ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Unique Case Observations

Editor
S. Ather Enam, MD, PhD
Aga Khan University, Karachi, Sindh, Pakistan

SNI
Open Access

Case Report

Invasive pituitary adenoma presenting with cerebrospinal fluid rhinorrhea and meningitis – A case report

Zanib Javed[1], Zunaira Saeed[1], Sibgha Khan[2], Altaf Ali Laghari[1]

Departments of [1]Neurosurgery and [2]Radiology, Aga Khan University Hospital, Karachi, Pakistan.

E-mail: *Zanib Javed - zanib.javed@aku.edu; Zunaira Saeed - zunairasaeed06@gmail.com; Sibgha Khan - sibgha.sk@gmail.com; Altaf Ali Laghari - altaf.alilaghari@aku.edu

***Corresponding author:**
Zanib Javed,
Department of Neurosurgery,
Aga Khan University Hospital,
Aga Khan University Hospital,
Karachi, Pakistan.

zanib.javed@aku.edu

Received: 26 March 2024
Accepted: 05 August 2024
Published: 06 September 2024

DOI
10.25259/SNI_224_2024

Quick Response Code:

ABSTRACT

Background: Most pituitary neuroendocrine tumors are benign, except some adenomas that show invasiveness and are called invasive pituitary adenomas. These are challenging and rare pathologies.

Case Description: We present a case of a 40-year-old male who presented to the emergency with seizures, rhinorrhea, headache, and drowsiness. Radiology images showed a sellar mass with supra-sellar extension and pneumocephalus. The pituitary profile was within normal limits. The patient underwent bifrontal craniotomy and maximum safe resection of the lesion with cerebrospinal fluid (CSF) leak repair and lumbar drain insertion. Histological examination and immunohistochemical stain were consistent with pituitary adenoma. Postoperatively, there was no CSF leak, and the patient's Glasgow Coma Scale improved.

Conclusion: Rhinorrhea is a unique presentation for pituitary adenoma. According to the current literature, surgery is the only effective treatment as part of the management of invasive pituitary adenomas, along with a multidisciplinary approach.

Keywords: Invasive pituitary adenomas, Meningitis, Pneumocephalus, Rhinorrhea

INTRODUCTION

Around 10–15% of all intracranial tumors will be pituitary adenomas, 80% of which will be benign pituitary adenomas, and the rest will be substantial risk adenomas or metastatic tumors.[8] Pituitary neuroendocrine tumors are slow-growing, noninvasive, and will remain in the sella. However, invasive pituitary adenomas are rare, with a tendency to invade the surrounding structures and show rapid progression as well as resistance to standard treatments, although histopathology is like benign adenoma.[1,9] These are associated with a higher risk of recurrence due to the challenges in surgical resection, such as the enormous size of the tumor, invasion into the suprasellar area, or the cavernous sinus or bone extension that renders it difficult to remove the tumor completely. Radiotherapy, chemotherapy, or medications are usually necessary after surgery, whether it is transcranial or transsphenoidal. Based on functionality, prolactinomas are the most common, followed by nonfunctional pituitary adenomas and growth hormone (GH) secreting adenomas, with thyroid-stimulating hormone and gonadotropin-releasing hormone adenomas being the rarest.[5] As part of this report, we will discuss a case of invasive pituitary adenoma along with a literature review on this tumor.

CASE PRESENTATION

A 40-year-old gentleman sought urgent medical attention at the emergency department, reporting a 2-year history of untreated seizures. He presented with a sudden onset of watery discharge from his nose, accompanied by a persistent headache and drowsiness over the past day. Upon arrival, his vital signs were stable, and a thorough general examination revealed no significant abnormalities. However, neurological evaluation disclosed concerning findings, including a Glasgow Coma Scale (GCS) score of E1V1M5, along with evident cerebrospinal fluid (CSF) leak and bilaterally reactive pupils. A computed tomography scan was done in the emergency department, which showed a significantly distended sella housing low attenuation mass lesion measuring 35 × 27 mm (about 1.06 in), causing significant thinning of the adjacent sella bone with erosion. On the left side of the suprasellar region, there was a soft tissue mass measuring 22 × 13 mm (about 0.51 in) with adjacent mild perilesional edema, an extension of the sellar lesion, or tumor bleed. Multiple small, scattered foci of air specks were noted, most of which were in the subarachnoid space representing pneumocephalus [Figure 1].

The patient was intubated in the emergency department due to low GCS and managed in the intensive care unit. Broad-spectrum IV antibiotics were started. The pituitary profile showed normal levels of thyroid-stimulating hormone and free thyroxine with slightly low free triiodothyronine. Follicle-stimulating hormone, luteinizing hormone, prolactin, testosterone, cortisol, and insulin-like growth factor-1 were within normal limits. Brain magnetic resonance imaging (MRI) demonstrated an expansile solid cum cystic lesion measuring 35 × 35 × 25 mm (about 0.98 in) in anteroposterior × transverse × craniocaudal in the sella with predominant cystic component and peripheral enhancing nodular soft-tissue rim dimensions. There was an obliteration of diaphragmatic sella with intracranial extension of the lesion in the left parasagittal location with mild surrounding edema. This part of the lesion showed postcontrast enhancement and restriction on diffusion-weighted images. Foci of signal dropout were noted on susceptibility-weighted imaging representing hemorrhage measuring 25 × 15.5 mm in axial dimensions. Abnormal patchy intra-ventricular enhancement was seen in the posterior horns of lateral ventricles. The cystic component was laterally abutting the internal carotid and cavernous sinus bilaterally. Anteriorly, it was reaching up to the cribriform plate. Posteriorly, it was abutting the pituitary gland; however, it was separately visualized and was being pushed by the lesion. The pituitary stalk was deviated to the right side. There was a diffuse meningeal enhancement. Anteriorly, the lesion reached up to the pterygopalatine fossa bilaterally (more on the right side) with erosion of the skull base anterior to the lacerum [Figure 1].

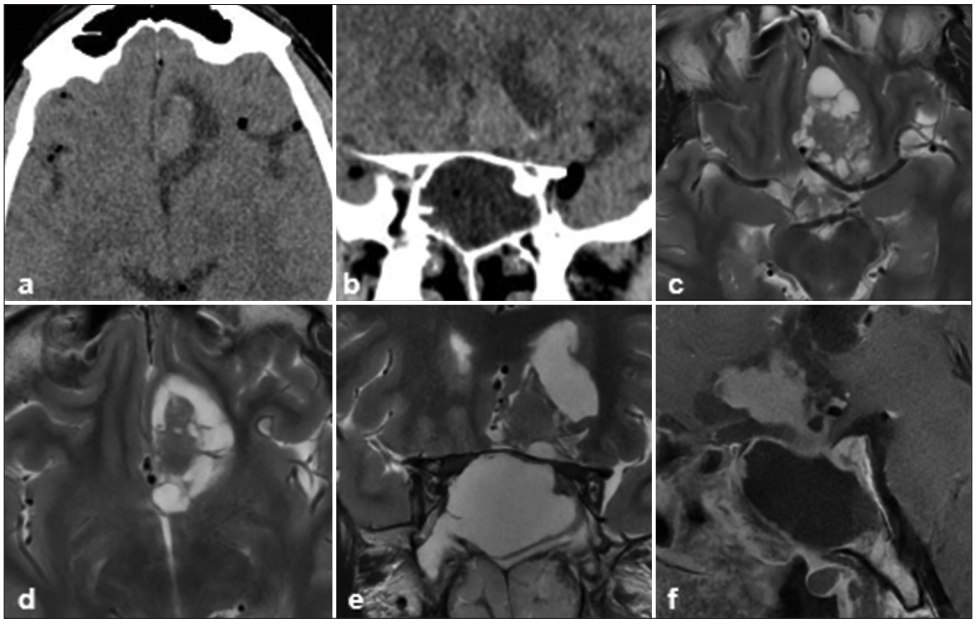

Figure 1: (a and b) Computed tomography scan axial sections showing the sella with pneumocephalus and lesion in suprasellar location. (c and d) axial T2-weighted images showing lobulated solid cum cystic lesion in the left suprasellar location, abutting the frontal lobe parenchyma and anterior cerebral arteries, (e) coronal T2-weighted image showing the same lesion in suprasellar location with expanded sella. (f) Sagittal T1 postcontrast image showing expanded sella with a lesion in suprasellar location and along posterior wall. The solid part of the lesion is showing homogenous enhancement.

The patient underwent a neuro-navigation guided bi-frontal craniotomy for the maximal safe resection of the lesion and repair of the cerebrospinal fluid (CSF) leak. The lesion was identified as a cystic and solid component within the sella, extended to the point of causing erosion of the sphenoid bone. A 5 mL sample of necrotic tumor, resembling thick purulent liquid, was aspirated and sent for microbiological culture. The tumor was then gradually debulked by piecemeal removal. Reconstruction and repair of the CSF leak involved covering the cribriform plate and sellar floor with a fascia lata graft, followed by the application of fat, surgical sealant, and Spongostan. Subsequent analysis of a frozen section of the tumor indicated a single piece of tissue measuring 0.5 × 0.4 cm, labeled as a neoplastic sellar lesion, with the potential for metastasis or lymphoma not entirely ruled out. The lumbar drain was kept for 5 days. Histopathological examination revealed fragments of a neoplastic lesion composed of sheets and nests of cells having round-to-oval hyperchromatic nuclei with stippled chromatin and moderate pale cytoplasm. Immunohistochemical stains were performed, which showed the following reactivity pattern: synaptophysin positive, CKAE1/AE3 negative, CD20 negative, CD3 negative, GFAP negative, and Ki-67 low. There was no evidence of malignancy, thereby confirming the diagnosis of pituitary adenoma based on morphological features and immunohistochemical profile [Figure 2]. Pus culture was negative for acid–fast bacilli and fungi but showed few colonies of multidrug-resistant *Acinetobacter baumannii* with sensitivity to gentamicin, tobramycin, and trimethoprim/cotrimoxazole.

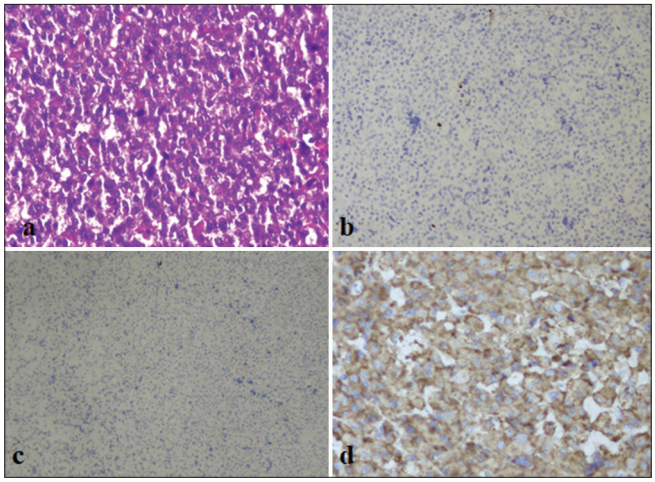

Figure 2: Histopathology. (a) Haematoxylin and eosin stain sections reveal fragments of neoplastic cells composed of sheets and nests of cells having round to oval hyperchromatic nuclei with stippled chromatin and moderate pale cytoplasm. (b) Immunohistochemical stains show low MIB, (c) CKAE1/AE3 negative and (d) Synaptophysin positive.

Postoperatively, the patient was managed in the intensive care unit with infectious disease and endocrinology on board. He developed partial left third nerve palsy. There was no CSF

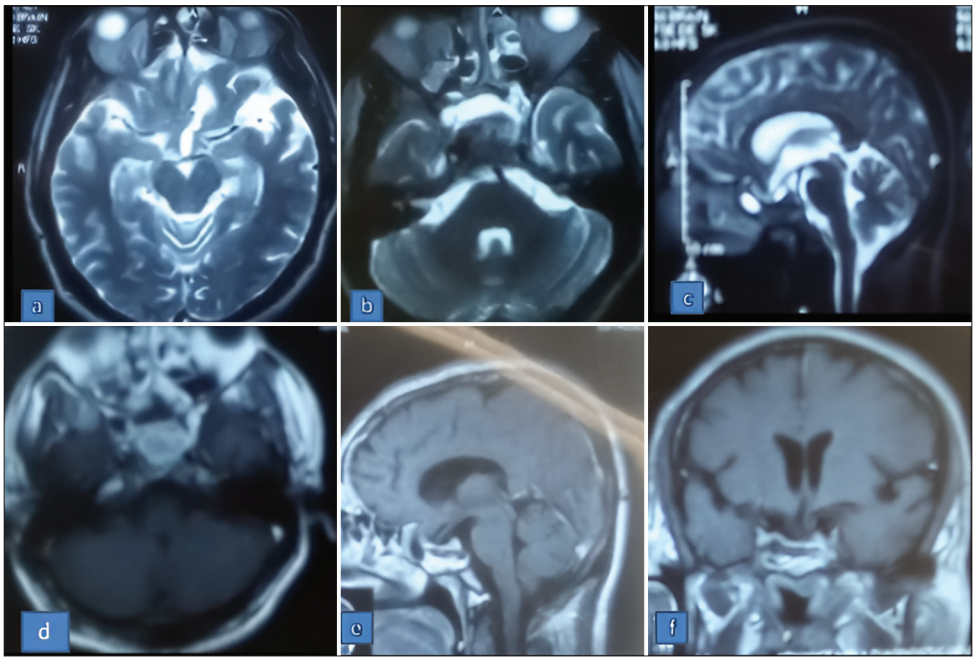

Figure 3: (a-c) Axial and sagittal T2-weighted images resection of previously seen solid cum cystic lesion in the left suprasellar location with postsurgical changes. (d-f) T1 postcontrast images axial, sagittal, and coronal showing small enhancing residual lesions in the suprasellar location. The residual sellar lesion shows homogenous enhancement.

leak or seizures. Due to difficulty in weaning, a tracheostomy was done on the 6th postoperative day. The patient's GCS improved to E4VTM6. Subsequent CSF cultures showed no growth of any organism. The lumbar drain was removed on the 5th postoperative day, and there were no complications. The patient was discharged on the 15th postoperative day. Postoperative MRI after 3 months showed some residual disease. He received stereotactic radiosurgery of 25 Gy in 5 fractions after 6 months of surgery. At his last follow-up 1 year after surgery, the patient's progress was encouraging, with stable disease progression noted [Figure 3], along with improvements in visual deficits and the restoration of pituitary function. This milestone marked a significant achievement in the patient's journey toward recovery, underscoring the importance of timely intervention, comprehensive care, and ongoing support in complex medical cases such as this one.

CASE DISCUSSION

About 5% of pituitary adenomas become locally invasive. Rapid progression of symptoms and invasiveness is the defining criterion that differentiates locally invasive pituitary adenomas from benign adenomas. The genetic make-up of these tumors may differ from more benign adenomas, even though the histology is similar.[1] Most of the invasive pituitary adenomas present with compression of the optic apparatus, extraocular muscle deficits with cavernous sinus invasion, and exophthalmos with orbital invasion due to compromise of orbital venous drainage. Hydrocephalus due to suprasellar extension obstructing one or both foramen of Monro is also common. Nasal blockage may result from skull base invasion. CSF rhinorrhea may be precipitated by tumor shrinkage in response to dopamine agonists (e.g., bromocriptine) due to uncovering areas of bone erosion. This carries the risk of ascending meningitis.[3] Our patient presented with intracranial extension, invasion of the sphenoid bone with CSF leak, no hydrocephalus, and normal endocrine parameters.

In the literature, most instances involving CSF leaks (73%) happened after the start of medical treatment, but in about 27% of the cases, the CSF leak emerged as a presenting symptom of a pituitary adenoma. 81% of patients who developed CSF leaks following initiation of medical therapy had prolactinomas. 11% had nonfunctioning pituitary adenoma, 4% had a GH-secreting adenoma, 2% had mammosomatotroph cell adenoma, and 2% had adrenocorticotrophic hormone (ACTH)-secreting adenoma.[6,11] In 97% of cases, dopamine agonists were associated with CSF leaks, and a somatostatin analog (lanreotide) in the rest of the cases.[7] Our patient was a case in point because the CSF leak was spontaneous, and he had a nonfunctioning pituitary adenoma.

Patients who developed spontaneous (noniatrogenic) CSF leaks, like our patient, had a variety of pituitary adenomas, with 42% having prolactinomas, 42% nonfunctioning pituitary adenomas (as in the case of our patient), 8% GH-secreting adenomas, and 8% ACTH-secreting adenomas.[7]

Wilson's system (modified from Hardy) of anatomic classification of pituitary adenoma grades these tumors according to the extent of suprasellar and parasellar extension as well as invasion into the floor of sella, sphenoid bone, and distant spread.[10] Our patient presented with grade D IV due to intracranial extension and diffuse destruction of the sellar floor. In the literature, GH-secreting adenomas and prolactinomas commonly invade the sellar floor and infrasellar space, whereas nonfunctioning pituitary adenomas invade the suprasellar space. Our patient's tumor had suprasellar invasion with intracranial extension. In some cases, the tumor occludes these openings due to invasion and serves as a "plug," and no CSF leak is observed. However, any major shrinkage of the tumor can act as a pathway for the CSF to escape. This can happen due to initiation of dopamine agonist therapy, intratumoral infarction or hemorrhage with subsequent reduction in tumor volume, ongoing invasion through the arachnoid or bony skull base, and a CSF fistula as a result of increases in intracranial pressure.[7] As per the literature, the prevalence of meningitis in conjunction with CSF rhinorrhea is uncommon (14%), unlike our patient, whose culture was positive.[2,7]

A review of treatment modalities showed surgical intervention as the definitive treatment for the CSF leak carried out in 88% of cases. The most common definitive procedures for CSF leaks included trans-sphenoidal surgery (70%). Craniotomy was done in 11% (also employed in the case of our patient), and lumboperitoneal shunt in 4%.[4] In patients who were presented after initiation of dopamine agonists, bed rest and withdrawal of medications seem to be the most common treatment modalities employed. Some patients were also successfully treated with temporary lumbar drainage. CSF rhinorrhea may persist in a small subset of patients in whom surgery is not performed, either due to the patient's personal choice or medical contraindications. In some minorities of patients, surgery might not be performed due to medical contraindications or patient preference, resulting in ongoing CSF rhinorrhea.[11] In the literature, rhinorrhea recurred despite initial surgical treatment in some patients (13%). Of these cases, rhinorrhea was ultimately resolved with a trans-sphenoidal approach in the majority of cases. The rest of the patients underwent a trans-frontal approach, a craniotomy, or a lumboperitoneal shunt placement. It also subsided without treatment in a minority of the patients.[7] As per the last follow-up of our patient, 12 months after the surgery, there were no complaints of nasal discharge or CSF leak.

CONCLUSION

Locally invasive pituitary adenomas, impacting 5% of cases, show rapid progression and often cause optic compression

and CSF leaks. Our patient, with a nonfunctioning pituitary adenoma, had an intracranial and extracranial extension and CSF leak without hydrocephalus. Surgery with tumor resection and skull base reconstruction is the main treatment for CSF leaks, with dopamine agonist withdrawal and bed rest as adjuncts in cases of prolactinomas. Recurrence, though rare, may require further surgery. Notably, our patient showed sustained improvement without CSF leak recurrence, even 1-year postsurgery, indicating successful management.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent is not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Amar AP, Hinton DR, Krieger MD, Weiss MH. Invasive pituitary adenomas: Significance of proliferation parameters. Pituitary 1999;2:117-22.
2. Boscolo M, Baleriaux D, Bakoto N, Corvilain B, Devuyst F. Acute aseptic meningitis as the initial presentation of a macroprolactinoma. BMC Res Notes 2014;7:9.
3. Cohn EM. Handbook of neurosurgery, 7th edition. Neuroophthalmology 2011;35:54.
4. Esposito D, Olsson DS, Ragnarsson O, Buchfelder M, Skoglund T, Johannsson G. Non-functioning pituitary adenomas: Indications for pituitary surgery and post-surgical management. Pituitary 2019;22:422-34.
5. Glezer A, Bronstein MD. Prolactinoma. Arq Bras Endocrinol Metabol 2014;58:118-23.
6. Kanemitsu T, Ikeda N, Fukumura M, Sakai S, Oku H, Furuse M, *et al*. Pituitary stone resulting in visual dysfunction and spontaneous rhinorrhea in nonfunctioning pituitary adenoma: Illustrative case. J Neurosurg Case Lessons 2021;1:CASE2029.
7. Lam G, Mehta V, Zada G. Spontaneous and medically induced cerebrospinal fluid leakage in the setting of pituitary adenomas: Review of the literature. Neurosurg Focus 2012;32:E2.
8. Møller MW, Andersen MS, Glintborg D, Pedersen CB, Halle B, Kristensen BW, *et al*. Pituitary adenoma. Ugeskr Laeger 2019;181:V05180331.
9. Sav A, Rotondo F, Syro LV, Di Ieva A, Cusimano MD, Kovacs K. Invasive, atypical and aggressive pituitary adenomas and carcinomas. Endocrinol Metab Clin North Am 2015;44:99-104.
10. Serioli S, Doglietto F, Fiorindi A, Biroli A, Mattavelli D, Buffoli B, *et al*. Pituitary adenomas and invasiveness from anatomo-surgical, radiological, and histological perspectives: A systematic literature review. Cancers (Basel) 2019;11:1936.
11. Vieira Neto L, Boguszewski CL, Araújo LA, Bronstein MD, Miranda PA, Musolino NR, *et al*. A review on the diagnosis and treatment of patients with clinically nonfunctioning pituitary adenoma by the neuroendocrinology department of the Brazilian society of endocrinology and metabolism. Arch Endocrinol Metab 2016;60:374-90.

How to cite this article: Javed Z, Saeed Z, Khan S, Laghari AA. Invasive pituitary adenoma presenting with cerebrospinal fluid rhinorrhea and meningitis – A case report. Surg Neurol Int. 2024;15:318. doi: 10.25259/SNI_224_2024