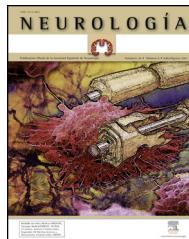




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ORIGINAL ARTICLE

Atypical pituitary adenomas: 10 years of experience in a reference centre in Portugal[☆]



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KEYWORDS

Pituitary adenoma;
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Abstract

Introduction: Primary pituitary tumours are classified by the World Health Organization as typical adenoma, atypical adenoma, or carcinoma. Information on the incidence and prevalence of these pituitary tumours is limited, and these data in Portugal are scarce, obsolete, or non-existent. Our study evaluates pituitary adenomas (PA) in the population of Lisbon, and it aims to describe the prevalence of all subgroups in order to revise the incidence of the 'atypical' histological type and its correlation to tumour subtype, invasion, and recurrence.

Patients and methods: A retrospective, descriptive analysis of patients with PA diagnosed between 2004 and 2013 was performed at Santa María University Hospital, a national reference centre.

Results: Of the 220 PA cases diagnosed, 28 (12.7%) fulfilled criteria for atypical lesions, and within that group, 23 were macroadenomas (82.1%) and 13 showed radiological evidence of invasion (46.4%). Ages ranged from 29 to 81 years (mean, 53.4 years). Eleven patients (39.3%) had functional tumours. Sixteen of the 28 patients (57.1%) experienced tumour recurrences; in the 100 adenomas monitored for more than 5 years, the recurrence rate in atypical PA was 7 times higher than in typical PA. Immunohistochemically, 28.6% of the tumours stained positively for ACTH, 25% for gonadotrophins, and 17.9% for prolactin. The proliferation index (Ki67) ranged from 3% and 25% (mean, 6.4%).

Conclusions: Atypical PAs make up 12.7% of all surgically treated PA cases, and they tend to be invasive and recurrent macroadenomas. We found no differences in metastatic potential between typical and atypical PA.

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PALABRAS CLAVE

Adenoma hipofisario;
Atípico;
Antígeno Ki67

Adenomas hipofisarios atípicos: experiencia de 10 años en un centro de referencia de Portugal**Resumen**

Introducción: Los tumores hipofisarios primarios son clasificados por la Organización Mundial de la Salud como adenoma típico, adenoma atípico y carcinoma. Existen datos limitados sobre la incidencia y la prevalencia de tumores hipofisarios, siendo en Portugal escasos, obsoletos o inexistentes. Presentamos un estudio que evalúa los adenomas hipofisarios (AH) basado en la población de Lisboa, cuyo objetivo es describir la prevalencia de todos los subgrupos, revisando la incidencia de este tipo histopatológico «atípico» y su correlación con el subtipo de tumor, invasión y recurrencia.

Pacientes y métodos: Se realizó un análisis descriptivo retrospectivo de pacientes diagnosticados de AH entre 2004 y 2013, en el Hospital Universitario de Santa María (Lisboa), un centro de referencia nacional.

Resultados: De 220 AH diagnosticados, 28 (12,7%) cumplían criterios de lesiones atípicas, 23 de los cuales (82,1%) fueron macroadenomas y 13 (46,4%) mostraron radiológicamente evidencia de invasión. La edad osciló entre 29-81 años (media 53,4 años). Once pacientes (39,3%) tenían tumores funcionantes. Dieciséis (57,1%) de los 28 pacientes presentaron tumores recurrentes; en 100 de los adenomas diagnosticados, con seguimiento superior a 5 años, se observó una tasa de recurrencia en AH atípicos hasta 7 veces superior. En estudios inmunohistoquímicos destacaron los positivos a ACTH (28,6%), a gonadotrofinas (25%) y a prolactina (17,9%). El índice proliferativo (Ki67) varió entre el 3 y el 25% (media 6,4%).

Conclusiones: Los AH atípicos corresponden al 12,7% de los AH resecados, tendiendo a ser macroadenomas, invasivos y recurrentes. No encontramos diferencias entre AH típicos y atípicos en cuanto al potencial metastásico.

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Introduction

Pituitary tumours account for 10% to 15% of all brain tumours.¹ Pituitary adenoma (PA) is the most common neoplasm of the sella turcica² and, from a neurosurgical perspective, the third most common intracranial primary tumour after gliomas and meningiomas.¹ Recent studies show that the prevalence of PAs is as much as 4 times higher than was previously believed.^{3,4} Data on PA incidence are limited, and data from series based on MR images and autopsies contrast with those from surgical series at tertiary hospitals.

PAs are composed of a monoclonal proliferation of anterior pituitary cells. They most frequently occur in women in their third to sixth decade, although they can be found in all age groups.^{1,5} PAs are not homogeneous; rather, each subtype has its own clinical presentation, hormone secretion profile, tendency towards invasiveness, histopathological characteristics, prognosis, and treatment.⁶

Since Cushing proposed the first morphological classification system in 1912, there have been numerous other attempts at classifying PAs histologically. Classification is based on: (a) histological criteria. Although tumour classification based on haematoxylin–eosin (HE) stain results does not correlate with functional status, this information is still valuable: it enables differential diagnosis with other entities, permits evaluation of cell atypia or mitotic activity, and reveals any haemorrhages or necrosis. (b) Immunohistochemical criteria. These constitute the gold standard for

diagnosis and for analysing the main pituitary hormones (PRL, GH, ACTH, FSH, LH, and TSH), to which we can add the alpha subunit of glycoprotein hormones (FSH, LH, and TSH). (c) Ultrastructural criteria, although electron microscopy is a time-consuming and expensive technique and not routinely performed.⁷ (d) Clinical and biochemical criteria, such as clinical presentation and pituitary function to determine whether or not the tumour is functioning. (e) Imaging criteria to determine tumour size and sellar/extrasellar extension. (f) Surgical findings.

The most controversial addition to the most recent classification system by the World Health Organization (WHO, 2004)⁸ is the rating scale for primary endocrine tumours of the pituitary. These tumours are classified as typical pituitary adenomas (ICD 8272/0), atypical pituitary adenomas (ICD 8272/1), and pituitary carcinomas (ICD 8272/3).⁸ Most PAs are typical, with a bland histological appearance; mitotic figures are rare, and the proliferation index (Ki67) is below 3%. Atypical PAs are borderline or uncertain, with atypical morphological characteristics indicative of aggressive behaviour (such as invasive growth), a high mitotic index, a cellular proliferation index (Ki67) greater than 3%, and extensive nuclear positivity for protein p53. Nevertheless, differences between 'typical' and 'atypical' adenomas are not clearly defined. There are no morphological criteria for distinguishing locally aggressive atypical PAs from carcinomas when the tumour is limited to the sella turcica.⁹ While pituitary carcinomas tend to exhibit the usual morphological characteristics associated with malignant neoplasms

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