

# Seeding of Pituitary Carcinoma Throughout the Neuraxis: Lessons from an Interesting Case

Masoud Shirvani<sup>1</sup>, Mohammadali Arami<sup>2\*</sup>, Behrang Kazeminezhad<sup>3</sup> and Zeynab Kishani Farahani<sup>4</sup>

<sup>1</sup>Department of Neurosurgery, Salamat Farda Hospital, Tehran, Iran

<sup>2</sup>Department of Neurology, Salamat Farda Hospital, Tehran, Iran

<sup>3</sup>Associate Professor of Pathology, Pediatric Pathology Research Center, Modarres Hospital. Shahid Beheshti University of Medical Sciences. Tehran, Iran

<sup>4</sup>Department of Pathology, Salamat Farda Hospital, Tehran, Iran

## \*Corresponding Author

Mohammadali Arami, Department of Neurology, Salamat Farda Hospital, Tehran, Iran.

Submitted: 2025, Mar 03; Accepted: 2025, Mar 10; Published: 2025, Mar 28

**Citation:** Shirvani, M., Arami, M., Kazeminezhad, B., & Farahani, Z.K. (2025). Seeding of Pituitary Carcinoma Throughout the Neuraxis: Lessons from an Interesting Case. *J Clin Rev Case Rep*, 10(3), 01-06.

## Abstract

**Background:** Pituitary neuroendocrine tumors are predominantly benign, although a minority may exhibit invasive tendencies. Only a small percentage of pituitary tumors show evidence of neuraxis seeding. Assessing the risk of spread and metastasis is crucial for timely diagnosis and effective treatment in these cases.

**Case Description:** This article presents a case of pituitary carcinoma diagnosed four years apart, following two surgeries for pituitary macroadenoma, and subsequent spread throughout the spinal canal. A third surgery was performed to address lumbosacral metastasis, and histopathological findings, including immunohistochemistry studies, confirmed the diagnosis of metastatic pituitary carcinoma.

**Conclusions:** This case can contribute to refining future clinically relevant definitions of the disease. Additionally, predicting aggressiveness and the potential for malignant transformation using clinical, imaging, histopathological, and molecular-genetic criteria is essential for managing these tumors.

**Keywords:** Non-functional pituitary macroadenoma, Tumor seeding, Neuraxis, Pituitary carcinoma

## 1. Introduction

The pituitary gland is a small gland located at the base of the skull, beneath the hypothalamus. It regulates growth, metabolism, stress response, and the function of the sex organs by controlling the thyroid gland, adrenal glands, ovaries, and testicles.

Pituitary tumors are among the most common tumors found at the base of the skull [1]. They are often diagnosed late because their symptoms are vague and can mimic those of many other common diseases. Treatment is generally determined by the type and size of the tumor, the pressure it exerts on surrounding structures such as the brain and visual pathways, as well as the

patient's age and overall health. Currently, three types of treatment are used: surgical removal of the tumor, radiation therapy, and drug therapy. In some cases, medications are employed to inhibit the tumor's hormone production, which may also lead to tumor shrinkage. Early diagnosis and appropriate treatment are crucial for improving prognosis.

While pituitary adenomas are typically benign, a large case series has reported a recurrence rate of 30% for those operated on via the transcranial approach [2]. In this article, we present a rare case of a pituitary adenoma or unusual pituitary carcinoma that has spread throughout the nervous system, including the brain and cervical,

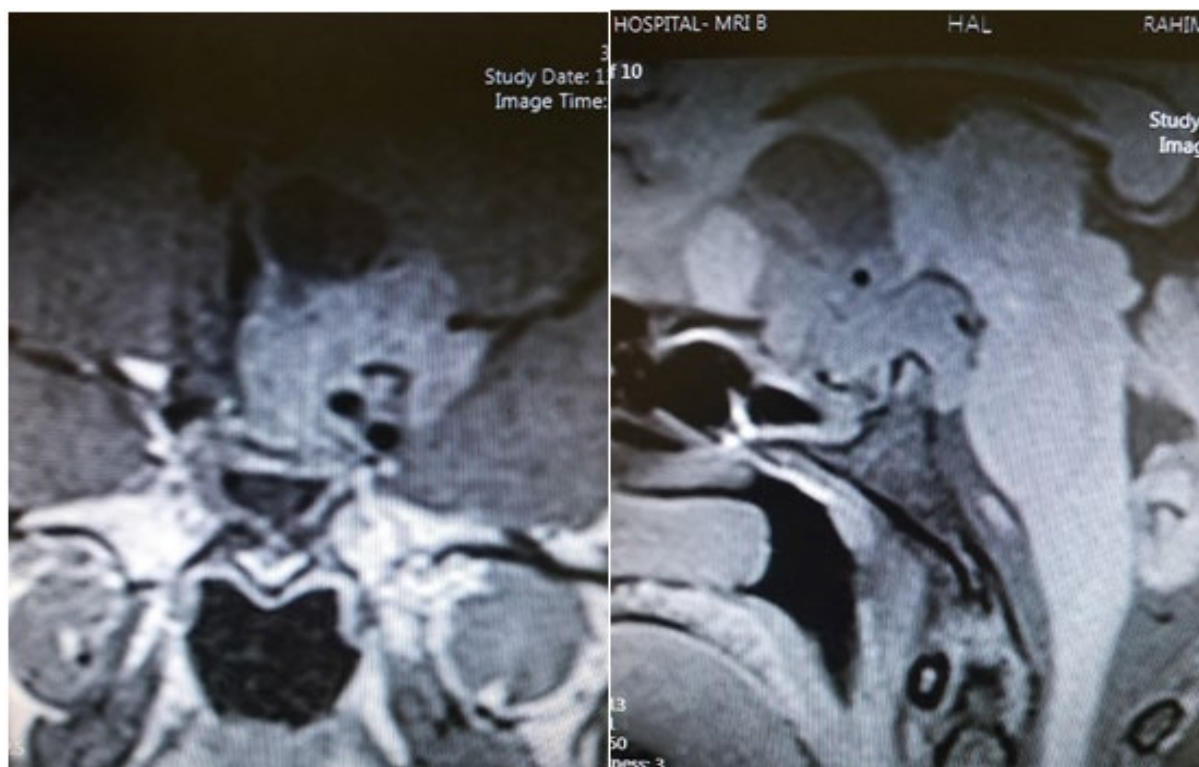
thoracic, and lumbosacral canals. We also review other reports to provide recommendations for better management of these invasive tumors.

## 2. Case Presentation

A 46-year-old man presented to the neurosurgery department of Milad General Hospital in 2018, reporting persistent headaches that had lasted for the past four months. During the history-taking, the patient described a gradual onset and progression of headaches without accompanying nausea or vomiting. He also experienced occasional transient blurred vision and brief episodes of dizziness. Neurological examination, including assessments of sensory and motor systems, cerebellar tests, and cranial nerve evaluation, revealed no deficits. Fundoscopy indicated slight pallor of the left

optic disc. Serum levels of prolactin, thyroid hormones, growth hormones, sex hormones, and electrolytes were within normal ranges.

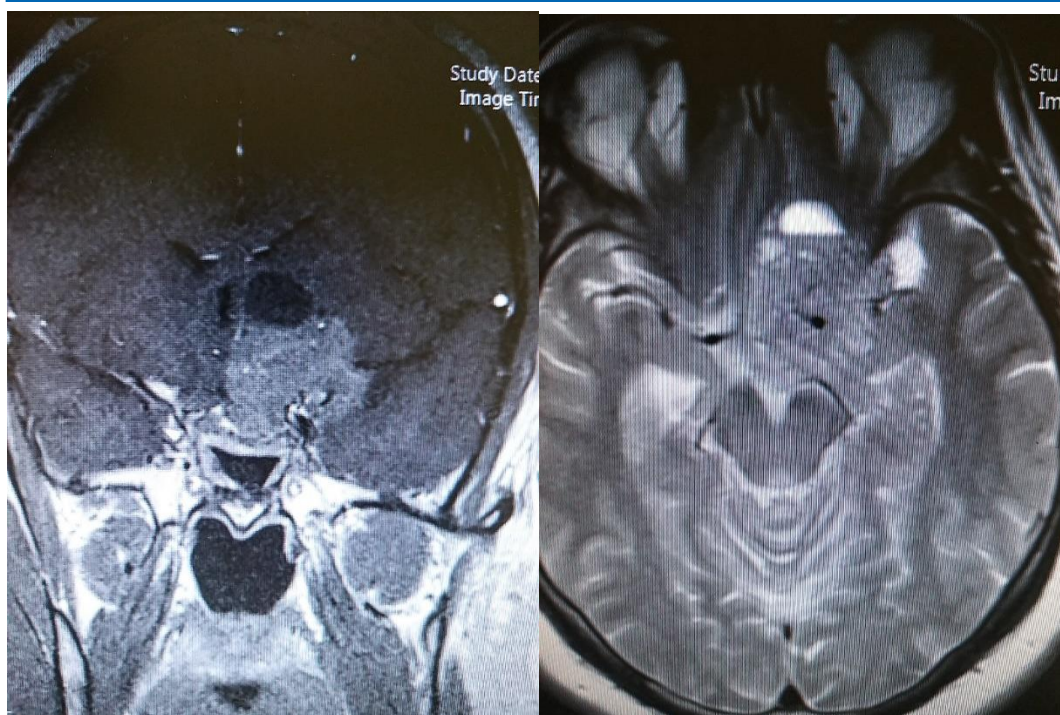
Further investigation through focused brain MRI with contrast revealed a large lobulated, heterogeneously enhancing lesion in the sellar, left parasellar, suprasellar, and left temporal regions (Figure 1), consistent with a pituitary macroadenoma. The patient was diagnosed with a nonfunctional pituitary macroadenoma and was considered a candidate for transnasal transsphenoidal endoscopic excision of the tumor under general anesthesia. The histopathological report confirmed a nonfunctional pituitary adenoma without immunohistochemical study.



**Figure 1:** Pituitary macroadenoma, coronal and sagittal MRI with contrast.

One year after surgery (2019), the patient returned with worsening vision problems. Perimetry revealed bitemporal hemianopia, and MRI indicated tumor recurrence (Figure 2). Laboratory tests showed a fourfold increase in serum prolactin levels. The patient then underwent a second transcranial microscopic surgery for

recurrent macroadenoma, during which the tumor was completely removed. The histopathological findings remained consistent with the previous report. Subsequently, the patient was referred for radiotherapy to the tumor region.



**Figure 2:** Recurrent pituitary macroadenoma, Axial and coronal MRI with contrast (2019)

Four years later, the patient presented for the third time, reporting symptoms of lumbosacral involvement, including lower limb paresthesia and back pain. An MRI of the brain and entire spinal cord was performed, revealing tumor seeding as multiple lesions

throughout the neuraxis, including the posterior border of the medulla, cervical, thoracic, and lumbosacral spinal canal (Figure 3). There was no recurrence of the pituitary tumor.

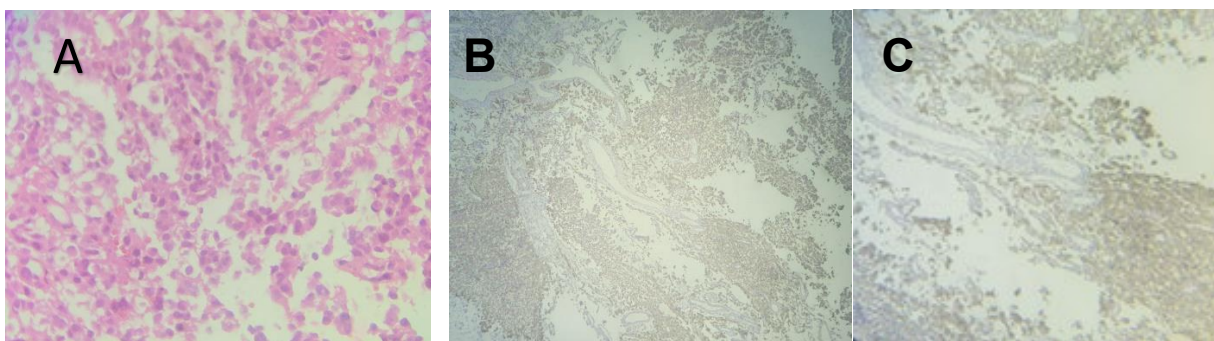


**Figure 3:** Cervical, thoracic and lumbosacral MRI with contrast shows multiple lesions throughout neuraxis.

Given the extensive and symptomatic nature of the lumbosacral lesion, surgery was performed to remove a large portion of the tumor. Histopathological findings, including immunohistochemistry

studies, were consistent with metastatic pituitary carcinoma (Ki67: proliferative activity index up to 10%). Figure 4 illustrates the pathological findings of the tumor.





**Figure 4:** A) Histologic evaluation reveals solid sheets to nests within a fibrovascular stroma and foci of dyscohesive growth. Cytologically uniform nuclear morphology with stippled chromatin, inconspicuous nucleoli and moderately abundant cytoplasm are evident. As other neuroendocrine tumors positivity for synaptophysin; B) and CK19; C) is seen, hence the name metastatic pituitary neuroendocrine tumor (formerly known as pituitary carcinoma) based on behavior applied.

The patient underwent total neuraxis radiotherapy and chemotherapy, and his last follow-up MRI in the summer of 2024 showed significant regression of the lesions (Figure 5).



**Figure 5:** Cervical, thoracic and lumbosacral MRI with contrast, sagittal views.

### 3. Discussion

The clinical manifestations of non-functioning pituitary macroadenomas primarily arise from the mass effect of the tumor [3, 4]. Throbbing headaches and visual field abnormalities are among the most commonly reported symptoms, occurring in 60–80% of patients, respectively [3, 5]. Although visual field defects, typically bitemporal hemianopia, are prevalent [6], the occurrence of oculomotor abnormalities due to involvement of cranial nerves III, IV, and VI is quite low (less than 5%), even in patients whose tumors invade the cavernous sinuses [7].

One of the most intriguing aspects of pituitary adenoma biology is that only 0.1–0.2% progress to malignant tumors with metastasis, despite some being highly invasive and exhibiting considerable recurrence rates [8]. The terms "atypical," "aggressive," "invasive," and "refractory" adenomas lack precise definitions and diagnostic criteria and are often used interchangeably, although there have been attempts to provide clarity. The term "atypical" pituitary

adenoma was introduced in 2004 by an expert panel of the World Health Organization to describe a subset of pituitary tumors that, while not meeting the diagnostic criteria for carcinoma (namely, the presence of distant metastasis), exhibit aggressive biological behavior [9]. Histopathologically, atypical adenomas are characterized by high mitotic activity, with Ki-67 indexes greater than 3%, excessive p53 immunoreactivity, and distinctive morphological features such as large pleomorphic nuclei and prominent nucleoli [10]. Virtually all atypical adenomas are large macroadenomas that invade either the cavernous or sphenoid sinuses and/or extend suprasellar.

Conversely, some authors propose the term "refractory" pituitary adenoma for aggressive-invasive tumors exhibiting a disease course distinct from benign adenomas and pituitary carcinomas. According to Dai et al., this type demonstrated a high Ki-67 index, rapid growth, frequent recurrence, and resistance to conventional treatments and/or temozolomide [11].

Pituitary carcinomas represent a rare clinical entity, constituting only 0.1–0.2% of all pituitary tumors, and are associated with a poor prognosis that is challenging to diagnose and treat. The limited number of cases hinders the design of randomized clinical trials; management is largely informed by retrospective studies and case series. Establishing molecular biomarkers and comprehensive genomic profiling could aid in the diagnosis and management of pituitary carcinoma. The malignant potential of oncological tumors is defined by their ability to metastasize (including craniospinal and/or systemic dissemination). Early identification of pituitary carcinoma is crucial for appropriate management, though it remains challenging [12]. While multiple reviews have explored the molecular pathogenesis of pituitary tumors, efforts to establish predictive and/or prognostic markers for clinical aggressiveness have largely been unsuccessful or controversial. Suspicion should be raised when patients present with aggressive tumor subtypes, concerning histological features, and multiple recurrences [13, 14].

In the analysis conducted by Yoo et al., metastases in pituitary carcinoma were found to be intracranial or spinal in 43.1% and 37.5% of cases, respectively. Liver metastases were observed in 13.9%, while cervical lymph node and bone metastases occurred in 11.1% and 9.7% of pituitary carcinoma cases, respectively. Central nervous system metastasis was identified in 58.3% of patients, systemic metastasis in 31.9%, and both central nervous system and systemic metastases in 8.3% of cases [15].

Lai Xu et al. (2020) reported two cases of pituitary carcinoma in men with a history of pituitary adenoma. In the first case, a 55-year-old man diagnosed with a pituitary macroadenoma underwent subtotal resection followed by adjuvant radiotherapy. He later developed relapsed disease and multifocal intracranial metastases. The second case involved a 52-year-old man diagnosed with atypical pituitary adenoma, who presented with sudden onset vision loss in the right eye and had recurrent pituitary carcinoma with spinal metastases [16].

Several case reports suggest that the latency between the initial presentation of a pituitary adenoma and its transformation into carcinoma varies based on the type of endocrine function of the tumor. The average latency period for ACTH-secreting carcinomas has been reported as 9.5 years, while for prolactin-secreting carcinomas, it is approximately 4.7 years [17]; however, this average time has not been reported for nonfunctional tumors. In our case, this duration was about four years.

At the second visit, our patient's serum prolactin (PRL) level had increased fourfold due to a recurrence of the pituitary tumor. Mild elevations in serum PRL, usually below 100 ng/mL, can be found in one-third of patients with non-functional pituitary adenomas. This hyperprolactinemia results from the interruption of descending dopaminergic tone due to stalk compression by the adenoma. It is crucial to differentiate this scenario from a PRL-secreting adenoma, as the treatment of choice for non-functional pituitary adenomas is surgery, whereas dopamine agonists are the mainstay of treatment for prolactinomas [18].

#### 4. Conclusion

Currently, despite various definitions for atypical and invasive pituitary tumors, significant controversy and challenges remain in this area. Since timely diagnosis before tumor spread and metastasis can greatly improve prognosis, efforts to establish a comprehensive and classified definition, along with appropriate diagnostic criteria, are essential.

#### References

- Ostrom, Q. T., Gittleman, H., Farah, P., Ondracek, A., Chen, Y., Wolinsky, Y., et al. (2013). CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2006-2010. *Neuro-Oncology*, 15(Suppl. 2), 1-56.
- Marguth, F., & Oeckler, R. (1985). Recurrent pituitary adenomas. *Neurosurgical Review*, 8, 221-224.
- Molitch, M. E. (2017). Diagnosis and treatment of pituitary adenomas: A review. *JAMA*, 317, 516-524.
- Jaffe, C. A. (2006). Clinically non-functioning pituitary adenoma. *Pituitary*, 9, 317-321.
- Dekkers, O. M., Pereira, A. M., & Romijn, J. A. (2008). Treatment and follow-up of clinically nonfunctioning pituitary macroadenomas. *Journal of Clinical Endocrinology & Metabolism*, 93, 3717-3726.
- Grochowicki, M., Vighetto, A., Berquet, S., Khalfallah, Y., & Sassolas, G. (1991). Pituitary adenomas: Automatic static perimetry and Goldmann perimetry. A comparative study of 345 visual field charts. *British Journal of Ophthalmology*, 75, 219-221.
- Molitch, M. E. (2008). Nonfunctioning pituitary tumors and pituitary incidentalomas. *Endocrinology and Metabolism Clinics of North America*, 37, 151-171.
- Pernicone, P. J., Scheithauer, B. W., Sebo, T. J., Kovacs, K. T., Horvath, E., Young, W. F. Jr., et al. (1997). Pituitary carcinoma: A clinicopathologic study of 15 cases. *Cancer*, 79, 804-812.
- Figarella-Bronger, D., & Trouillas, J. (2006). The WHO classification of human pituitary tumors: Comments. *Acta Neuropathologica*, 111, 71-72.
- DeLellis, R., Lloyd, R. V., Heitz, P., & Eng, C. (2004). *World Health Organization classification of tumours: Tumours of the endocrine organs*. Lyon: IARC Press.
- Dai, C., Feng, M., Liu, X., Ma, S., Sun, B., Bao, X., Yao, Y., Deng, K., Wang, Y., Xing, B., et al. (2016). Refractory pituitary adenoma: A novel classification for pituitary tumors. *Oncotarget*, 7, 83657–83668.
- Heaney, A. (2014). Management of aggressive pituitary adenomas and pituitary carcinomas. *Journal of Neuro-Oncology*, 117, 459–468.
- Robertson, A. M., & Heaney, A. P. (2016). Molecular markers in pituitary tumors. *Current Opinion in Endocrinology, Diabetes and Obesity*, 23, 324–330.
- Wierinckx, A., Roche, M., Legras-Lachuer, C., Trouillas, J., Raverot, G., & Lachuer, J. (2017). MicroRNAs in pituitary tumors. *Molecular and Cellular Endocrinology*, 456, 51–61.
- Yoo, F., Kuan, E. C., Heaney, A. P., Bergsneider, M., & Wang,

- 
- M. B. (2018). Corticotrophic pituitary carcinoma with cervical metastases: Case series and literature review. *Pituitary*, 21, 290–301.
16. Xu, L., Khaddour, K., Chen, J., Rich, K. M., Perrin, R. J., & Campian, J. L. (2020). Pituitary carcinoma: Two case reports and review of literature. *World Journal of Clinical Oncology*, 11(2), 91-102.
17. Yang, Z., Zhang, T., & Gao, H. (2016). Genetic aspects of pituitary carcinoma: A systematic review. *Medicine*, 95, e5268.
18. Arafah, B. M., Neik, K. E., Gold, R. S., & Selam, W. R. (1995). Dynamics of prolactin secretion in patients with hypopituitarism and pituitary macroadenomas. *Journal of Clinical Endocrinology & Metabolism*, 80, 3507-3512.

**Copyright:** ©2025 Mohammadali Arami, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original authors and source are credited.