

DOI: <http://dx.doi.org/10.12996/gmj.2026.4680>

A Case of Acromegaly Diagnosed After Pituitary Apoplexy Presenting as Polycystic Ovary Syndrome

Polikistik Over Sendromu gibi Prezente Olan ve Hipofiz Apopleksisi Sonrasında Tanı Konulan Bir Akromegali Olgusu

İb Seyit Murat Bayram, İb Özgür Özçelik, İb Hüseyin Demirci, İb Revah Çankaya, İb Erman Çakal

Department of Endocrinology Clinic, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye

ABSTRACT

Pituitary apoplexy (PA) is an uncommon neuroendocrine emergency resulting from hemorrhage or infarction of a pituitary adenoma. Dopaminergic agents are well-established precipitants; however, the role of synthetic progestins remains insufficiently characterized. Acromegaly may present with clinical features that overlap considerably with those of polycystic ovary syndrome (PCOS), thereby complicating and delaying its diagnosis. We report a 26-year-old woman with a two-year history of secondary amenorrhea and hirsutism who had previously been evaluated by gynecology and diagnosed with PCOS on the basis of oligomenorrhea, clinical hyperandrogenism, and polycystic ovarian morphology on ultrasonography. Markedly elevated prolactin (127 µg/L) and a low free T4 level were also documented; however, the possibility of an underlying pituitary pathology was not investigated at that time. Dydrogesterone was commenced, and twelve days later the patient developed thunderclap headache and acute complete visual loss. Emergency evaluation demonstrated markedly elevated insulin-like growth factor-1 (984 ng/mL) and growth hormone (20 µg/L). Pituitary magnetic resonance imaging revealed a 50x25 mm macroadenoma with signal characteristics consistent with acute hemorrhage and infarction. Emergency transsphenoidal surgery was performed, and histopathology confirmed a sparsely granulated somatotroph pituitary neuroendocrine tumor of the Pit-1 lineage (Ki-67: 8%). The postoperative course was complicated by panhypopituitarism and permanent bilateral visual loss. This case underscores the importance of excluding sellar pathology before

Öz

Hipofiz apopleksisi (HA), hipofiz adenomunun kanaması veya enfarktüsü sonucunda gelişen, nadir görülen bir nöroendokrin acil durumdur. Dopaminerjik ajanlar iyi bilinen tetikleyici faktörler arasında yer almakla birlikte, sentetik progestinlerin bu süreçteki rolü henüz yeterince aydınlatılamamıştır. Akromegali, polikistik over sendromu (PKOS) ile belirgin klinik örtüşme gösteren bulgularla prezente olabilmekte; bu durum tanıyı güçleştirmekte ve geciktirmektedir. İki yıldır süren sekonder amenore ve hirsutizm şikayetiyle başvuran 26 yaşındaki kadın hasta, daha önce jinekoloji tarafından değerlendirilmiş; oligomenore, klinik hiperandrogenizm ve ultrasonografide polikistik over morfolojisi temelinde PKOS tanısı almıştı. Belirgin düzeyde yüksek prolaktin (127 µg/L) ve düşük serbest T4 değeri saptanmış olmakla birlikte, altta yatan hipofizer patoloji olasılığı o dönemde araştırılmamıştı. Didrogesteron başlanmasının ardından on ikinci günde hasta gök gürültüsü baş ağrısı ve akut tam görme kaybı ile başvurdu. Acil değerlendirmede belirgin derecede yüksek insülin benzeri büyüme faktörü-1 (984 ng/mL) ve büyüme hormonu (20 µg/L) düzeyleri saptandı. Hipofiz manyetik rezonans görüntülemesinde akut kanama ve enfarktüsle uyumlu sinyal özelliklerine sahip 50x25 mm'lik bir makroadenom izlendi. Acil transsfenoidal cerrahi uygulandı; histopatoloji, Pit-1 soyundan seyrek granüllü somatotrop hipofiz nöroendokrin tümörü tanısını doğruladı (Ki-67: %8). Postoperatif dönem panhipopituitarizm ve kalıcı bilateral görme kaybı ile komplike oldu. Bu olgu; menstrüel düzensizliği ve hafif endokrin bozuklukları olan hastalarda hormonal tedaviye başlamadan önce sellar patolojinin dışlanması önemini vurgulamaktadır. Ayrıca

Cite this article as: Bayram SM, Özçelik Ö, Demirci H, Çankaya R, Çakal E. A case of acromegaly diagnosed after pituitary apoplexy presenting as polycystic ovary syndrome. Gazi Med J. 2026;37(4):576-582

Address for Correspondence/Yazışma Adresi: Seyit Murat Bayram, Department of Endocrinology Clinic, University of Health Sciences Türkiye, Ankara Etlik City Hospital, Ankara, Türkiye

E-mail / E-posta: drmurat.endokrin@yandex.com

ORCID ID: orcid.org/0000-0003-1459-5765

Received/Geliş Tarihi: 02.04.2026

Accepted/Kabul Tarihi: 08.09.2026

Publication Date/Yayınlanma Tarihi: 15.10.2026



©Copyright 2026 The Author(s). Published by Galenos Publishing House on behalf of Gazi University Faculty of Medicine. Licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

©Telif Hakkı 2026 Yazar(lar). Gazi Üniversitesi Tıp Fakültesi adına Galenos Yayınevi tarafından yayımlanmaktadır. Creative Commons Atıf-GayriTicari-Türetilemez 4.0 (CC BY-NC-ND) Uluslararası Lisansı ile lisanslanmaktadır.

ABSTRACT

initiating hormonal therapy in patients with menstrual irregularities and subtle endocrine disturbances, particularly when features suggestive of acromegaly are present. It also highlights the need for broader awareness of acromegaly's clinical manifestations among non-endocrinology specialists.

Keywords: Pituitary apoplexy, acromegaly, dydrogesterone, PCOS

Öz

endokrinoloji dışı uzmanlık alanlarında akromegalinin klinik bulgularına yönelik farkındalığın artırılması gerektiğine dikkat çekmektedir.

Anahtar Sözcükler: Hipofiz apopleksisi, akromegali, didrogesteron, PCOS

INTRODUCTION

Pituitary apoplexy (PA) is a potentially life-threatening clinical syndrome caused by acute hemorrhage or infarction of a pituitary adenoma. It presents as a neuroendocrine emergency characterized by the sudden onset of severe headache, visual disturbances, ophthalmoplegia, and altered consciousness, frequently accompanied by acute hypopituitarism (1). Although the term "PA" classically refers to this dramatic clinical presentation, subclinical or silent apoplexy—detected incidentally on imaging or histopathological examination—is in fact considerably more prevalent (2). The estimated incidence of clinically overt PA is approximately 0.17 episodes per 100,000 individuals per year, occurring in 2-12% of patients with known pituitary adenomas (3). The pathophysiology of PA, while incompletely understood, is thought to involve a combination of factors: A mismatch between the elevated metabolic demands of a rapidly enlarging tumor and its blood supply, intrinsic vascular abnormalities within the adenoma, and compression of the superior hypophyseal vessels against the diaphragma sellae (4). Overexpression of vascular endothelial growth factor in certain adenomas has been identified as a contributing mechanism, potentially leading to the formation of fragile, fenestrated vessels prone to hemorrhage (5). A precipitating factor is identified in up to 30-40% of cases; recognized triggers include arterial hypertension, major surgery, dynamic pituitary function testing, coagulopathy, head trauma, and various pharmacological agents, of which dopamine agonists are the best-documented (6).

The association between sex steroid hormones and PA is less well established but has been reported. Two main pathophysiological mechanisms have been proposed. First, estrogens are known to induce pituitary hyperemia and increase glandular vascularity, potentially imposing hemodynamic stress on the fragile vasculature of an adenoma (5). Second, both estrogens and progestins increase the risk of thrombotic events by promoting a prothrombotic coagulation state, which may predispose to ischemic infarction within tumor tissue (7). While most reported cases have involved combined oral contraceptives, the independent contribution of synthetic progestins administered in isolation has not been systematically studied. Dydrogesterone is a retroprogestogen with a molecular structure closely resembling that of endogenous progesterone; it is widely used for the management of menstrual disorders, endometriosis, and luteal phase support owing to its favorable tolerability profile. Its potential to precipitate PA in the context of an undiagnosed pituitary macroadenoma remains inadequately documented, making individual case reports especially valuable for delineating this uncommon risk.

Acromegaly is a chronic disorder resulting from sustained excess secretion of growth hormone (GH), responsible for the characteristic peripheral manifestations, including progressive acral enlargement, coarsening of facial features, soft tissue hypertrophy, and a broad range of systemic complications. In more than 95% of cases, the source is a GH-secreting pituitary neuroendocrine tumor (PitNET). Because the onset is insidious and symptom progression is gradual, the diagnosis is frequently delayed by a decade or more (8). Consequently, approximately 75% of somatotroph adenomas are already at the macroadenoma stage (>1 cm) at the time of diagnosis, conferring greater potential for mass-related complications, including apoplexy (9,10). The co-occurrence of acromegaly and PA is uncommon; when it does occur, spontaneous biochemical remission of acromegaly may follow, but this is the exception rather than the rule, and most GH-secreting adenomas remain hormonally active after an apoplectic event (11,12). Critically, PA may occasionally represent the initial clinical presentation of a previously undiagnosed somatotroph adenoma.

We present a case of a young woman whose undiagnosed acromegaly, initially misattributed to PCOS by her gynecologists, was dramatically unmasked by the onset of PA shortly after dydrogesterone was initiated for secondary amenorrhea. This case illustrates the potential of synthetic progestins—and dydrogesterone in particular—to precipitate PA and emphasizes the critical importance of excluding sellar pathology prior to commencing hormonal therapy in patients with unexplained menstrual disturbances and hormonal abnormalities.

CASE PRESENTATION

A 26-year-old woman presented to the gynecology outpatient clinic in December 2024 with a two-year history of secondary amenorrhea and progressive hirsutism. She was a mother of three with no significant past medical history and no regular medications. Her body mass index was 35 kg/m², consistent with class II obesity. The preoperative gynecology notes documented obesity and non-specific constitutional complaints, without reference to acromegalic features. At the time of our endocrinology consultation—obtained following the apoplectic event—directed history taking revealed that the patient had noticed an increase in ring size and an increase in shoe size over the preceding two years, and physical examination demonstrated mild acral enlargement of the hands and feet. These findings, in retrospect, were consistent with chronic GH excess, though they had not been elicited or recognized at the time of the initial gynaecological assessment.

Laboratory investigations revealed a free thyroxine (T4) of 0.75 ng/dL (reference: 0.8-1.8 ng/dL), thyroid-stimulating hormone

(TSH) of 0.02 mIU/L (reference: 0.4-4.0 mIU/L), and a markedly elevated prolactin of 127 µg/L (reference: 3-27 µg/L) (Table 1). Transabdominal pelvic ultrasonography demonstrated bilateral polycystic ovarian morphology with a thin, regular endometrium. On the basis of secondary amenorrhea, clinical hyperandrogenism (hirsutism), and polycystic ovarian morphology on ultrasound—satisfying two of the three 2003 Rotterdam consensus criteria for PCOS (oligo-/anovulation and polycystic ovaries)—a clinical diagnosis of PCOS was established by the gynecology team (13). It is important to note that this diagnosis was made outside our endocrinology department; the patient was not referred to endocrinology at this juncture. The substantially elevated prolactin level, which raises the differential of a pituitary pathology such as a prolactinoma or a GH-secreting adenoma with co-secretion of prolactin, was not pursued further before initiating hormonal therapy. Dydrogesterone was commenced.

Five days after commencing dydrogesterone, the patient developed a headache and was advised to continue treatment. Twelve days after initiation, she returned with a markedly worsening headache and acute-onset visual loss, prompting an urgent referral to neurosurgery. Ophthalmological assessment at this point documented visual acuity of 0.25 in the right eye and absence of light perception (P-) in the left eye, with a relative afferent pupillary defect on the left. Fundoscopic examination showed normal optic discs bilaterally, and no acute ocular pathology was identified; retrobulbar neuritis and PA were raised as differential diagnoses by the ophthalmology team. Repeat laboratory investigations showed TSH 1.32 mIU/L, free T4 0.78 ng/dL, and prolactin 130 µg/L. Additional testing revealed a markedly elevated IGF-1 of 984 ng/mL (reference: 100-300 ng/mL) and GH of 20 µg/L (reference: <5 µg/L). Adrenocorticotrophic hormone (ACTH) was 19 ng/L, and morning cortisol was critically low at 2.49 µg/dL (reference: 5-25 µg/dL), indicating adrenal insufficiency secondary to pituitary compromise.

Preoperative pituitary magnetic resonance imaging (MRI) demonstrated a 50×25 mm lesion occupying the pituitary fossa and extending into the sellar, suprasellar, and sphenoid sinus regions. The mass was in close proximity to both internal carotid arteries and the Circle of Willis and exerted significant compression on the optic chiasm, with superior extension to the level of the third ventricle. The lesion demonstrated heterogeneous signal characteristics on both T1- and T2-weighted sequences. On T2-weighted imaging, the presence of hypointense areas within the mass is consistent with the paramagnetic effects of deoxyhemoglobin or intracellular methemoglobin, indicating subacute hemorrhagic transformation. This pattern supports the interpretation of a hemorrhagic apoplectic event of recent onset, as hyperacute hemorrhage tends to appear isointense or hyperintense on T2 sequences, whereas the T2 hypointensity observed here is more characteristic of an evolving hemorrhage in the early subacute phase. The overall signal heterogeneity is consistent with mixed hemorrhagic and ischemic infarction within the adenoma (Figure 1).

Given the acute onset of complete visual loss and severe headache—both established indications for emergency surgical intervention in PA—the patient underwent emergency transnasal transsphenoidal pituitary surgery within hours of presentation. The decision to proceed with urgent decompression was guided by the presence of progressive neuro-ophthalmological compromise, in accordance with current management guidelines for PA (14). Published evidence further supports early surgery in patients with visual acuity impairment or visual field defects, as prompt decompression of the optic chiasm is associated with meaningful visual recovery (15).

Postoperatively, the patient was monitored in the intensive care unit. Day 1 laboratory results showed improvement in GH to 0.5 µg/L, prolactin below 2 µg/L, and IGF-1 at 554 ng/mL. However, hyponatremia developed (serum sodium 154 mmol/L, urine specific gravity 1.004), consistent with central antidiuretic hormone

Table 1. Preoperative and postoperative laboratory findings.

Parameter (reference range)	Pre-op (gynecology visit)	Pre-op (day before surgery)	Post-op day 1	Post-op day 3	Post-op week 1	Post-op month 1	Post-op month 6
Sodium (135-145 mmol/L)	—	139	154	145	143	143	—
Potassium (3.5-5.1 mmol/L)	—	4.2	3.6	3.2	—	—	—
Urine specific gravity (1.005-1.030)	—	—	1.004	1.020	—	1.025	1.020
TSH (0.4-4.0 mIU/L)	0.02	1.32	0.06	—	<0.005	<0.005	<0.005
Free T4 (0.8-1.8 ng/dL)	0.75	0.78	0.96	—	0.5	0.5	0.8
Cortisol (5-25 µg/dL)	—	2.49	4	—	0.8	0.2	0.5
ACTH (10-60 ng/L)	—	19	<1.5	—	<1.5	<1.5	<1.5
GH (<5 µg/L)	—	20	0.5	—	0.9	1.02	0.5
IGF-1 (100-300 ng/mL)	—	984	554	—	279	300	248
PRL (3-27 µg/L)	127	130	<2	—	<2	<2	<2
LH (2-12 IU/L)	—	<0.3	<0.3	—	<0.3	<0.3	<0.3
FSH (3-10 IU/L)	—	1	<0.3	—	<0.3	<0.3	<0.3
E2 (30-400 ng/L)	—	<5	16	—	<5	—	—

ACTH: Adrenocorticotrophic hormone, E2: Estradiol, FSH: Follicle-stimulating hormone, GH: Growth hormone, IGF-1: Insulin-like growth factor-1, LH, Luteinizing hormone, Post-op: Postoperative, Pre-op: Preoperative, PRL: Prolactin, T4: Thyroxine, TSH: Thyroid-stimulating hormone. Note: Empty cells indicate that the parameter was not measured or that data were not available for that time point.

(ADH) deficiency. Anterior pituitary function remained severely impaired, with undetectable gonadotropins, TSH of 0.06 mIU/L, and morning cortisol of 4 µg/dL. Following endocrinology consultation, a diagnosis of panhypopituitarism with central ADH deficiency was established. Replacement therapy was initiated with levothyroxine, hydrocortisone, and desmopressin. By postoperative day 3, serum sodium had normalized to 145 mmol/L and urine specific gravity had increased to 1.020, indicating a therapeutic response.

Postoperative MRI (day 1) demonstrated a 31×22×18 mm postoperative cavity with peripheral enhancement, containing air and hemorrhagic material, and continuing to exert a mass effect on the optic chiasm. A 5×3 mm nodular area of enhancement adjacent to the left frontal base was observed, raising the possibility of

residual tumor (Figure 2). Ophthalmological reassessment in the postoperative period documented bilateral fixed dilated pupils with no perception of light bilaterally (P-/P-) and bilateral optic nerve atrophy on fundoscopy, indicating irreversible ischemic injury to the anterior visual pathway.

One week post-surgery, TSH remained suppressed (<0.005 mIU/L), free T4 was 0.5 ng/dL, ACTH was below 1.5 ng/L, morning cortisol 0.8 µg/dL, and IGF-1 had decreased to 279 ng/mL. The patient was discharged on postoperative day 13 on desmopressin acetate 60 mcg twice daily, hydrocortisone 10 mg in the morning and 5 mg in the afternoon, and levothyroxine 25 mcg once daily.

Pathological analysis of the resected specimen identified a PitNET with positive immunostaining for synaptophysin, Pit-1, estrogen

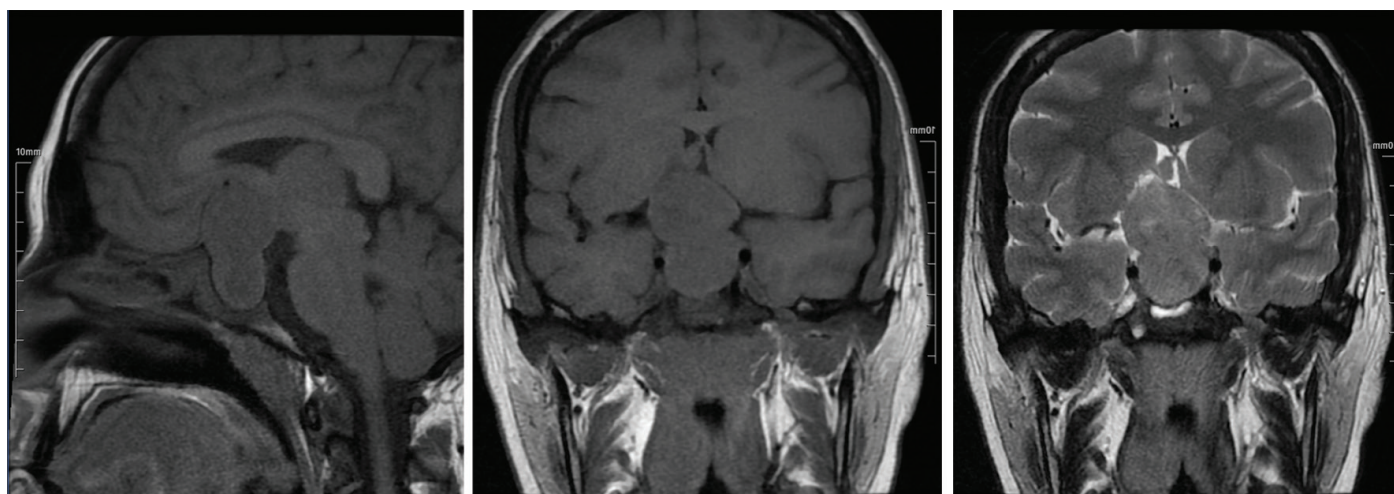


Figure 1. Preoperative pituitary MRI. From left to right: sagittal T1-weighted, coronal T1-weighted, and coronal T2-weighted images demonstrate a large macroadenoma (50×25 mm) filling the sella and suprasellar region. The lesion extends into the sphenoid sinus, compresses the optic chiasm, and abuts both internal carotid arteries. Heterogeneous signal intensity, including hypointense areas on T2-weighted imaging, is consistent with hemorrhagic transformation in the early subacute phase of apoplexy.

MRI: Magnetic resonance imaging.

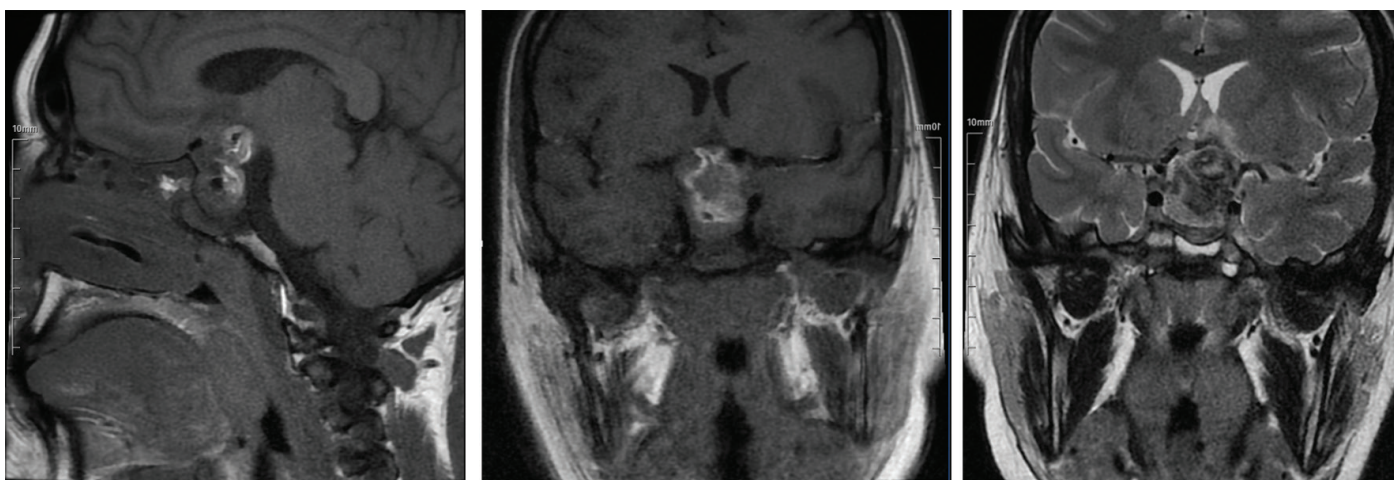


Figure 2. Postoperative day 1 pituitary MRI. From left to right: sagittal T1-weighted, coronal T1-weighted, and coronal T2-weighted images show a 31×22×18 mm postoperative cavity with peripheral enhancement, containing air and hemorrhagic material. A 5×3 mm nodular area of enhancement adjacent to the left frontal base raises the possibility of residual tumor. The optic chiasm remains compressed.

MRI: Magnetic resonance imaging.

receptor (ER), and GH. No staining for other pituitary hormones was detected. Cytokeratin 8-18 demonstrated a dot-like cytoplasmic pattern, and reticulin staining revealed disruption of the normal acinar architecture. The Ki-67 proliferation index was approximately 8%. The final pathological diagnosis was a sparsely granulated somatotroph PitNET of the Pit-1 lineage.

One month post-surgery, the patient remained on full pituitary hormone replacement with stable biochemistry. At four months, follow-up MRI showed the postoperative cavity had decreased in size to 20×14×13 mm and was partly occupied by fat packing material with peripheral enhancement. A 3×3 mm nodular area of enhancement adjacent to the right frontal base persisted, representing a possible residual tumor focus. The optic chiasm remained morphologically deformed (Figure 3).

At six months, anterior pituitary function remained globally deficient. The patient continued on her existing replacement regimen. GH was 0.5 µg/L, IGF-1 was 248 ng/mL, and all other hormonal axes remained suppressed (Table 1). She continues under combined outpatient follow-up by neurosurgery and endocrinology.

Written informed consent was obtained from the patient for publication of this case report and the accompanying clinical images.

DISCUSSION

This case illustrates how the insidious clinical presentation of acromegaly can result in diagnostic delays and misattribution to more common conditions such as PCOS, with potentially catastrophic consequences. The patient's presenting features of obesity, secondary amenorrhea, and hirsutism are well-recognized overlapping manifestations of both PCOS and acromegaly, and the clinical overlap between the two conditions has been described in the literature (16,17). A retrospective review of the preoperative gynecology documentation revealed subtle acromegalic features, including a reported increase in ring size and increase in shoe size over the preceding two years and mild indeterminate enlargement of the hands and feet on physical examination. Although non-specific in isolation, such findings—particularly in the context of markedly

elevated prolactin and an isolated low free T4 with suppressed TSH, suggesting central rather than primary hypothyroidism—warrant systematic exclusion of pituitary pathology before initiating hormonal therapy. Non-endocrinology clinicians, including gynecologists and primary care physicians, should maintain awareness of the somatic features of acromegaly, as early recognition outside specialist settings is essential to reduce the well-documented diagnostic delay that characterizes this condition.

The markedly elevated prolactin level (127 µg/L) documented at initial presentation warrants specific discussion. When prolactin is substantially elevated in a patient with menstrual irregularities, the differential diagnosis should include prolactinoma, compression of the pituitary stalk by a non-functioning mass (the “stalk effect”), and co-secretion of prolactin by a GH-secreting adenoma. GH and prolactin co-secretion occurs in approximately 30-40% of acromegaly cases, either through a mammosomatotroph adenoma or a mixed somatotroph-lactotroph tumor, both of which fall within the Pit-1 transcription factor lineage (18). In the present case, the immunohistochemical profile of the resected tumor—strongly positive for GH, Pit-1, and ER, without prolactin staining—suggests that hyperprolactinemia was most likely the result of a stalk effect due to the large macroadenoma rather than true co-secretion. Irrespective of mechanism, a prolactin level of this magnitude in a young woman with menstrual disturbance should prompt pituitary imaging prior to the initiation of any hormonal treatment. The failure to investigate further before prescribing dydrogesterone was a critical missed opportunity (19).

The initial diagnosis of PCOS deserves careful consideration in this context. PCOS is the most common endocrinopathy in women of reproductive age, and its diagnosis is based on the 2003 Rotterdam consensus criteria, which require the presence of at least two of the following three features: oligo- and/or anovulation; clinical and/or biochemical signs of hyperandrogenism; and polycystic ovarian morphology on ultrasonography—after exclusion of other relevant endocrinopathies such as congenital adrenal hyperplasia, Cushing's syndrome, androgen-secreting tumors, hyperprolactinemia, and

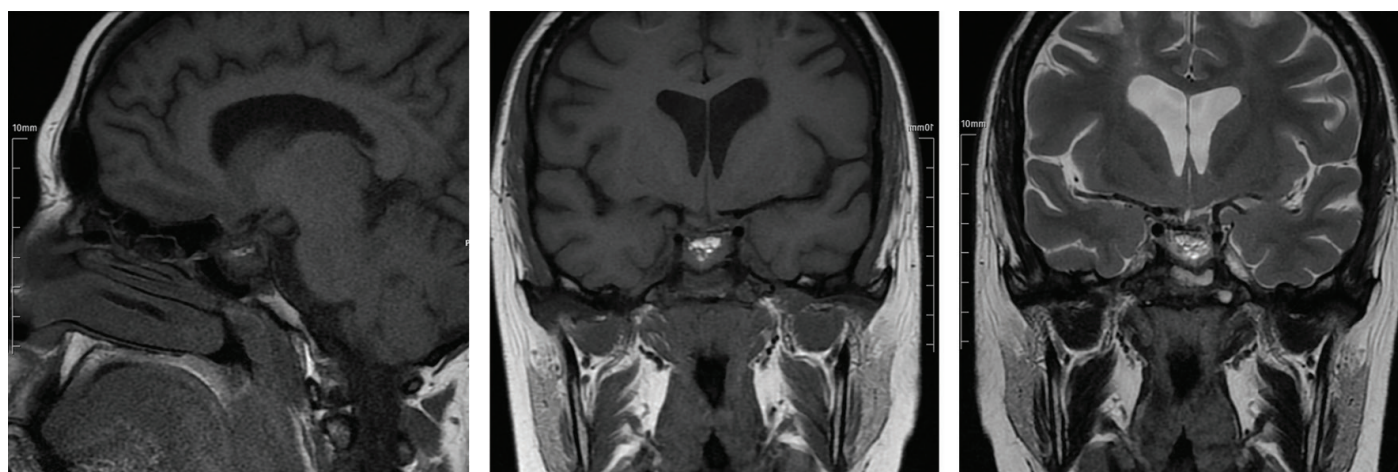


Figure 3. Postoperative month 4 pituitary MRI. From left to right: sagittal T1-weighted, coronal T1-weighted, and coronal T2-weighted images demonstrate a 20×14×13 mm postoperative cavity containing fat packing material with peripheral enhancement. A 3×3 mm nodular area of enhancement persists adjacent to the right frontal base, consistent with possible residual tumor. The optic chiasm remains morphologically deformed.

MRI: Magnetic resonance imaging.

thyroid dysfunction (13). Polycystic ovarian morphology, as defined by the Rotterdam criteria, requires the presence of 12 or more follicles measuring 2-9 mm in diameter in at least one ovary and/or an ovarian volume exceeding 10 mL. In the present case, the gynecology team identified oligomenorrhea and polycystic ovarian morphology on transabdominal ultrasound, satisfying two Rotterdam criteria. However, the exclusion steps integral to a rigorous PCOS workup—particularly the evaluation of markedly elevated prolactin and the abnormal thyroid function pattern suggestive of central hypothyroidism—were not completed. This serves as a reminder that PCOS is, by definition, a diagnosis of exclusion and that the presence of elevated prolactin or atypical hormonal patterns mandates further investigation before the diagnosis is confirmed and treatment initiated.

The temporal relationship between the initiation of dydrogesterone and the onset of PA in this case raises the possibility that this progestogen may have acted as a precipitating factor, though this association is based on temporal evidence rather than established causality. The precise mechanism by which sex steroids might trigger PA has not been fully elucidated. The proposed pathophysiological pathways include estrogen-mediated pituitary hyperemia with resultant vascular congestion and a procoagulant effect of exogenous progestins promoting thrombotic infarction within the adenoma (5,7). The majority of published cases linking hormonal agents to PA have involved combined oral contraceptives containing both estrogen and progestin components. Kobayashi et al. (20) reported a case of ischemic PA in a 33-year-old woman following 18 months of combined oral contraceptive use, proposing that the estrogen-induced hypercoagulable state was the underlying mechanism. More broadly, case series and reviews have documented PA in the setting of various sex steroid exposures, including combined oral contraceptives, anabolic androgenic steroids, and GnRH agonists, each mediated by distinct but potentially overlapping mechanisms (4,20-22).

The specific contribution of dydrogesterone as a sole precipitant of PA has not been established in the literature, and no controlled data exist. This case should therefore be interpreted cautiously: While the temporal sequence is compelling and consistent with a drug-related precipitant, a causal relationship cannot be confirmed from a single case report. The possibility that the apoplectic event was spontaneous within a large and hemorrhage-prone adenoma and coincidentally occurred shortly after dydrogesterone was started cannot be excluded. Despite extensive review of the available literature, no prior published case definitively attributing PA to dydrogesterone as an isolated agent was identified. The absence of evidence of causation does not, however, diminish the clinical lesson: In any patient with suspected pituitary pathology, hormonal agents capable of altering pituitary blood flow or coagulation status should not be initiated without adequate exclusion of a sellar mass.

The decision to proceed with emergency transsphenoidal surgery was made on the basis of acute-onset complete visual loss and thunderclap headache—both of which are accepted indications for urgent surgical decompression in the current management

guidelines for PA. Published evidence supports early surgery (within 7 days) in patients with visual acuity impairment or visual field defects, as prompt decompression of the optic chiasm is associated with meaningful visual recovery in a significant proportion of patients (14,15). Unfortunately, in the present case, the severity of the apoplectic insult resulted in irreversible bilateral optic nerve atrophy with permanent loss of visual function, emphasizing the necessity of early recognition and rapid intervention.

Following surgery, the patient developed panhypopituitarism with central ADH deficiency, requiring comprehensive hormonal replacement with hydrocortisone, levothyroxine, and desmopressin. These complications are well recognized sequelae of PA, particularly after large apoplectic events, and reflect the extent of ischemic damage to the anterior and posterior pituitary parenchyma. Endocrine function did not recover over the six-month follow-up period, consistent with published reports indicating that pituitary insufficiency after PA is often permanent when the apoplectic injury is extensive (11).

To our knowledge, this case is the first reported case of a somatotroph macroadenoma presenting as PA potentially precipitated by dydrogesterone administered for a presumed diagnosis of PCOS. This case adds to a modest but growing literature on sex steroid-associated PA and highlights several important principles: The clinical overlap between acromegaly and PCOS mandates systematic pituitary evaluation in atypical cases; markedly elevated prolactin should always be investigated before commencing hormonal therapy; and the diagnosis of PCOS, as a diagnosis of exclusion, requires the formal exclusion of pituitary pathology. Non-endocrinology practitioners should be familiar with the somatic features of acromegaly—including acral enlargement, coarsening of facial features, change in ring or shoe size, soft tissue hypertrophy, and macroglossia—as their recognition in primary or specialist gynecological care has the potential to prevent delayed diagnosis and its consequences.

This case illustrates how an undiagnosed somatotroph macroadenoma presenting with clinical features mimicking PCOS was dramatically revealed by PA following the initiation of dydrogesterone therapy. It underscores the diagnostic challenges inherent to acromegaly; the potential for synthetic progestins to precipitate apoplexy in the presence of a pre-existing adenoma—though causality in this individual case cannot be confirmed—and the critical need for comprehensive pituitary evaluation before commencing hormonal treatment in patients with menstrual disturbances and unexplained endocrine abnormalities. Clinicians across specialties should maintain a low threshold for suspecting pituitary pathology when features overlap with PCOS, particularly when prolactin is markedly elevated or when subtle somatic features of acromegaly are present. When clinical suspicion is raised, measurement of IGF-1 and dedicated pituitary imaging should be obtained prior to initiating any hormonal therapy. This case contributes to the limited literature on progestin-associated PA and reinforces the importance of careful risk stratification in clinical practice.

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Acknowledgments

AI tools were used for language correction. The authors reviewed and edited all AI-assisted text and take full responsibility for the content of the manuscript.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.M.B., Ö.Ö., H.D., R.Ç., E.Ç., Concept: S.M.B., E.Ç., Design: S.M.B., H.D., Supervision: H.D., E.Ç., Patient Follow-up: S.M.B., Ö.Ö., R.Ç., Literature Search: S.M.B., R.Ç., Critical Review: H.D., E.Ç., Ö.Ö., R.Ç., Writing: S.M.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

- Briet C, Salenave S, Bonneville JF, Laws ER, Chanson P. Pituitary apoplexy. *Endocrine Reviews*. 2015; 36: 622-45.
- Bonicki W, Kasperlik-Załuska A, Koszewski W, Zgliczyński W, Wisławski J. Pituitary apoplexy: endocrine, surgical and oncological emergency. Incidence, clinical course and treatment with reference to 799 cases of pituitary adenomas. *Acta Neurochir (Wien)*. 1993; 120: 118-22.
- Raappana A, Koivukangas J, Ebeling T, Pirilä T. Incidence of pituitary adenomas in Northern Finland in 1992-2007. *J Clin Endocrinol Metab*. 2010; 95: 4268-75.
- Iglesias P. Pituitary apoplexy: an updated review. *J Clin Med*. 2024; 13.
- Cardoso ER, Peterson EW. Pituitary apoplexy: a review. *Neurosurgery*. 1984;14: 363-73.
- Semple PL, Jane JA, Laws ER. Clinical relevance of precipitating factors in pituitary apoplexy. *Neurosurgery*. 2007; 61: 956-61; discussion 961-2.
- Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the women's health initiative randomized controlled trial. *JAMA*. 2002; 288: 321-33.
- Zahr R, Fleseriu M. Updates in diagnosis and treatment of acromegaly. *Eur Endocrinol*. 2018; 14: 57-61.
- Lavrentaki A, Paluzzi A, Wass JA, Karavitaki N. Epidemiology of acromegaly: review of population studies. *Pituitary*. 2017; 20: 4-9.
- Fernandez A, Karavitaki N, Wass JA. Prevalence of pituitary adenomas: a community-based, cross-sectional study in Banbury (Oxfordshire, UK). *Clin Endocrinol (Oxf)*. 2010; 72: 377-82.
- Capatina C, Inder W, Karavitaki N, Wass JA. Management of endocrine disease: pituitary tumour apoplexy. *Eur J Endocrinol*. 2015; 172: R179-90.
- Fraser LA, Lee D, Cooper P, Van Uum S. Remission of acromegaly after pituitary apoplexy: case report and review of literature. *Endocr Pract*. 2009; 15: 725-31.
- Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod*. 2004;19: 41-7.
- Rajasekaran S, Vanderpump M, Baldeweg S, Drake W, Reddy N, Lanyon M, et al. UK guidelines for the management of pituitary apoplexy. *Clin Endocrinol (Oxf)*. 2011; 74: 9-20.
- Brown NJ, Patel S, Gendreau J, Abraham ME. The role of intervention timing and treatment modality in visual recovery following pituitary apoplexy: a systematic review and meta-analysis. *J Neurooncol*. 2024; 170: 469-82.
- Joham AE, Tay CT, Laven J, Louwers YV, Azziz R. Approach to the patient: diagnostic challenges in the workup for polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2025; 110: e2298-308.
- Khiyami AM, Jokar TO, Abdallah HM, Gardner PA, Zenonos GA, Styer AK, et al. Polycystic ovary syndrome preceding the diagnosis of acromegaly: a retrospective study in 97 reproductive-aged women. *Reprod Biol Endocrinol*. 2023; 21: 14.
- Araujo-Castro M, Biagetti B, Menéndez E, Novoa-Testa I, Cordido F, Rodríguez Berrocal V, et al. Predictors of therapeutic failure in GH and prolactin co-secreting pituitary adenomas. *Endocr Connect*. 2025; 14.
- Petersenn S, Fleseriu M, Casanueva FF, Giustina A, Biermasz N, Biller BMK, et al. Diagnosis and management of prolactin-secreting pituitary adenomas: a Pituitary Society International Consensus Statement. *Nat Rev Endocrinol*. 2023; 19: 722-40.
- Kobayashi J, Miyashita K, Tamanaha T, Kobayashi N, Iihara K, Nagatsuka K. Pituitary ischemic apoplexy in a young woman using oral contraceptives: a case report. *J Stroke Cerebrovasc Dis*. 2013; 22: e643-4.
- Donegan D, Erickson D. Revisiting pituitary apoplexy. *J Endocr Soc*. 2022; 6: bvac113.
- Raj R, Elshimy G, Jacob A, Arya PVA, Unnikrishnan DC, Correa R, et al. Pituitary apoplexy induced by gonadotropin-releasing hormone (GnRH) agonist administration for treatment of prostate cancer: a systematic review. *J Cancer Res Clin Oncol*. 2021; 147: 2337-47.