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Case Report

A Case of Invasive Pituitary Prolactinoma Misdiagnosed as Nasopharyngeal Carcinoma: Diagnostic Lessons and Management

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Abstract

Invasive pituitary adenomas with infrasellar extension can present with symptoms such as epistaxis and nasal obstruction, closely mimicking the clinical and radiological characteristics of nasopharyngeal carcinoma, which frequently leads to misdiagnosis. This report discusses the case of a 32-year-old male who was initially misdiagnosed with nasopharyngeal carcinoma for approximately one month and subsequently underwent radiotherapy and chemotherapy. However, a multidisciplinary assessment at our institution, incorporating magnetic resonance imaging findings of an invasive sellar mass, serum prolactin levels exceeding 2,000 ng/mL, and positive immunohistochemistry for PIT-1 and prolactin, established the diagnosis of an invasive prolactinoma. Treatment with bromocriptine led to significant tumor reduction. However, this was complicated by cerebrospinal fluid leakage, which subsequently resulted in an intracranial infection. The patient underwent surgical resection of the tumor and repair of the cerebrospinal fluid leak, with postoperative pathology confirming a PIT1-lineage, densely granulated, prolactin-secreting adenoma. The patient experienced a favorable recovery, with prolactin levels normalizing under continued bromocriptine therapy. This case highlights the critical importance of routine hormonal screening, thorough evaluation of nasopharyngeal mucosal integrity, and multidisciplinary collaboration in the diagnostic process.

Introduction

Pituitary adenomas represent a prevalent category of benign neoplasms originating from the anterior pituitary gland, with an estimated annual incidence of approximately 1 per 1,000 individuals.[1] These tumors are categorized into functional and non-functional subtypes based on their hormone secretory activity. Among these, prolactin (hereinafter referred to as PRL)-secreting adenomas are the most common functional subtype. The clinical manifestations of pituitary adenomas are bifurcated: functional adenomas lead to endocrine abnormalities due to hormone hypersecretion, while the mass effect of the tumor can cause symptoms such as headaches and visual field deficits.[2] Notably, approximately 30–40% of pituitary adenomas exhibit invasive growth behavior.[3] When tumors extend inferiorly, eroding the skull base and invading the nasopharynx, initial symptoms may include epistaxis and nasal obstruction, rather than the typical endocrine or visual disturbances.[4]

These atypical symptoms overlap significantly with the core clinical presentation of nasopharyngeal carcinoma (NPC), a prevalent head and neck malignancy in certain regions, including China. NPC typically arises from the nasopharyngeal mucosa and commonly presents with symptoms such as blood-stained sputum, epistaxis, nasal obstruction, and tinnitus. A characteristic feature of NPC is its tendency for superior extension through natural foramina, leading to skull base destruction and cranial nerve involvement, resulting in headache, facial numbness, and diplopia—symptoms that closely resemble those of invasive pituitary adenomas.[5] Radiologically, both entities can demonstrate extensive skull base destruction.

This significant overlap in clinical and radiological presentations creates considerable diagnostic challenges. When evaluating patients presenting with epistaxis and skull base destruction, clinicians may readily anchor their diagnosis to the more prevalent NPC, potentially overlooking a pituitary origin and leading to inappropriate management. Immunohistochemical detection of the pituitary lineage-defining transcription factor pituitary-specific positive transcription factor 1 (PIT-1) serves as a powerful tool for establishing a definitive diagnosis. This report details a case of

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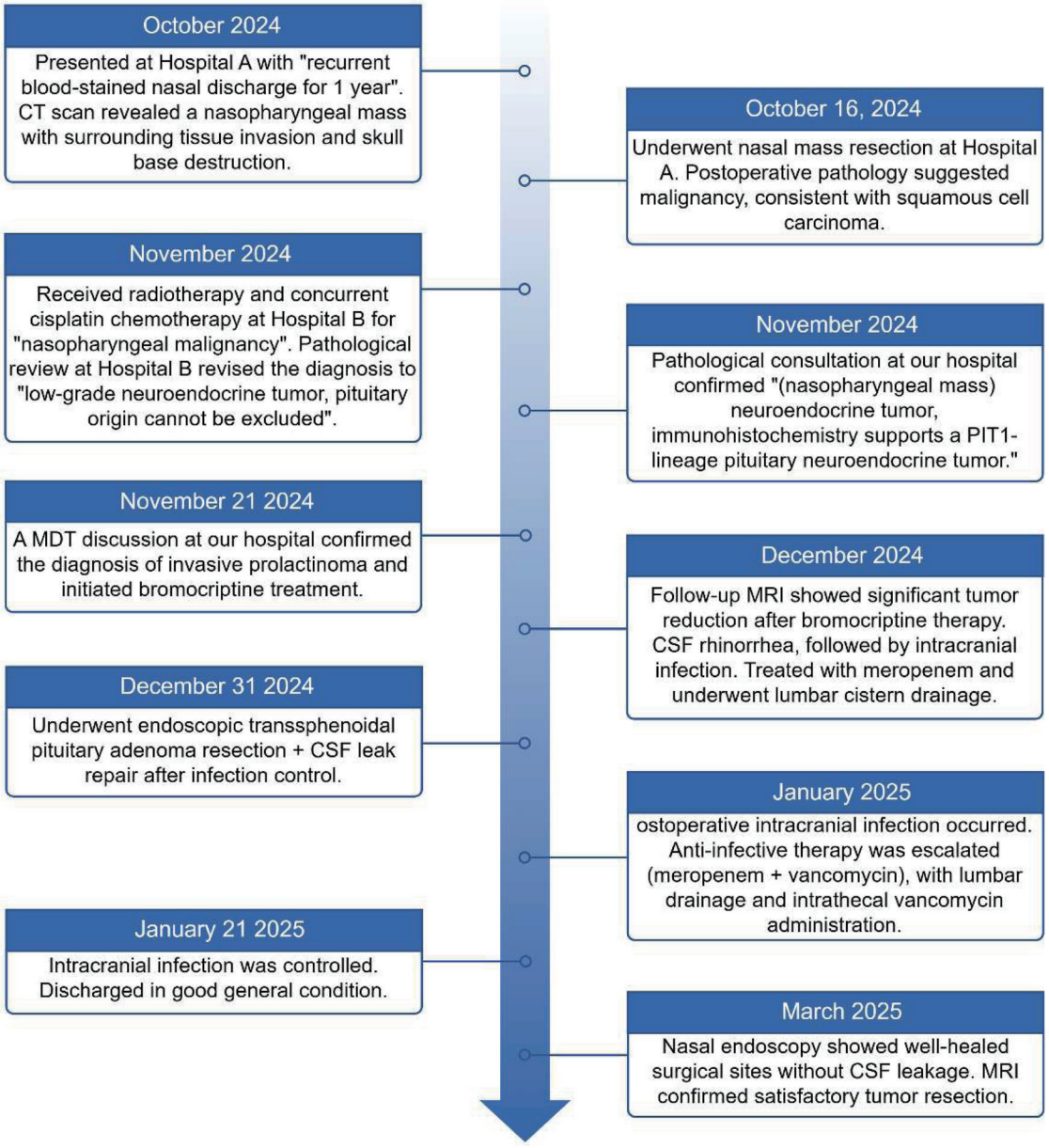

Fig. 1. Diagnostic and therapeutic timeline of the patient's clinical course. CSF, cerebrospinal fluid; CT, computed tomography; MDT, multidisciplinary team; MRI, magnetic resonance imaging; PIT1, pituitary-specific positive transcription factor 1.

invasive prolactinoma initially misdiagnosed as NPC and treated with chemoradiotherapy (Fig. 1). Through analyzing the reasons for misdiagnosis and summarizing key diagnostic points for sellar lesions, this study aims to enhance clinicians' capability in recognizing and managing such complex cases.

Case presentation

This case report was prepared in accordance with the CARE guidelines.

History and initial management

A 32-year-old male presented to a local hospital in October 2024 with a one-year history of recurrent blood-stained nasal discharge, bloody sputum, and left orbital pain. Cranial computed tomography (CT) revealed a nasopharyngeal mass with surrounding tissue invasion and skull base destruction. On October 16, 2024, he underwent resection of the nasal mass at this institution. Postoperative pathology was reported as "malignancy, consistent with squamous cell carcinoma." Subsequently, the patient was transferred to another center, where he received radiotherapy and concurrent cisplatin chemotherapy in November 2024 for "nasal and nasopharyngeal malignancy." After receiving less than one week of chemoradiotherapy, his symptoms showed no significant improvement. Pathological review at that institution revised the diagnosis to "low-grade neuroendocrine tumor, pituitary origin cannot be ex-

cluded." For further evaluation, the patient sought a pathological consultation at our hospital. Our pathological assessment indicated a neuroendocrine tumor, with immunohistochemical staining supporting a PIT1-lineage pituitary neuroendocrine tumor. The patient was admitted to our neurosurgery department on November 15, 2024, for comprehensive management.

Re-evaluation and treatment

Upon admission, a specialized neurological examination revealed no significant abnormal signs. Further investigations were then performed. Paranasal sinus CT with 3D reconstruction showed a soft tissue density lesion in the sphenoid sinus and sellar region, accompanied by destruction of the clivus, sellar floor, and sphenoid sinus walls (Fig. 2). Pituitary contrast-enhanced magnetic resonance imaging (MRI) (performed on a 3.0-T scanner, including sagittal and coronal T1- and T2-weighted sequences before and after gadolinium administration) revealed a large mass (47×39×44 mm) in the sphenoid-sellar region with marked enhancement. The lesion encased both cavernous sinuses and segments C4–6 of the internal carotid arteries, extended superiorly to involve the adenohypophysis, displaced the pituitary stalk, and elevated the optic chiasm (Fig. 2). Endocrine evaluation demonstrated a prolactin level > 2,000 ng/mL, with low testosterone (1.27 ng/mL) and estradiol (10.11 ng/mL) levels.

Subsequently, a multidisciplinary team discussion was held. The radiology expert noted that despite its invasive nature and skull base destruction, the nasopharyngeal mucosa remained intact, suggesting a sellar origin rather than a primary nasopharyngeal tumor. The pathology expert confirmed strong positivity for PIT-1 on immunohistochemistry, and combined with the markedly elevated serum prolactin, supported the diagnosis of a prolactin-secreting pituitary adenoma. The otorhinolaryngology specialist, based on nasopharyngeal endoscopy, confirmed the absence of primary nasopharyngeal tumor evidence. The endocrinology specialist integrated these findings and diagnosed an invasive prolactinoma, recommending bromocriptine as first-line treatment according to clinical guidelines. Treatment was initiated with bromocriptine at a starting dose of 2.5 mg daily, given in two divided doses.

One month after starting bromocriptine, follow-up MRI demonstrated substantial tumor regression, confirming responsiveness to medical therapy. Nevertheless, the patient developed clear nasal discharge consistent with cerebrospinal fluid (CSF) rhinorrhea. Endoscopic examination identified leakage from the left olfactory cleft and sphenoid sinus ostium; imaging confirmed CSF flow (Fig. 2). Shortly thereafter, the patient developed fever (38.9°C) and meningeal irritation signs, consistent with intracranial infection. He received meropenem and lumbar CSF drainage, which yielded clear, colorless fluid. Analysis of the CSF revealed a white blood cell count of 1/μL, a protein level of 0.34 g/L, and a glucose level of 5.06 mmol/L. Cultures were negative. Following infection control, he underwent endoscopic transsphenoidal tumor resection and CSF leak repair on December 31, 2024.

Postoperatively, he experienced a second episode of intracranial infection with fever (39°C) and neck stiffness. Combined meropenem and vancomycin therapy was initiated, along with lumbar drainage and intrathecal vancomycin administration. Initially, the CSF appeared slightly turbid and reddish. Laboratory analysis showed a markedly elevated white blood cell count of 6,475/μL, an increased protein level of 2.75 g/L, and a glucose level of 2.21 mmol/L, although cultures remained negative. After two weeks of treatment, the CSF gradually cleared and became colorless. A repeat analysis showed significant improvement: the white blood cell count dropped to 27/μL, protein decreased to 0.37 g/L, and glucose increased to 3.10 mmol/L. The patient's temperature normalized by January 15, 2025.

Histopathologic examination confirmed a pituitary neuroendocrine tumor/adenoma. Immunostaining revealed Syn (+), PRL (diffuse cytoplasmic +), PIT-1 (+), ER (partial +), and Ki-67 < 5% (Fig. 3). This immunoprofile, particularly the co-expression of PIT-1 and prolactin, confirmed the diagnosis of a PIT1-lineage, densely granulated prolactin-producing adenoma. At the three-month follow-up in March 2025, nasal endoscopy showed well-healed surgical sites with no recurrent CSF leakage, and MRI confirmed satisfactory tumor removal (Fig. 3). The patient remained on bromocriptine therapy, with serum prolactin levels stable within the normal range.

Discussion

Invasive pituitary adenomas pose significant diagnostic challenges due to their variable clinical presentations and biological behavior. This case illustrates a complex diagnostic journey, from initial misdiagnosis as NPC and inappropriate chemoradiation to eventual correct diagnosis and management. Analyzing the reasons for misdiagnosis, key differential diagnostic points, and treatment strategies provides valuable insights for recognizing atypical pituitary adenomas.

The diagnostic challenges in this case stemmed from three main areas: overlapping clinical presentations, misleading radiological features, and complexities in pathological interpretation. The patient's symptoms—blood-stained nasal discharge, hemoptysis, and orbital pain—are highly characteristic of NPC. Radiologically, the initial CT demonstrating a nasopharyngeal mass with skull base destruction reinforced the suspicion of NPC, overshadowing the critical observation that the main tumor bulk originated from the sella. However, a recent case report described an invasive NPC that presented as a sellar mass on MRI and was initially misdiagnosed as a pituitary macroadenoma.[6] This illustrates that reliance on imaging alone, without comprehensive assessment, can lead to diagnostic anchoring. Retrospective analysis highlighted the importance of the intact nasopharyngeal mucosa, a key radiological clue against a primary nasopharyngeal lesion. Pathological misinterpretation initially labeled the tumor as squamous cell carcinoma, likely due to superficial biopsy sampling that captured only the tumor's extension into the nasopharyngeal submucosa. The definitive diagnosis in this case relied on comprehensive immunohistochemical profiling, including the pituitary-specific transcription factor PIT-1, underscoring its critical role in diagnosing sellar region tumors.[7]

Mastering the fundamental principles for differentiating sellar lesions is essential in clinical practice. NPC originates from the nasopharyngeal mucosa and is typically characterized by mucosal irregularity in its early stages. In contrast, pituitary adenomas generally maintain the integrity of the nasopharyngeal mucosa, even when they invasively affect the skull base. Craniopharyngiomas often manifest as suprasellar cystic-solid masses, frequently accompanied by characteristic calcifications visible on CT imaging. Meningiomas are typically identified by a broad dural base and the presence of a "dural tail sign" on contrast-enhanced MRI. Chordomas, which originate from the midline clivus, exhibit marked hyperintensity on T2-weighted MRI sequences.[8,9] Additionally, laboratory studies play a crucial role in the differential diagnosis of sellar lesions. In this case, a significantly elevated prolactin level (>2,000 ng/mL) strongly indicates the presence of a prolactin-

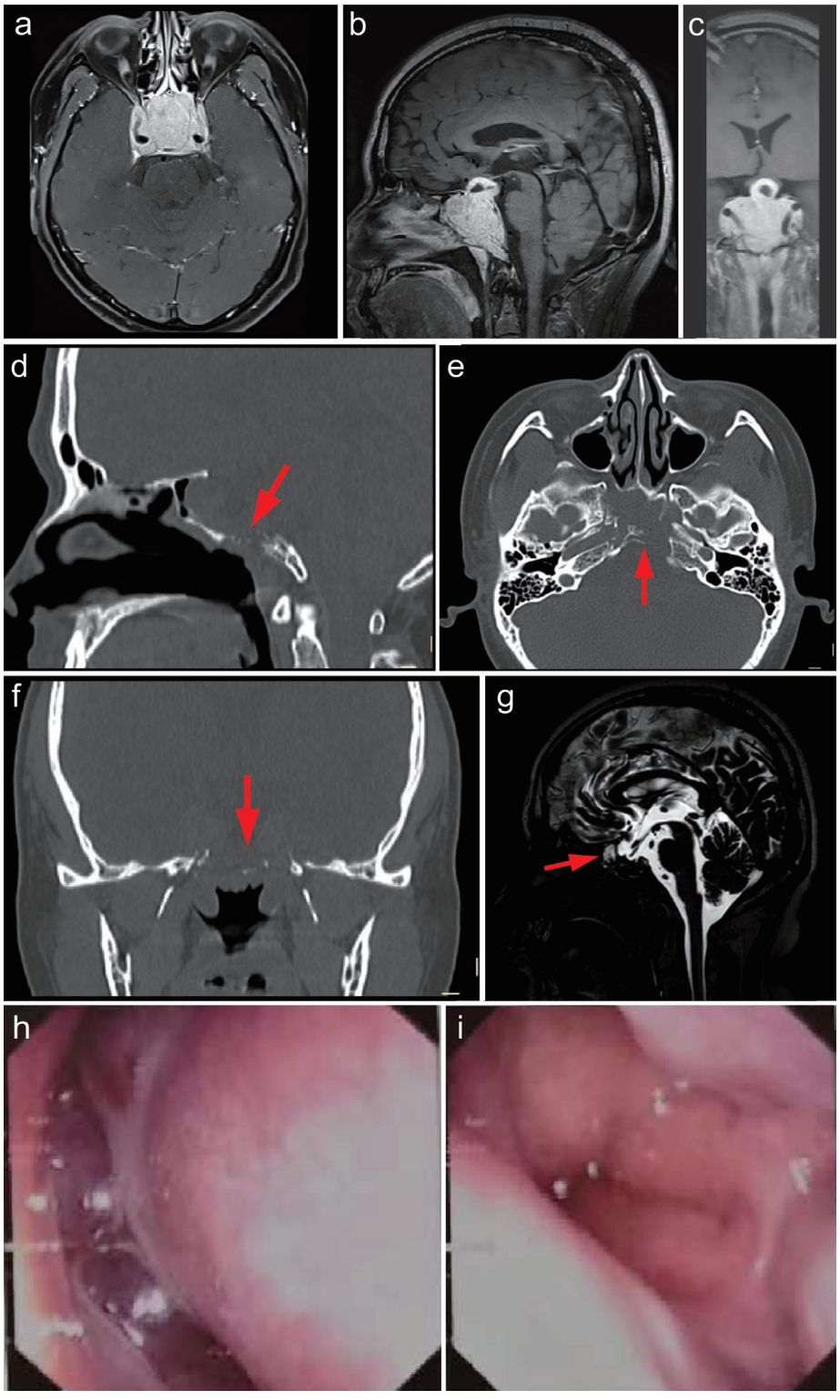

Fig. 2. Preoperative imaging and endoscopic findings. MRI shows a mass (approx. 47×39×44 mm) with marked enhancement in the sphenoid sinus and sellar region. The lesion elevates and displaces the pituitary stalk to the right, pushes the optic chiasm superiorly, and encases both bilateral cavernous sinuses along with segments C4–6 of the internal carotid arteries (a, b, c). CT reveals bony destruction of the clivus, sellar floor, and sphenoid sinus walls (d, e, f, *red arrows*). CSF hydrography demonstrates a small patch of high signal intensity in the left sphenoid sinus, suggestive of communication with the suprasellar cistern, which confirms that CSF rhinorrhea has led to intracranial infection (g *red arrow*). Nasal endoscopy shows copious secretions in the left olfactory cleft and pulsatile discharge from the left sphenoid sinus ostium (h, i). CSF, cerebrospinal fluid; CT, computed tomography; MRI, magnetic resonance imaging.

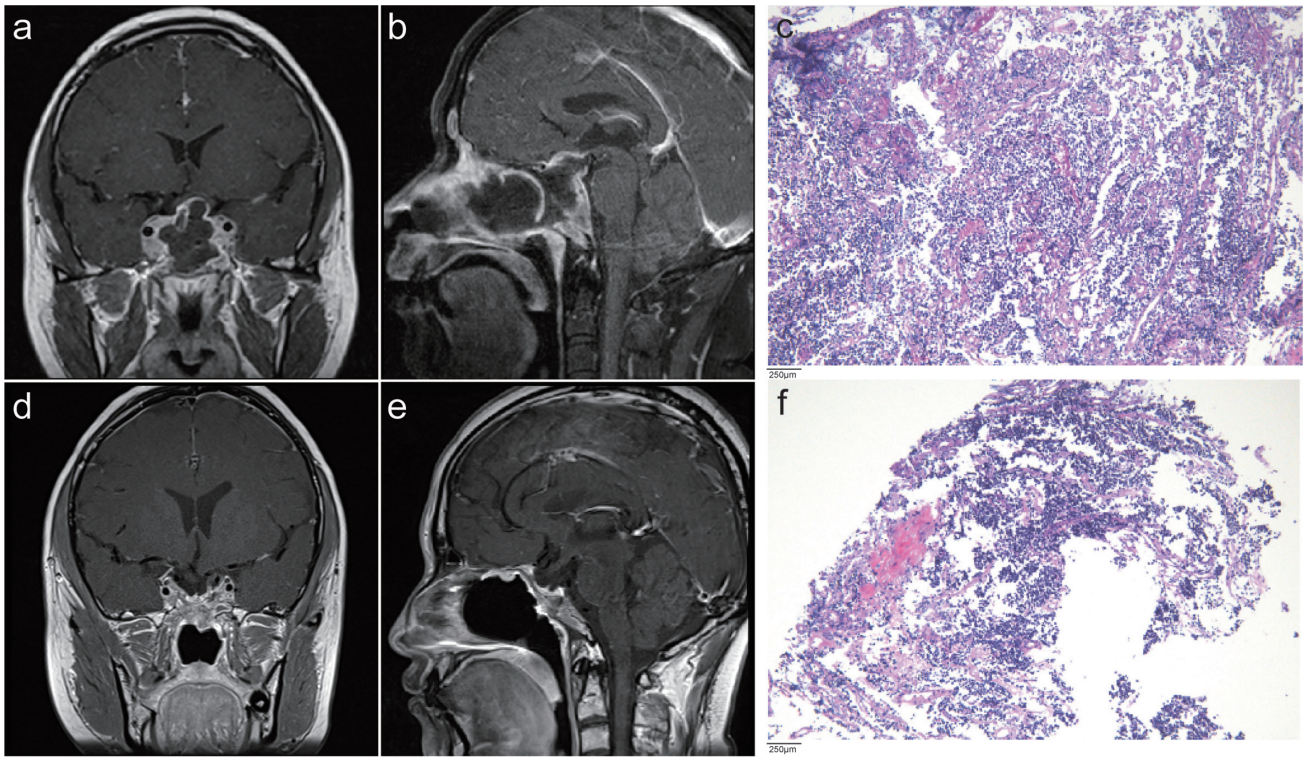

Fig. 3. Postoperative imaging and histopathological findings. Postoperative day 3 MRI demonstrates a partially empty sella with residual, markedly enhancing tumor tissue at the margins, involving bilateral cavernous sinuses and encasing the internal carotid arteries (a, b). Three-month follow-up MRI shows inferior displacement of the sella floor with a thinned pituitary gland closely apposed to the sella base, exhibiting relatively homogeneous enhancement (d, e). Histopathological diagnosis was pituitary neuroendocrine tumor (PitNET)/pituitary adenoma. Combined with immunohistochemical staining results, the findings are consistent with a PIT1-lineage tumor (favoring a densely granulated lactotroph tumor) (c, f). MRI, magnetic resonance imaging; PIT1, pituitary-specific positive transcription factor 1.

secreting macroadenoma. Consequently, routine preoperative hormonal screening for skull base lesions can substantially enhance diagnostic accuracy. Pala *et al*., in a retrospective clinical study of 47 rare sellar lesions, found that relying solely on preoperative imaging resulted in a remarkably high misdiagnosis rate (38%). Multidisciplinary evaluation and image-guided biopsy were identified as key measures for achieving a definitive diagnosis.[10] Ultimately, integrating imaging characteristics, clinical presentation, and laboratory findings within a multidisciplinary team framework is vital for accurate diagnosis and management.

This case also highlights the complexities in managing invasive prolactinomas. Following guideline recommendations, a dopamine agonist was the initial treatment. The significant tumor reduction with bromocriptine confirmed the central role of medical therapy for prolactinomas.[11] However, rapid shrinkage of invasive macroadenomas carries a well-documented risk of CSF leakage and subsequent intracranial infection.[12] Invasive prolactinomas often erode skull base structures, such as the sphenoid sinus and clivus, causing bony defects and dural penetration. The pharmacologically induced rapid tumor regression can expose these pre-existing dural and osseous defects, leading to CSF rhinorrhea.[13] Therefore, for patients with these high-risk features, close monitoring for symptoms such as rhinorrhea, headache, or fever during medical treatment is crucial. Surgical repair is the recommended initial treatment for definitive management of dopamine agonist-induced rhinorrhea.[14] For patients who are not immediate surgical candidates, a temporary cessation of medication combined with lumbar drainage might be considered.[14] In this case, surgical intervention was undertaken, achieving both tumor resection and successful skull base reconstruction. Although postoperative intracranial infection occurred, it was effectively managed with tailored antibiotics and CSF drainage. This sequence underscores the importance of a comprehensive treatment strategy for invasive adenomas. The final pathological diagnosis of a PIT1-lineage, densely granulated prolactinoma aligns with the observed favorable response to dopamine agonist therapy.

The absence of a multidisciplinary team (MDT) approach during the initial diagnostic process contributed significantly to the misdiagnosis in this case. This experience reinforces the indispensable value of the MDT model in managing complex sellar lesions. Integrating radiologic, pathologic, endocrinologic, and surgical expertise facilitated accurate diagnosis, guided individualized treatment, and improved patient outcomes. For complex sellar lesions with atypical presentations, an MDT approach mitigates cognitive bias and ensures comprehensive care.

This study has several limitations that should be acknowledged. First, the findings and conclusions are derived from a single case, which inherently limits their generalizability. Second, the retrospective design may introduce biases in data collection and interpretation. Furthermore, the follow-up period of three months is relatively short to assess long-term tumor recurrence and hormonal stability. Future prospective studies with larger cohorts and longer follow-up are needed to validate our observations and refine the management strategies for such complex cases.

Conclusions

This case underscores that pituitary tumors should be included in the differential diagnosis of lesions presenting with nasopharyngeal symptoms and skull base destruction, even when imaging suggests extensive invasion. A thorough preoperative evaluation, including detailed imaging and serum hormonal assessments, should be routinely performed. It is imperative to avoid anchoring the diagnosis solely on initial pathology results while neglecting routine serum hormonal screening for invasive skull base lesions. The MDT approach serves as an effective means to enhance diagnostic accuracy when facing diagnostic challenges. Furthermore, this case demonstrates the necessity for clinicians to anticipate and manage associated complications throughout the disease course. The insights gained from this case provide valuable experience in enhancing clinicians' capability to recognize atypical presentations of pituitary adenomas and effectively manage related complications.

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Conflict of interest

Prof. Hongyang Zhao is an Editor-in-Chief and Prof. Xiaobing Jiang is an Executive Associate Editor of *Neurosurgical Subspecialties*. The authors have no other conflict of interest to note.

Author contributions

Writing-original draft preparation, image processing (QL, YZ, KQ, XH), project administration, and supervision (HZ, XJ, HW). All authors have made significant contributions to this study and have approved the final manuscript.

Ethical statement

The study was conducted in accordance with the ethical standards of the institutions to which we are affiliated and with the Declaration of Helsinki (as revised in 2024). Written informed consent was obtained from the patient for reporting the case and accompanying images.

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