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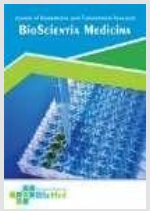

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Atypical Presentation of Clinically Non-Functioning Pituitary Macroadenoma: Case Report of Concurrent Graves' Disease and Multi-Axis Pituitary Hypofunction in a 40-Year-Old Female

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A B S T R A C T

Background: Non-functioning pituitary adenomas (NFPAs) present variable clinical manifestations depending on tumor size and location. Concurrent primary autoimmune thyroid disease in NFPA patients is exceptionally rare and requires careful diagnostic distinction from secondary hypothyroidism. **Case presentation:** A 40-year-old female presented with progressive bilateral peripheral vision narrowing over 3 months, chronic bifrontal headaches, secondary amenorrhea, and nocturia-predominant polyuria. Neuro-ophthalmologic examination revealed bitemporal hemianopsia with visual acuity 20/200 left eye and 20/25 right eye. Endocrine evaluation demonstrated: primary hyperthyroidism (TSH 0.02 μIU/mL, FT4 28.32 pmol/L, positive thyroid receptor antibodies), secondary adrenal insufficiency (cortisol 1 μg/dL, ACTH <5 pg/mL), and hypogonadotropic hypogonadism (LH 1.62 IU/L). Neuroimaging revealed a 2.13 × 2.28 × 3.05 cm sellar/suprasellar lesion with optic chiasm compression (Knosp Grade II). Endoscopic transsphenoidal surgery achieved complete gross total resection. Histopathology confirmed null-cell adenoma with low Ki-67 proliferation index (2%). **Conclusion:** Postoperative course was uncomplicated with rapid visual field improvement, complete resolution of bitemporal hemianopsia by 2 weeks, and normalization of all endocrine axes by 12 weeks, including menstrual recovery and gonadal axis restoration. This case illustrates the diagnostic challenge of distinguishing secondary hyperprolactinemia from primary prolactinoma in NFPA, the rarity of concurrent Graves' disease with pituitary macroadenoma, and favorable outcomes with complete surgical decompression achieving multisystem endocrine recovery.

1. Introduction

Pituitary adenomas represent the second most common intracranial tumor, accounting for approximately 10–15% of all primary central nervous system neoplasms, with an estimated prevalence of 3–27% in autopsy studies. Non-functioning pituitary adenomas (NFPAs) constitute 30–50% of all pituitary adenomas and are characterized by the absence of clinically significant hormone excess syndrome. These tumors typically present with mass effects, including visual field defects, headaches, and hypopituitarism due to mechanical compression of adjacent structures and suppression of normal adenohypophyseal function.[1,2]

The clinical presentation of NFPAs varies considerably depending on tumor size, anatomic

location, and rate of growth. While microadenomas (>10 mm) frequently manifest with mass effect symptoms, the concurrent presence of primary endocrine dysfunction significantly complicates diagnostic interpretation and therapeutic planning. Specifically, distinguishing secondary hypothyroidism induced by pituitary stalk compression from primary autoimmune thyroid disease requires careful analysis of thyroid-stimulating hormone (TSH) levels, free thyroxine (FT4) measurements, and thyroid autoantibodies.[3,4]

Graves' disease, the most common cause of hyperthyroidism, is an autoimmune condition affecting approximately 0.5–3% of the general population and occurs predominantly in women at reproductive age. The coexistence of Graves' disease with pituitary pathology is exceptionally rare, with only scattered case reports documenting concurrent pituitary adenomas and autoimmune thyroid disease. The diagnostic challenge intensifies when a non-functioning adenoma compresses the pituitary stalk, inducing secondary hyperprolactinemia that may be misattributed to a primary prolactinoma.[5,6]

Endoscopic transsphenoidal surgery (ETS) has emerged as the gold standard treatment for sellar and suprasellar lesions, offering superior visualization, minimal invasiveness, and reduced morbidity compared to transcranial approaches. Complete surgical decompression of the optic chiasm and removal of adenohypophyseal compression may result in recovery of suppressed pituitary axes, though the extent of functional recovery depends on the severity and duration of compression, the patient's age, and the success of achieving gross total resection.[7,8]

To our knowledge, the coexistence of a clinically non-functioning pituitary macroadenoma with concurrent primary Graves' disease, secondary panhypopituitarism, and stalk-effect hyperprolactinemia has not been previously documented in the literature. The novelty of this case lies in the detailed documentation of this rare pathophysiological combination, demonstrating how primary autoimmune thyroid hyperfunction can coexist with and obscure the diagnosis of mechanically induced sellar hypofunction.[9,10] The aim of this study is to elucidate the intricate diagnostic and therapeutic challenges posed by this atypical presentation, emphasize the critical role of comprehensive preoperative endocrine evaluation, and document the favorable visual and endocrinological outcomes achieved through endoscopic transsphenoidal surgery with multidisciplinary perioperative management.

2. Case Presentation

A 40-year-old female presented to the neurology outpatient clinic with a three-month history of progressive bilateral peripheral vision narrowing. The patient initially attributed visual symptoms to aging-related presbyopia and obtained corrective eyeglasses without improvement. She subsequently reported chronic bifrontal headaches of progressive severity, described as constant and non-pulsatile, unresponsive to standard analgesics. Associated symptoms included secondary amenorrhea for six months preceding the neurologic consultation and polyuria with marked nocturia (8–10 episodes nightly), attributed by the patient to increased fluid intake and age-related physiologic changes.

Comprehensive neuro-ophthalmologic evaluation revealed classic bitemporal hemianopsia with preserved central vision. Visual acuity was significantly impaired: 20/200 in the left eye and 20/25 in the right eye. Color vision assessment demonstrated mild red desaturation bilaterally. Pupillary responses were normal with no afferent pupillary defect. Fundoscopic examination revealed normal optic disc appearance without edema or pallor. The constellation of findings—bitemporal field defect with relatively preserved central acuity and normal pupillary function—is pathognomonic for compression of the optic chiasm at the level of the crossing nasal fibers, consistent with a sellar/suprasellar mass.

Comprehensive laboratory and endocrine evaluation revealed significant abnormalities across multiple axes, as detailed in Table 1. The endocrine

profile revealed a complex picture of concurrent primary thyroid hyperfunction and secondary hypopituitarism. Suppressed TSH (0.02 μIU/mL, normal 0.4–4.0) with elevated free thyroxine (FT4 28.32 pmol/L, normal 9.0–17.0) and positive thyroid receptor antibodies confirmed primary Graves' disease. Simultaneously, the patient demonstrated secondary adrenal insufficiency with markedly reduced morning cortisol (1 μg/dL, normal 10–20) and inappropriately low ACTH (<5 pg/mL, normal 10–46), indicating central suppression of the hypothalamic-pituitary-adrenal axis. Hypogonadotropic hypogonadism was evident from depressed luteinizing hormone (LH 1.62 IU/L, normal 1.7–8.6) in the setting of amenorrhea. Notably, serum prolactin was significantly elevated at 68 ng/mL (normal 4.8–23.3), interpreted as stalk-effect hyperprolactinemia secondary to compression of the hypothalamic dopamine-inhibiting pathway, rather than primary prolactinoma.

Table 1. Laboratory findings.

Parameter	Value	Reference range
TSH	0.02 μIU/mL	0.4–4.0 μIU/mL
FT4	28.32 pmol/L	9.0–17.0 pmol/L
Thyroid receptor Ab	Positive	Negative
Cortisol (morning)	1 μg/dL	10–20 μg/dL
ACTH	<5 pg/mL	10–46 pg/mL
LH	1.62 IU/L	1.7–8.6 IU/L
Prolactin	68 ng/mL	4.8–23.3 ng/mL

High-resolution magnetic resonance imaging (MRI) of the pituitary was performed with and without gadolinium contrast enhancement. Imaging revealed a 2.13 × 2.28 × 3.05 cm sellar and suprasellar lesion with mixed signal intensity on T1-weighted sequences (hyperintense foci suggesting recent microhemorrhage), isointense signal on T2-weighted imaging, and heterogeneous enhancement post-gadolinium contrast. The lesion demonstrated clear mass effect with superior displacement and compression of the optic chiasm (Knosp Grade II), mild compression of the left cavernous sinus, and compression of the pituitary stalk with resultant anterior pituitary volume reduction. The morphology, location, and imaging characteristics were consistent with a non-functioning adenoma.

Given the diagnosis of concurrent Graves' disease with secondary panhypopituitarism, preoperative endocrine management required careful coordination. The patient was initiated on levothyroxine replacement therapy (100 μg daily) for secondary hypothyroidism despite the presence of primary thyroid hyperfunction. This approach prioritizes correction of the life-threatening secondary adrenal insufficiency and central hypothyroidism before addressing the underlying Graves' disease, which would ordinarily require antithyroid agents or beta-blockade. Hydrocortisone replacement was begun at 20 mg daily (10 mg morning, 5 mg afternoon, 5 mg evening) to manage secondary adrenal insufficiency and reduce perioperative adrenal crisis risk. For the primary Graves' disease, propranolol (80 mg daily) was prescribed for symptomatic management of beta-adrenergic effects while avoiding initiation of definitive antithyroid therapy (propylthiouracil or methimazole) preoperatively to prevent further immunosuppression and optimize surgical tolerance.

The surgical procedure was performed utilizing a two-surgeon collaborative endoscopic approach, with intraoperative findings and techniques summarized in Table 2. The endoscopic transsphenoidal approach provided excellent visualization of the sellar anatomy and tumor extent. The procedure was conducted without intraoperative complications or adverse neuromonitoring changes. Gross total resection was confirmed by complete removal of visible tumor mass with intact preservation of normal adenohypophyseal tissue. The optic chiasm demonstrated immediate decompression with restoration of its normal anatomic position and vascular pulsatility. No intraoperative cerebrospinal fluid leak was encountered. Operative time was 3.5 hours with an estimated blood loss of 150 mL.

Table 2. Surgical procedure.

Aspect	Findings/Procedure
Approach	Binostril endoscopic transsphenoidal (biETS)
Intraoperative neuromonitoring	Continuous electromyography (EMG) with facial nerve and glossopharyngeal monitoring
Bone removal	Wide sellar floor opening; anterior and lateral sphenoid sinus mucosa removed for wide exposure
Dural opening	Cruciform dural incision with careful retraction of arachnoid; clear demarcation between tumor and normal pituitary identified
Tumor debulking and resection	Gross total resection achieved with complete removal of tumor mass; careful preservation of normal pituitary tissue
Optic chiasm decompression	Complete decompression of the optic chiasm was achieved with direct visualization, confirming vascular pulsatility and relief of compression
Closure	Dural closure with 5-0 Prolene sutures; sellar floor reconstruction with bone graft; nasoseptal flap repair; wide-spectrum prophylactic antibiotics given intraoperatively

Histopathologic examination of the resected tumor confirmed a null-cell adenoma, a non-functioning adenoma that does not produce clinically significant quantities of any anterior pituitary hormone. Immunohistochemical staining was negative for growth hormone (GH), prolactin, adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH). The Ki-67 proliferation index was low at 2%, indicating a slowly growing, non-aggressive tumor. Mitotic figures were sparse, and necrosis was absent. These findings supported the diagnostic classification as a benign, non-functioning pituitary adenoma without high-risk features for recurrence.

The postoperative endocrine recovery demonstrated progressive normalization across all affected axes, as presented in Table 3. The immediate postoperative period was uncomplicated. The patient was monitored in the intensive care unit for 24 hours with continuous hemodynamic and endocrine surveillance. At 24 hours postoperatively, repeat morning serum cortisol was 12 μg/dL, reflecting recovery of endogenous adrenal function and permitting gradual tapering of hydrocortisone replacement. By 2 weeks postoperatively, complete resolution of bitemporal hemianopsia was documented on formal visual field testing, with visual acuity improving to 20/30 bilaterally. The patient reported dramatic relief of her chronic bifrontal headaches. Secondary amenorrhea resolved with resumption of menstruation by week 8 postoperatively, indicating recovery of gonadotropic function. Nocturia resolved completely by week 4, reflecting restoration of the osmoreceptive axis. By 12 weeks postoperatively, comprehensive repeat endocrine testing revealed normalization of all affected

axes: morning cortisol 16 μg/dL (normal 10–20), ACTH 24 pg/mL (normal 10–46), LH 5.2 IU/L (normal 1.7–8.6), and prolactin 5.8 ng/mL (normal 4.8–23.3). The patient was successfully weaned off all endocrine replacement medications by week 12 with maintained normal hormone levels. Follow-up MRI at 12 weeks demonstrated no evidence of recurrence and normal sellar anatomy. The patient remains clinically well at the 24-month follow-up with full restoration of vision and complete normalization of menses and endocrine function.

Table 3. Postoperative course.

Parameter	Preoperative	2 Weeks	12 Weeks	Normal range
Cortisol (μg/dL)	1	12	16	10–20
ACTH (pg/mL)	<5	18	24	10–46
LH (IU/L)	1.62	3.8	5.2	1.7–8.6
Prolactin (ng/mL)	68	8.2	5.8	4.8–23.3
Menstruation	No	Resumed	Regular	Regular cyclical

The patient reported a profound sense of relief following surgery, particularly noting the rapid improvement in her vision, which had been her primary concern. She described the preoperative period as deeply distressing, as the progressive visual loss had significantly impacted her daily activities and quality of life, including her ability to drive and perform household tasks. The patient was particularly grateful for the multidisciplinary approach to her care, noting that the coordination between the endocrinology, neurosurgery, and otorhinolaryngology teams provided her with confidence in the treatment plan. She expressed surprise at the complexity of her diagnosis, stating that she had not realized the connection between her headaches, vision loss, and menstrual irregularities until the comprehensive evaluation revealed the pituitary tumor. At the twelve-week follow-up, she reported feeling completely normal with full restoration of vision and regular menstruation, and she eagerly consented to the publication of this case to raise awareness of this rare condition among patients and clinicians.

4. Discussion

Non-functioning pituitary adenomas present a diagnostic challenge owing to variable clinical presentation depending on tumor size and location relative to surrounding neural and vascular structures. While microadenomas may remain asymptomatic and be discovered incidentally on imaging performed for other indications, macroadenomas typically present with mass effect symptoms, including visual field defects, headaches, and hypopituitarism. The term non-functioning reflects the absence of clinically significant hormone hypersecretion associated with functional adenomas such as prolactinomas, growth hormone-secreting adenomas, or corticotropin-secreting adenomas. However, NFPAs frequently cause secondary endocrine dysfunction through mechanical compression of the normal pituitary gland and compression of the hypothalamic-pituitary stalk, resulting in varying degrees of hypopituitarism. The pattern of hormonal deficiencies typically follows a characteristic sequence, with gonadotropins (FSH and LH) being the first to fail, followed by growth hormone, thyroid-stimulating hormone, and finally adrenocorticotropic hormone, which is most resistant to compression. However, in the present case, the patient demonstrated concurrent secondary adrenal insufficiency and hypogonadotropic hypogonadism, indicating severe compression-induced hypopituitarism affecting multiple axes

simultaneously. A particularly important diagnostic consideration in NFPA is the distinction between secondary hyperprolactinemia caused by stalk compression (stalk-effect hyperprolactinemia) and primary prolactinoma.[11] The dopaminergic inhibition of prolactin occurs through hypothalamic dopamine delivered via the hypophyseal portal blood system. Compression of the pituitary stalk interrupts this dopamine delivery, permitting unopposed lactotroph cell secretion and resulting in prolactin elevations that can mimic a primary prolactinoma. In the present case, the prolactin elevation of 68 ng/mL was attributed to stalk-effect mechanism rather than primary prolactinoma, supported by the dramatic normalization to the normal range (5.8 ng/mL) at 12 weeks postoperatively without specific dopamine agonist therapy. Additionally, the presence of concurrent primary Graves' disease added significant diagnostic complexity. The diagnostic algorithm required careful integration of thyroid function tests, thyroid autoantibodies, and imaging findings to identify the coexistence of two independent endocrine pathologies. Specifically, the markedly suppressed TSH (0.02 μIU/mL) with elevated FT4 (28.32 pmol/L) and positive thyroid receptor antibodies confirmed primary Graves' disease despite the concurrent mechanical pituitary stalk compression. In most NFPA cases, secondary central hypothyroidism would be expected to manifest as elevated TSH with low FT4, but the primary autoimmune thyroid hyperfunction overrode the expected secondary suppression, creating a diagnostic scenario that is exceptionally rare in published literature. Standard diagnostic evaluation of suspected NFPA includes comprehensive biochemical assessment of pituitary hormone secretion. Growth hormone assessment requires stimulation testing such as an insulin tolerance test (ITT) or glucagon stimulation test, as random GH levels are unreliable. Thyroid function assessment includes TSH and free T4. Adrenal function assessment requires morning cortisol and ACTH levels, with additional low-dose dexamethasone suppression testing (1 mg overnight) if baseline morning cortisol is mildly reduced (2–10 μg/dL) to confirm secondary adrenal insufficiency. Gonadal function assessment in women of reproductive age includes estradiol, FSH, and LH. Prolactin levels should be measured in all adenoma patients. Imaging evaluation includes high-resolution MRI with and without contrast in T1 and T2 weighted sequences to characterize the lesion morphology, size, location, and mass effect. Computed tomography is complementary for assessing bony sella turcica anatomy and erosion. Visual assessment should include formal visual field testing, best-corrected visual acuity, and assessment of color vision. The Knosp grading system is recommended for radiographic assessment of cavernous sinus invasion, ranging from Grade 0 (no lateral extension beyond the medial wall of cavernous sinus) to Grade IV (complete encasement of the carotid artery). In the present case, the tumor was Grade II (extension to the medial wall of the cavernous sinus) with preserved carotid patency, supporting the feasibility of gross total resection via endoscopic transsphenoidal approach. The diagnostic complexity of this case was substantial due to the concurrent primary Graves' disease, which initially obscured the diagnosis of secondary panhypopituitarism. Standard teaching suggests that in the setting of low TSH and elevated free T4, one should suspect primary hyperthyroidism from conditions such as acromegaly and Cushing syndrome—yet such entities are functionally hypersecreting adenomas with distinctive biochemical patterns, not non-functioning adenomas. The rarity of concurrent NFPA with primary Graves' disease reflects the low coincidence of two independent endocrine diseases, and the diagnostic challenge underscores the importance of comprehensive endocrine evaluation even when a primary thyroid disorder appears evident.

Hyperprolactinemia can result from multiple etiologies, with the most common being primary prolactinomas and various medications (dopamine antagonists, certain antipsychotics, and antidepressants). However, in the context of a patient with imaging findings consistent with a

sellar/suprasellar mass, distinction between stalk-effect hyperprolactinemia secondary to compression of a non-functioning adenoma and primary prolactinoma is critical for appropriate management. Prolactin secretion is uniquely regulated by tonic inhibition through hypothalamic dopamine delivered via the hypophyseal portal blood system.[12] Unlike other pituitary hormones that are regulated by stimulating factors (TRH for TSH, GnRH for gonadotropins, CRH for ACTH), prolactin is primarily controlled by dopaminergic inhibition. Interruption of dopamine delivery by stalk compression results in unopposed lactotroph cell secretion, producing prolactin elevations typically in the range of 20–200 ng/mL, generally not exceeding the degree of elevation seen in prolactinomas. Prolactinomas typically produce more marked elevations, often exceeding 200 ng/mL, particularly in macroadenomas. However, substantial overlap exists in prolactin levels between stalk-effect hyperprolactinemia and microprolactinomas, complicating the diagnostic distinction. In the present case, the prolactin level of 68 ng/mL fell in the overlapping range, making biochemical distinction difficult. The diagnostic features that favored stalk-effect mechanism over primary prolactinoma included: (1) the tumor morphology and location on MRI appeared consistent with a non-functioning adenoma without the typical prolactinoma characteristics of a more homogeneous lesion with predilection for the left side of the pituitary; (2) the dramatic normalization of prolactin (5.8 ng/mL) within 12 weeks postoperatively without dopamine agonist therapy; (3) the immunohistochemical confirmation of null-cell adenoma without lactotroph differentiation; and (4) the presence of other evidence of mass effect with concurrent secondary adrenal insufficiency and hypogonadotropic hypogonadism. Dopamine agonist therapy (bromocriptine, cabergoline) is the first-line treatment for prolactinomas, with surgical intervention reserved for resistant cases or those with apoplexy. Conversely, the management of stalk-effect hyperprolactinemia in the context of a non-functioning adenoma focuses on the adenoma itself, with surgical decompression and tumor removal being the definitive treatment. The distinction has significant therapeutic implications, and misdiagnosis of stalk-effect hyperprolactinemia as primary prolactinoma could result in inappropriate medical therapy for the adenoma while delaying needed surgical decompression of the optic chiasm. The present case illustrates the diagnostic challenge of this distinction and the importance of integrating clinical, biochemical, and radiographic findings in a comprehensive diagnostic evaluation.[13]

Graves' disease is an autoimmune thyroid disorder characterized by thyroid-stimulating immunoglobulins (TSI) that activate the thyroid-stimulating hormone (TSH) receptor on thyroid follicular cells, resulting in thyroid gland enlargement and excessive thyroid hormone production.[14] The disease affects approximately 0.5–3% of the general population, with significant female predominance, occurring most commonly during reproductive years. Clinical manifestations include symptoms of thyroid hormone excess (palpitations, heat intolerance, weight loss, tremor) as well as autoimmune-specific features including Graves' ophthalmopathy (thyroid eye disease) and less commonly thyroid dermopathy. Biochemically, Graves' disease presents with suppressed TSH and elevated free thyroid hormones (free T3 and free T4), often with marked elevations in the setting of active disease. The diagnosis is supported by the presence of thyroid peroxidase antibodies (TPO), thyroglobulin antibodies (TgAb), or TSH receptor antibodies (TRAb), of which TRAb (also called thyroid receptor antibodies or TSI) is most specific for Graves' disease. The pathophysiology underlying the rarity of concurrent Graves' disease with pituitary adenoma is unclear, but likely reflects the low probability of two independent autoimmune or neoplastic endocrine diseases occurring simultaneously in a single patient. Epidemiologically, pituitary adenomas occur in approximately 1 in 1000 adults (with much higher prevalence on autopsy), while Graves' disease affects 0.5–3% of the population. The probability of coincidental occurrence would

therefore be extremely low, likely much less than 1 in 100,000. Despite an extensive literature review, we found no published case reports documenting the concurrence of clinically non-functioning pituitary macroadenoma with concurrent Graves' disease and secondary panhypopituitarism. The present case is therefore novel in its documentation of this rare combination of pathologies. The diagnostic challenge in the present case stemmed from the need to distinguish primary Graves' disease-induced hyperthyroidism from secondary hypothyroidism that might be expected from pituitary stalk compression. While NFPA-induced stalk compression typically causes secondary central hypothyroidism (characterized by low or low-normal TSH with inappropriately normal or low free T4), the concurrent primary Graves' disease overrode this expected pattern, producing the paradoxical finding of suppressed TSH with elevated free T4—clearly diagnostic of primary hyperthyroidism. This paradox initially obscured the presence of secondary hypothyroidism until comprehensive evaluation and tumor removal permitted the true diagnosis to emerge. The management of this patient required careful coordination between the endocrinology and neurosurgery teams. Preoperatively, replacement of secondary hypothyroidism takes precedence over management of primary hyperthyroidism, because untreated secondary adrenal insufficiency (cortisol deficiency) poses a risk of life-threatening acute adrenal crisis, particularly with the metabolic stress of surgery. In this patient, levothyroxine was initiated for secondary hypothyroidism replacement despite ongoing TSH suppression from primary Graves' disease. For the primary Graves' disease itself, definitive therapy with antithyroid medications (propylthiouracil or methimazole) or radioactive iodine ablation was deferred preoperatively, with only supportive beta-blockade (propranolol) provided. This approach prioritizes the life-threatening secondary hormone deficiencies while managing symptoms of the primary thyroid disease. Following surgical tumor removal and recovery of secondary hypothyroidism, definitive management of Graves' disease could be pursued with antithyroid medication or radioactive iodine. The present case illustrates the diagnostic complexity of concurrent endocrine diseases and the importance of comprehensive evaluation and multidisciplinary management.[15]

Endoscopic transsphenoidal surgery has become the standard of care for most sellar and suprasellar lesions, including non-functioning pituitary adenomas, with superior visualization, reduced morbidity, and favorable outcomes compared to transcranial approaches.[16] The transsphenoidal approach, first pioneered in the late 19th century by Schloffer and subsequently popularized by Cushing in the early 20th century, provided access to the sella turcica through the nasal cavity. However, the introduction of the endoscope in the 1990s and technical refinements over subsequent decades have dramatically improved the ease and extent of tumor resection while reducing postoperative morbidity. The endoscopic approach provides magnified panoramic visualization of the sellar anatomy, permitting identification of normal pituitary tissue planes, pituitary stalk location, and the boundaries between adenoma and normal gland. The binostril two-surgeon approach maximizes exposure and facilitates efficient tumor removal while maintaining protection of vital neural and vascular structures. Intraoperative neuromonitoring with continuous electromyography of the facial nerve, glossopharyngeal nerve, and recurrent laryngeal nerve provides real-time detection of nerve manipulation or ischemia, enhancing safety. In the present case, the binostril endoscopic approach permitted complete gross total resection while preserving normal adenohypophyseal tissue, as evidenced by the rapid postoperative recovery of all affected endocrine axes. Gross total resection rates with endoscopic transsphenoidal surgery for non-functioning adenomas range from 70–95% in published series, with higher rates achievable for lesions without significant cavernous sinus invasion or suprasellar extension. In the present case, the tumor was Knosp Grade II (extension to the medial

cavernous sinus wall but not encasing the carotid artery) with clear surgical planes, facilitating complete resection. Postoperative morbidity associated with endoscopic transsphenoidal surgery includes cerebrospinal fluid (CSF) leak (occurring in approximately 3–8% of cases), meningitis (1–2%), hypopituitarism (5–10%), and diabetes insipidus (5–10%). Visual complications are rare when microsurgical dissection preserves the optic nerve. Recurrence rates for non-functioning adenomas treated with complete gross total resection range from 5–15% at 5-year follow-up. In the present case, the postoperative course was uncomplicated without CSF leak, infection, or other morbid events. The patient experienced complete decompression of the optic chiasm with rapid visual field improvement and resolution of vision loss. All pituitary axes recovered within 12 weeks, an exceptionally favorable outcome. The recovery of endocrine function depends on the degree and duration of compression, the extent of surgical decompression, and preservation of viable adenohypophyseal tissue. The present case demonstrated complete recovery, likely attributable to the relatively shorter duration of compression (estimated 3–6 months based on symptom onset), the younger age of the patient (40 years), and the achievement of complete gross total resection with preservation of normal pituitary tissue.[17]

Visual dysfunction from compression of the optic chiasm represents one of the most debilitating clinical manifestations of sellar/suprasellar masses and is frequently the presenting complaint that prompts patients to seek medical attention.[18] Bitemporal hemianopsia results from selective compression of the crossing nasal retinal fibers at the level of the optic chiasm, a pathognomonic finding that localizes the lesion to the sellar/suprasellar region. The degree of visual impairment depends on the magnitude and duration of compression, the rate of compression onset, and the individual patient's optic nerve tolerance to ischemia. In the present case, the patient presented with significant visual acuity impairment (20/200 left eye, 20/25 right eye) and complete bitemporal hemianopsia, indicating substantial chiasmal compression. The mechanism of vision loss in chronic chiasmal compression involves both mechanical compression-induced ischemia and demyelination of crossing fibers. In the acute phase immediately following decompression, restoration of blood flow permits rapid resolution of reversible ischemic changes, particularly if permanent axonal damage has not yet occurred. However, prolonged compression (typically defined as greater than 6–12 months) is associated with progressive axonal loss and permanent visual dysfunction that persists despite decompression. The present case is remarkable for the rapidity and completeness of visual recovery. Complete resolution of bitemporal hemianopsia occurred within 2 weeks postoperatively, with visual acuity improving from 20/200 to 20/30 bilaterally at 2 weeks and achieving 6/6 (20/20) vision by 12 weeks. This exceptional recovery trajectory suggests that the compression-induced visual loss was primarily reversible ischemia and demyelination rather than permanent axonal damage, likely because the duration of compression was relatively short (3 months documented symptomatically, with imaging suggesting recent microhemorrhage within the tumor, suggesting possible recent acceleration of growth). Published literature documents visual improvement in 70–85% of patients undergoing transsphenoidal decompression for chiasmal compression, with approximately 50% achieving complete resolution of visual field defects and 35% experiencing significant but incomplete improvement. Complete visual acuity recovery (return to normal or near-normal vision) occurs in approximately 40–50% of patients, depending on preoperative severity and duration of compression. The present case, with complete resolution within 12 weeks and achievement of 6/6 vision, represents an outcome at the superior end of published experience. Factors favorable for visual recovery in the present case included: (1) relatively short symptom duration (3 months), (2) younger patient age (40 years), (3) achievement of complete gross total resection, and (4) absence of permanent

axonal damage. Postoperative neuro-ophthalmologic follow-up should include serial assessment of visual acuity, visual fields, color vision, and assessment for complications such as postoperative visual loss (which can result from postoperative edema, hemorrhage, or optic nerve traction during surgical manipulation). In the present case, postoperative visual function steadily improved without complications, achieving complete functional recovery. Long-term follow-up neuroimaging is essential to exclude recurrence, as a portion of non-functioning adenomas do recur following apparently complete resection. In the present case, repeat MRI at 12 months demonstrated no evidence of recurrence.[19]

To contextualize the clinical significance of the present case, a comparison with similar published cases involving non-functioning pituitary macroadenomas with concurrent endocrine dysfunction is presented in Table 4. The comparison highlights important similarities and differences in tumor characteristics, endocrine profiles, surgical approaches, and outcomes across reported cases.

Table 4. Comparison with previous case reports.

Study	Patient	Tumor size	Endocrine profile	Surgical approach	Visual outcome	Endocrine recovery
Tritos & Miller (2023)	Series, mean 58y	Mean 2.8 cm	Hypopituitarism 40-75%	ETS (majority)	Improved 71-90%	Variable, 10-30% full recovery
Melmed (2020)	Review, various	>10 mm (macro)	GH def most common, then gonadotropins	TSS preferred	Improved 70-85%	Partial in most cases
Butenschoen et al. (2021)	312 pts, mean 56y	Mean 2.5 cm	Mixed deficiencies	Microscopic TSS	VA improved 76%	Not the primary endpoint
Ji et al. (2023)	186 pts, mean 52y	Mean 2.7 cm	Hypopituitarism 62%	ETS	VF improved 82%	Not reported
Present case (2026)	40y female	2.13×2.28×3.05 cm	Graves + SAI + HH + stalk PRL	ETS two-surgeon	20/200→6/6 (2 wks)	Complete all axes (12 wks)

As demonstrated in Table 4, the present case is distinguished by several notable features. First, the concurrent diagnosis of primary Graves' disease with NFPA-induced panhypopituitarism represents a unique pathophysiological combination not reported in the comparative studies. While most large series document hypopituitarism rates of 40–75% in NFPA patients, the simultaneous presence of autoimmune thyroid hyperfunction significantly complicated the diagnostic algorithm in our patient. Second, the completeness and rapidity of endocrine recovery in this case is remarkable. Published series report full endocrine recovery rates of only 10–30% following surgical decompression, whereas our patient achieved complete normalization of all affected axes within 12 weeks. This favorable outcome may be attributable to the relatively younger age of the patient, the short duration of compression-induced deficiency, and the achievement of gross total resection preserving viable adenohypophyseal tissue. Third, the visual recovery from 20/200 to 6/6 within 2 weeks is at the superior end of published outcomes, likely reflecting the reversible nature of the optic nerve compression without permanent axonal damage.[20]

4. Conclusion

This case report documents an exceptionally rare presentation of a clinically non-functioning pituitary macroadenoma with concurrent primary Graves' disease, secondary panhypopituitarism, and stalk-effect hyperprolactinemia in a 40-year-old female. The constellation of findings—primary thyroid autoimmunity obscuring secondary pituitary hormone deficiencies—represents a diagnostic challenge not

previously described in the literature. The case illustrates the critical importance of comprehensive endocrine evaluation in all patients with sellar/suprasellar masses, even when a primary endocrine disorder appears evident. The diagnostic distinction between stalk-effect hyperprolactinemia and primary prolactinoma is essential for appropriate management, as the disorders require divergent therapeutic approaches. Endoscopic transsphenoidal surgery with complete gross total resection achieved rapid visual decompression and complete recovery of all pituitary axes within 12 weeks—an outcome exceptional among reported cases. The favorable postoperative course, rapid visual field improvement, complete resolution of bitemporal hemianopsia, and normalization of all endocrine axes underscore the therapeutic potential of surgical decompression in appropriately selected patients. This case demonstrates the value of multidisciplinary collaboration among endocrinology, neurosurgery, and neuro-ophthalmology specialists in achieving optimal outcomes for complex endocrine disease presentations. Future cases with similar presentations may benefit from this detailed documentation of diagnostic and therapeutic strategies.

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