Invasive, Atypical and Aggressive Pituitary Adenomas and Carcinomas

Prof Dr Aydin Sav, MD[a,*], Fabio Rotondo, BSc[b], Luis V. Syro, MD[c], Antonio Di Ieva, MD, PhD[d], Michael D. Cusimano, MD, PhD[d], Kalman Kovacs, MD, PhD[b]

KEYWORDS

• Aggressive pituitary adenoma • Atypical adenoma • Invasive adenoma
• Noninvasive adenoma • Pituitary carcinoma • Diagnosis

KEY POINTS

- Pituitary adenomas can be classified according to pathologic, radiological, or clinical behavior as typical or atypical, invasive or noninvasive, and aggressive or nonaggressive adenomas.
- World Health Organization classification categorizes pituitary adenomas as typical and atypical. Pathologic features of atypical adenoma are defined as a Ki-67 labeling index greater than 3%, and/or extensive p53 immunoreactivity.
- Invasive adenomas show pathologic or radiological signs of invasion to the cavernous or sphenoid sinuses, bone, or nasal mucosa.
- According to clinical behavior, a pituitary adenoma can be either aggressive or nonaggressive, and the use of biomarkers in differentiating aggressive adenomas has a limited place in determining the prognosis.
- Pituitary carcinomas are rare, show cerebrospinal and/or systemic metastasis, show a higher index of Ki-67 and p53 protein than aggressive adenomas, and they usually are resistant to radiotherapy.

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[a] Department of Pathology, Acibadem University, School of Medicine, Kerem Aydinlar Yerleskesi, Icerenkoy Mahallesi, Kayisdagi Caddesi, No: 32, Atasehir, Istanbul, Turkey; [b] Division of Pathology, Department of Laboratory Medicine, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; [c] Department of Neurosurgery, Hospital Pablo Tobon Uribe and Clinica Medellin, Medellin, Colombia; [d] Department of Neurosurgery, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada
* Corresponding author.
E-mail address: muratay dinsav@gmail.com

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INTRODUCTION

Pituitary adenomas constitute 10% to 15% of intracranial neoplasms.[1] Although pituitary adenomas are benign, some of them are known to show aggressive clinical behavior, such as invading adjacent tissues and proliferating rapidly.[2] Invasion of surrounding structures by pituitary adenomas complicates complete resection and is an important cause for postoperative recurrence.[3] Biological markers for the aggressive nature of pituitary adenomas have been investigated, but none of them are widely accepted as being responsible for invasiveness.[4] Pathogenic mechanisms underlying pituitary adenoma formation, progression, and invasion remain poorly understood. Mutations in oncogenes and tumor suppressor genes (TSGs) that might be prognostic predictors or gene therapy targets are rarely found in pituitary tumors.[5] Thus, further investigation of new oncogenes and TSGs is needed. Pituitary carcinoma is restricted to tumors of adenohypophyseal cells that show cerebrospinal and/or systemic metastasis. They are rare and account for only 0.1% to 0.2% of pituitary tumors.[6] Their prognosis is poor and about 80% of these patients die within 8 years.[7]

ATYPICAL, INVASIVE, AND AGGRESSIVE PITUITARY ADENOMAS

Pituitary adenomas can be classified according to their pathologic features, radiological findings, or clinical behavior as typical or atypical, invasive or noninvasive, and aggressive or nonaggressive adenomas. The terminology aggressive has been used synonymously with invasive or atypical when evaluating pituitary adenomas and has produced different interpretations.[8] Clear definitions are therefore required.

According to the World Health Organization (WHO), pituitary tumors are classified as typical or atypical adenomas and pituitary carcinomas.[8] Pituitary adenomas that show higher mitotic activity, a Ki-67 labeling index (LI) greater than 3%, and/or extensive p53 immunoreactivity are considered atypical adenomas. Typical adenomas are tumors with monotonous cells and lack these findings. Pituitary carcinomas are defined when metastases are present even if they do not show common histologic malignant features such as higher mitotic activity.[9]

Aggressive adenoma has been used to define a high risk of recurrence or lack of therapeutic response. This pituitary tumor group advances to multiple recurrences[2] and is resistant to conventional treatment. These tumors are larger in size, faster in growth, or both.[9] Diverse potential biomarkers used in differentiating aggressive adenomas have not yet been fully validated.[10] So far, histopathologic biomarkers have yielded unconvincing results in predicting invasive adenomas.[11,12] Because of a lack of complete validation, correlation between polysialic neural cell adhesion molecule and pituitary tumor transforming gene with invasive potential seems to be unreliable.[13]

Invasive adenomas are considered tumors with proven growth to adjacent structures, such as the cavernous sinuses, bone, and sphenoid sinus.[14,15] Suprasellar extension is not considered a criterion of invasiveness. Invasion can be detected with preoperative MRI, during surgery, or with histologic demonstration of tumor spread to the dura, bone, or nasal mucosa.[16,17] MRI is the most practical common approach to classifying invasion and the Knosp grading system is widely used.[18]

Dural invasion detected by microscopic examination is common, therefore it is not regarded as a consistent indicator of aggressive tumor behavior.[16] The overall rate of invasion into the cavernous sinus is 35% and macroadenomas tend to invade more frequently than microadenomas.[16] Microscopy shows that dural invasion of pituitary