupt menin's tumor-suppressor function [8,10]. The identification of such rare variants highlights the importance of genetic counseling and surveillance for family members and individuals at risk [1,8,10].

Despite the remarkable advances in understanding MEN-1, definitive genotype-phenotype correlations remain ambiguous. Most genetic variants of MEN-1 are unique, with only a tiny proportion reported more than once, limiting the ability to predict clinical manifestations based solely on genotype and thereby posing multiple challenges [10,11]. However, specific familial variants, such as the MEN-1-Burin variant described in Newfoundland families, suggest that certain recurrent mutations may be associated with specific phenotypic patterns [1,8]. Therefore, systematic case reporting and collaborative research are critical to identifying subtle associations between clinical manifestations and specific mutations. Reporting rare variants, such as in our case, expands the limited knowledge base of genotype-phenotype correlation in MEN-1 in order to enrich the collective understanding of MEN-1 genetics, disease penetrance, and tumor spectrum, ultimately supporting more knowledgeable clinical decision-making, and personalized management [8,10,13].

Management of MEN-1 is tumor-specific and varies according to tumor type, size, functionality, and hormone overproduction. Management options include surgery, medical therapy, and radiotherapy, chosen based on tumor characteristics, comorbidities, and patient-related factors [8,10,11]. Current evidence indicates that treatment strategies for sporadic and MEN-1-associated pituitary tumors are similar. In this patient, pregnancy required temporary discontinuation of her medical therapy; the tumor remained stable, which highlights the need for vigilant post-pregnancy monitoring. Therefore, close clinical and radiological surveillance is strongly recommended [8,10,11].

This case report is limited by the unavailability of detailed histopathological data from the initial pituitary surgery and the absence of documented genetic screening results for family members at the time of manuscript preparation. In addition, long-term biochemical surveillance for other MEN-1-associated tumors is ongoing. Despite these limitations, this report highlights an uncommon clinical presentation of MEN-1 and contributes to the understanding of rare genotype-phenotype associations.

Conclusions

This case is novel due to the presentation of acromegaly caused by a growth hormone-secreting pituitary macroadenoma as the initial manifestation of MEN-1, preceding the development of clinically overt hyperparathyroidism, in association with a rare pathogenic in-frame MEN-1 deletion. Such an atypical onset emphasizes the importance of considering MEN-1 in patients with pituitary tumors, particularly when additional endocrine abnormalities are present. The detection of the uncommon MEN-1 mutation c.1087_1089delAGG (p.E363del) further contributes to the limited body of knowledge regarding genotype-phenotype correlations in MEN-1, and highlights the importance of genetic counseling, family screening, and vigilant follow-up. Early recognition of MEN-1 through clinical suspicion, biochemical testing, and genetic evaluation is critical, as timely diagnosis allows for proactive surveillance of associated tumors, reduces morbidity, and improves long-term outcomes.

Department and Institution Where Work Was Done

Department of Endocrinology, Yusuf Aydın Clinic, Istanbul, Türkiye.

Patient Consent

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.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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References:

1. Marques TF, Vasconcelos R, Diniz ET, et al. Multiple endocrine neoplasia type 1 revealed by a hip pathologic fracture. Clin Rheumatol. 2012;31(3):585-88
2. van Leeuwaarde RS, Pieterman CRC, Bleiker EM, et al. Care for patients with multiple endocrine neoplasia type 1: The current evidence base. Fam Cancer. 2016;15(1):157-71
3. Stratakis CA, Kamilaris CD. Multiple endocrine neoplasia type 1 (MEN1): An update and the significance of early genetic and clinical diagnosis. Front Endocrinol (Lausanne). 2019;10:339
4. Singh G, Mulji NJ, Jialal I. Multiple Endocrine Neoplasia Type 1. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. Updated July 10, 2023
5. Giusti F, Marini F, Brandi ML. Multiple endocrine neoplasia type 1. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025
6. Brandi ML, Pieterman CRC, English KA, et al. Multiple endocrine neoplasia type 1 (MEN1): Recommendations and guidelines for best practice. Lancet Diabetes Endocrinol. 2025;13(8):699-721
7. Waguespack SG. Beyond the "3 Ps": A critical appraisal of the non-endocrine manifestations of multiple endocrine neoplasia type 1. Front Endocrinol (Lausanne). 2022;13:1029041
8. Syro LV, Scheithauer BW, Kovacs K, et al. Pituitary tumors in patients with MEN1 syndrome. Clinics (Sao Paulo). 2012;67(Suppl. 1):43-48
9. Nachtigall LB, Guarda FJ, Lines KE, et al. Clinical MEN1 among a large cohort of patients with acromegaly. J Clin Endocrinol Metab. 2020;105(6):e2271-81
10. Marini F, Falchetti A, Luzi E, et al. Multiple endocrine neoplasia type 1 (MEN1) syndrome. In: Riegert-Johnson DL, Boardman LA, Hefferon T, et al, editors. Cancer Syndromes [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2009
11. Thakker RV. Multiple endocrine neoplasia type 1. Indian J Endocrinol Metab. 2012;16(Suppl. 2):S272-74
12. Sun M, Chang X, Huang X, Chen L, et al. Case report: a novel likely pathogenetic variant of the MEN1 gene in multiple endocrine neoplasia type 1. Front Endocrinol (Lausanne). 2025;16:1551087
13. National Center for Biotechnology Information. ClinVar; Variation ID: 18165 (MEN1 c.1087_1089delAGG, p.E363del) [Internet]. Bethesda (MD): National Center for Biotechnology Information; 2025 [cited 2025 Sep 26]. Available from: https://www.ncbi.nlm.nih.gov/clinvar/

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