

# Pituitary adenoma: A case report with special emphasis on approach to diagnosis

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## ABSTRACT

Pituitary tumors are common in sellar area. The prevalence of clinically apparent pituitary lesions is estimated to comprise approximately 10% of all intracranial lesions, while incidental pituitary tumors are detected in approximately 11% of individuals at autopsy. Pituitary tumors are mostly found to be benign adenomas, however pituitary carcinoma has been reported to comprise about 0.5% of pituitary tumors. Pituitary adenomas are associated with an immense diversity in their endocrine manifestations secondary to hypo or hyperfunction of pituitary gland and ophthalmological manifestations due to mass effect. Progress in the diagnostic examination of pituitary adenomas and advances in the treatment of these tumors offers excellent prospects for a successful therapeutic outcome. We hereby discuss a case of pituitary macro-adenoma in a young adult male and review the recent advances in the classification and diagnosis of pituitary adenoma.

**Key words:** Pituitary adenoma, diagnosis, recent advances

## INTRODUCTION

Pituitary tumors are common in the sellar area. The prevalence of clinically apparent pituitary lesions is estimated to comprise approximately 10% of all intracranial lesions,<sup>[1]</sup> while incidental pituitary tumors are detected in approximately 11% of individuals at autopsy.<sup>[2]</sup> Pituitary tumors are virtually always benign adenomas, however pituitary carcinomas are reported to comprise about 0.5% of pituitary tumors. Micro-adenomas are tumors measuring less than 10 mm in diameter and those of more than 10 mm are termed macro-adenomas. Diffuse adenomas are ones that lead to sellar expansion; often compressing the residual gland into a thin membrane. Massive adenomas often replace the sellar floor; displace surrounding structures and undergo suprasellar extension. Endocrinologically functional tumors are often small; whereas silent or non-functioning tumors are large, detected only as a result of mass effects. Macro-adenomas

compress normal pituitary and cause panhypopituitarism. Macro-adenomas often produce stalk effect, in which mild to moderate elevations of prolactin (PRL) hormone result from stalk compression caused by growing tumor mass. This mass blocks the transport of dopamine and thus releases the anterior pituitary from the inhibitory control by the hypothalamus.

In this article, we will discuss a case of pituitary macro-adenoma in a young adult male and review the recent advances in the classification and diagnosis of pituitary adenoma.

## CASE REPORT

A 25-year-old young male patient presented to neurosurgery out-patient department with the complaints of chronic headache and diminution of vision of left eye. General examination was found to be normal. No thyroid enlargement was found. Systemic examination was found to be normal. Ocular examination revealed that visual acuity in the right eye was 6/6, in the left eye was 9/36 respectively. Extraocular movements were of full range. Fundus examination was within normal limits. There was no mass palpable in the orbit or no bruit.

On investigation computed tomography scan revealed sellar mass with suprasellar extension and involvement

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of adjacent structures and vessels suggesting pituitary macro-adenoma.

MRI showed large intense homogenously enhancing dumbbell shaped sellar and suprasellar mass lesion with bilateral parasellar extension enclosing the cavernous segment of the internal carotid artery on both sides, suggesting the possibility of pituitary macro-adenoma.

Hormonal assay was carried out. Prolactin (PRL) level was found to be 180 ng/ml (normal range: Male 4.6-21.4 ng/ml). Thyroid profile was found to be normal. On the basis of clinical examination and investigations, a clinical diagnosis of pituitary macro-adenoma was made. The tumor was surgically excised and submitted for histopathological examination.

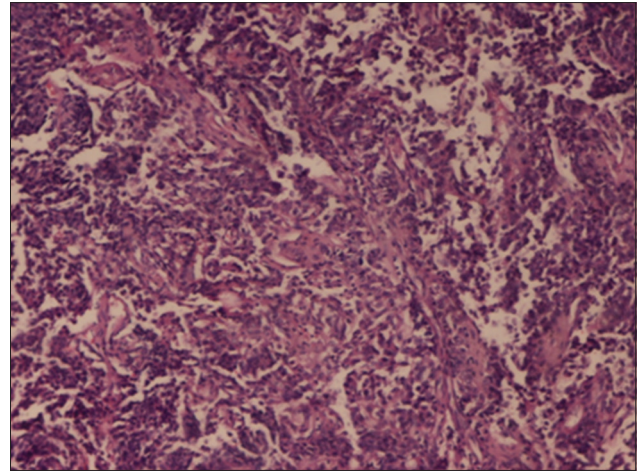
Gross examination showed multiple yellowish white soft-tissue aggregate measuring 0.7 cm. Microscopic examination showed tumor cells arranged in sheets and nests with focal glandular/rosette arrangement [Figure 1]. Two cell types were identifiable with some groups consisting of acidophilic cells with hyperchromatic nuclei and other cells showing delicate lightly staining (chromophobic) cytoplasm and vesicular nuclei with coarse chromatin and nucleoli [Figure 2]. Nuclear atypia was present, but mitotic activity was not evident. Stroma was fibrovascular and fibrous bands were seen. Hemorrhage was seen also.

## DISCUSSION

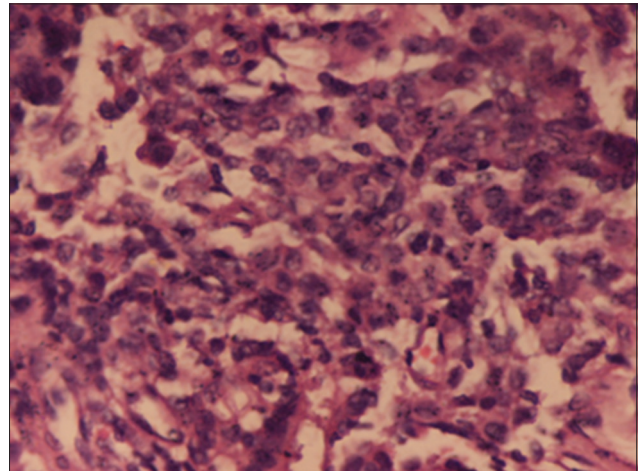
Pituitary tumors comprise 10-15% of intracranial neoplasm.<sup>[3]</sup> They can be broadly classified on the basis of tumor size. Micro-adenomas are less than 10 mm in diameter and those of more than 10 mm are called macro-adenomas. The tumors can also be classified as chromophobic, acidophilic and basophilic adenoma on the basis of their histologic appearance.<sup>[3]</sup> On the basis of immunohistochemical staining or by serum hormone measurement, tumors can be divided into secreting and non-secreting types. The secreting (functional tumor) comprises of 75% of pituitary adenomas.<sup>[3]</sup> They include:

- Growth hormone (GH) cell adenoma
- PRL cell adenoma/prolactinoma
- Mixed GH and PRL adenoma
- Thyrotropin releasing hormone cell adenoma
- Adrenocorticotrophic hormone (ACTH) cell adenoma
- Gonadotroph (LSH) and (follicle-stimulating hormone) cell adenoma.

Symptoms of these pituitary neoplasms depend on the presence of pituitary hypersecretion or hyposecretion caused by destruction of pituitary gland or direction of tumoral expansion and invasion of adjacent structures.



**Figure 1:** Medium power view showing focal glandular/rosette arrangement of tumor cells



**Figure 2:** High power view showing dual population of cells with one showing acidophilic cytoplasm with hyperchromatic nuclei and other showing chromophobic cytoplasm and vesicular nuclei with prominent nucleoli

Very occasionally, some pituitary tumors demonstrate their functional differentiation toward the production of hormones belonging to different cell lineages, i.e., ACTHomas with GH production, GHomas with ACTH production. It has been postulated that aberrant expressions of transcription factors could be the cause of this abnormal differentiation in the tumors.<sup>[4]</sup>

Prolactinomas constitutes 40% to 50% of pituitary adenoma. PRL secreting micro-adenomas generally occur in reproductive-aged females and they manifest with amenorrhea, galactorrhea or both. In males and post-menopausal females, prolactinomas often appear to be clinically non-functional, growing to macro-adenoma and exhibit invasion. Due to various syndromes produced by secreting tumors, they are detected early. Non-secreting tumors are larger when diagnosed and present with various symptoms and signs such as headache, visual field defects, typically bi-temporal field loss and cranial

nerve palsies, due to invasion into cavernous sinus or with epistaxis due to downward extension through the floor of sella.<sup>[5]</sup> The mass can extend to orbit leading to proptosis.<sup>[6]</sup> They can present with sudden onset of headache/loss of vision due to hemorrhage or necrosis of tumor as pituitary apoplexy.<sup>[7]</sup>

The diagnosis of prolactinoma is based on measurement of serum PRL level and neuroradiological imaging. Hyperprolactinemia at level less than 150 ng/ml does not indicate tumoral PRL production. Instead it may be the result of stalk section effect. If the lack of PRL staining is not demonstrated, valuable time may be wasted in useless endocrine therapy directed at a presumed prolactinoma. Immunohistochemically, PRL activity couldn't be demonstrated in our case as facility of immunomarkers for PRL is not available in our department.

Ectopic pituitary adenomas, though rare, can occur outside the sella turcica, most frequently in the sphenoid sinuses. The differential diagnoses include olfactory neuroblastoma, germinoma, rhabdomyosarcoma. Immunomarkers such as chromogranin, synaptophysin, pituitary hormones can be helpful to establish diagnosis in these tumors.<sup>[8]</sup>

Pituitary carcinomas are very rare. The tumor cells show atypia and high MIB-1 proliferative indices. The tumors are frequently functioning; such as PRL producing and ACTH producing.<sup>[9,10]</sup> Macro-adenomas are more often invasive than micro-adenomas.

### Recent update on the classification of pituitary adenoma

Pituitary adenomas are recently classified by their hormonal content. The hormonal activity is the basis for the diagnosis and treatment from the clinical perspective. Biologically, however, it remains to be established, whether other characteristics; such as proliferation markers (Ki-67/MIB-1 index), growth factors and receptors expression, or oncogene product expression will prove to be the most reliable predictors of tumor behavior, such as invasive growth, recurrence or metabolism. However, the application of immunohistochemical staining methods to determine tumor cytogenesis and pathogenesis is currently the mainstay of morphological classification.

Ultrastructural classification based on electron microscopy is useful to characterize the cytological differentiation of tumor cells.<sup>[11]</sup> The application of electron microscopy with immunohistochemistry allows structural-functional correlations that provide the basis for a morphological classification.

Majority of pituitary adenoma formation is dependent on a no of oncogenes and tumor suppressor gene such as

cyclinD1, multiple endocrine neoplasia type 1 (MEN-1), RAS, P53, retinoblastoma gene. The most important gene involved in the sporadic tumorigenesis is *gsp*, which encodes the  $GS\alpha$  subunit,<sup>[12]</sup> a stimulatory guanine binding protein that regulates hypothalamic GH releasing hormone effects in somatotrophs. Mutations in *gsp* have been most closely associated with somatotropinomas and they are found to occur in 40% of these tumors.

Pituitary adenomas that occur in a familial setting account for 4-5% of all pituitary adenomas. They can be a part of endocrine related tumor syndromes such as MEN-1,<sup>[13]</sup> carney complex (CNC), familial isolated pituitary adenomas (FIPA) and McCune-Albright syndrome.

## CONCLUSION

Pituitary tumors are most frequently encountered sellar neoplasms. They exhibit a wide range of biological behavior in terms of hormone production and tumor growth. The young patients with pituitary adenoma should be thoroughly evaluated for the association with genetic syndromes such as MEN-1, FIPA, CNC and McCune-Albright syndrome. The family of a young patient diagnosed with pituitary adenoma as a part of genetic syndrome should be offered genetic counseling. Recent advances in immunohistochemistry and molecular techniques have improved our concepts regarding pathogenesis of tumors. Classification of these tumors is likely to develop in future with growing knowledge of pathways of adeno-hypophyseal cytodifferentiation.

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