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Management of ACTH-Dependent Cushing's disease with Resistant Hypertension and "Kissing Carotids": A Challenging Pituitary Case

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Abstract

Background:
Cushing's disease (CD), caused by an ACTH-secreting pituitary adenoma, remains one of the most challenging endocrine disorders to diagnose and treat. The coexistence of resistant hypertension, metabolic complications, and complex vascular anatomy such as "kissing carotids" further complicates management.

Case Presentation:
We report a 40-year-old man with long-standing hypertension referred for evaluation of resistant blood pressure. Physical examination revealed classical Cushingoid features. Endocrine testing confirmed ACTH-dependent Cushing's syndrome. Pituitary MRI was limited by a rare vascular variant medialized internal carotid arteries ("kissing carotids") which obscured visualization of the adenoma. The patient underwent endoscopic transsphenoidal surgery in a specialized neurosurgical center, confirming a corticotroph adenoma. Postoperatively, cortisol levels normalized, and metabolic and cardiovascular comorbidities markedly improved.

Conclusion:
This case highlights the diagnostic and therapeutic complexity of ACTH-dependent Cushing's disease with challenging pituitary anatomy. Expert multidisciplinary management remains essential to achieve remission and prevent long-term sequelae.

Introduction

Cushing's syndrome (CS) is a rare endocrine disorder characterized by chronic exposure to excess glucocorticoids, resulting in multisystem complications such as hypertension, diabetes, dyslipidemia, osteoporosis, and psychiatric disturbances. Its incidence is estimated at 1–2 cases per million population per year, with Cushing's disease (CD) caused by an ACTH-secreting pituitary adenoma representing approximately 70% of endogenous cases (1,2).

Hypertension occurs in up to 80% of patients with CS and contributes significantly to cardiovascular morbidity and mortality (3). The mechanisms are multifactorial, involving activation of mineralocorticoid receptors, vascular remodeling, and metabolic dysregulation (4).

Although transsphenoidal pituitary surgery remains the cornerstone of treatment, success depends on accurate localization of the adenoma and the surgeon's expertise (5,6). Anatomical variations, such as "kissing carotids," can pose additional surgical challenges and increase operative risk (7).

We present an unusual case of ACTH-dependent Cushing's disease with resistant hypertension and a complex vascular anatomy that rendered surgical management particularly difficult.

Case Presentation

A 40-year-old man with a past history of coronary artery spasm and arterial hypertension since age 34 was referred to our endocrinology department for investigation of **resistant hypertension**. Despite optimal triple therapy (angiotensin receptor blocker, calcium channel blocker, and thiazide diuretic), his blood pressure remained poorly controlled.

On admission, **blood pressure** measured 130/80 mmHg under treatment. He exhibited typical Cushingoid features: **moon face, facial plethora, purple abdominal striae, dorsocervical "buffalo hump," truncal obesity, proximal muscle wasting**, and **telangiectasias**. No clinical signs of infection or venous thrombosis were present.

Laboratory evaluation revealed:

- Fasting plasma glucose: 5.9 mmol/L; HbA1c: 6.0% (prediabetic range).
- Serum triglycerides: 1.7 mmol/L (mild hypertriglyceridemia).
- Serum potassium: normal.
- Morning serum cortisol: elevated (615 nmol/L).
- Plasma ACTH: 23 pg/mL, repeated at 30 pg/mL.

Dynamic endocrine tests:

- **1-mg overnight dexamethasone suppression test**: serum cortisol post-test 130 nmol/L (non-suppressed).
- **Low-dose dexamethasone suppression test**: cortisol 273 nmol/L, confirming **Cushing's syndrome**.
- These findings, along with detectable ACTH, established an **ACTH-dependent** etiology.

Pituitary MRI demonstrated **medialization of both intracavernous internal carotid arteries ("kissing carotids")**, compressing and elevating the pituitary gland and rendering detailed visualization of the adenoma impossible. No discrete contrast defect could be confirmed.

The **systemic work-up** included:

- **24-hour ambulatory blood pressure monitoring (Holter):** confirmed resistant hypertension.
- **Echocardiography:** no left ventricular hypertrophy.
- **Bone mineral density (DXA):** T-score −2.8, consistent with osteoporosis.
- **Gonadal axis:** hypogonadotropic hypogonadism (testosterone 1.3 ng/mL; FSH 3.4 mIU/mL; LH 3.39 mIU/mL).

- **Psychological assessment:** revealed depressive symptoms.

Given the **high surgical risk** associated with the kissing carotids and limited visualization of the lesion, the case was discussed in a multidisciplinary team. After consultation with a specialized neurosurgical center in Germany, the patient underwent **endoscopic transsphenoidal pituitary surgery**.

Intraoperatively, the anatomical configuration required careful navigation between the medialized carotids. **Histopathology confirmed a corticotroph adenoma positive for ACTH** on immunostaining. Postoperative serum cortisol levels normalized (<100 nmol/L), confirming biochemical remission.

At **6-month follow-up**, MRI no longer showed the previously suspected left-sided lesion. Metabolic and cardiovascular parameters improved:

- Fasting glucose: 4.8 mmol/L; HbA1c: 5.4%.
- Triglycerides normalized.
- Blood pressure: grade I hypertension, well controlled on dual therapy (ARB + calcium channel blocker).
- Psychological and muscle strength improved significantly.

This case underscores the complex interplay of endocrine, cardiovascular, and anatomical factors that complicate the diagnosis and management of Cushing's disease.

Discussion

1. Diagnostic Challenges in ACTH-Dependent Cushing's Disease

Diagnosing CD remains challenging, especially when MRI fails to reveal a discrete adenoma. Up to 40% of microadenomas are not visible on routine imaging (8). In such cases, inferior petrosal sinus sampling (IPSS) is typically recommended to confirm pituitary origin of ACTH secretion (9). However, in our patient, anatomical distortion due to kissing carotids made IPSS technically risky. This highlights the importance of individualized diagnostic strategies and referral to expert centers for complex cases (10).

2. Resistant Hypertension and Cardiovascular Risk

Hypertension is among the earliest and most persistent features of Cushing's syndrome. It results from multiple mechanisms: mineralocorticoid receptor activation due to 11β-HSD2 saturation, vascular remodeling, and sympathetic nervous system activation (3,4). Chronic hypercortisolism also impairs endothelial function and increases vascular stiffness (11). In our patient, resistant hypertension at a young age was the key clue leading to endocrine investigation. Following surgical remission, blood pressure improved markedly, consistent with evidence that curative surgery reduces but does not always normalize blood pressure (3,12).

3. Anatomical Variants: The Challenge of "Kissing Carotids"

"Kissing carotids" refer to a rare variant where the intracavernous internal carotid arteries are medially displaced, approaching or contacting each other in the midline (7). This occurs in less than 1% of individuals and poses significant surgical risk due to the proximity of critical vascular structures (13). In our case, this malformation obscured visualization of the adenoma on MRI

and increased the complexity of transsphenoidal access. Endoscopic techniques and neuronavigation are essential to minimize complications (14).

4. Surgical Outcome and Postoperative Improvement
Transsphenoidal surgery is the treatment of choice for Cushing's disease, achieving remission in approximately 70–90% of microadenomas (5,6). Our patient's postoperative course was favorable, with normalization of cortisol, improvement in blood pressure, lipid profile, bone density, and psychological well-being. These findings align with previous studies reporting substantial improvement in metabolic parameters following surgical cure (12,15).

5. Lessons for Clinical Practice
This case emphasizes several practical messages:

- Resistant hypertension in a young patient should always prompt evaluation for secondary causes, including Cushing's syndrome.
- Pituitary MRI can be misleading in the presence of vascular anomalies; additional imaging modalities or IPSS may be necessary.
- Referral to high-volume pituitary centers is crucial when anatomical variations complicate surgery.
- Post-cure monitoring of metabolic, cardiovascular, and psychological parameters is vital, as recovery is gradual and incomplete in some cases (12,16).

Conclusion

This report describes a rare and challenging case of ACTH-dependent Cushing's disease associated with resistant hypertension and a "kissing carotids" vascular variant. The case illustrates the complexity of diagnosis when MRI is inconclusive and the increased surgical risk posed by altered vascular anatomy. Multidisciplinary management and referral to specialized centers are essential to achieve successful outcomes. Following endoscopic transsphenoidal surgery, our patient experienced complete biochemical remission and significant improvement of metabolic and cardiovascular comorbidities.
Ultimately, this case reinforces the importance of early recognition, tailored surgical planning, and comprehensive postoperative follow-up in patients with Cushing's disease, particularly when anatomical variants complicate management.

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