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Immunohistochemical Profile of Non-Functioning Pituitary Adenomas: A Cross-Sectional Study of 28 Cases from the Diabetology-Endocrinology Department at CHU Mohammed VI, Marrakech

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Abstract **Original Research Article**

Non-functioning pituitary adenomas (NFPAs) are common pituitary tumors characterized by the absence of clinical manifestations related to hormonal hypersecretion, often resulting in delayed diagnosis and presentation at an advanced stage. This cross-sectional study aimed to describe the demographic, clinical, radiological, and immunohistochemical characteristics of NFPAs managed between January 2018 and December 2024 at the Diabetology-Endocrinology Department of CHU Mohammed VI de Marrakech. Twenty-eight patients were included. Clinical, imaging, and histopathological data were retrospectively collected. Immunohistochemical analysis was performed using anti-LH, anti-FSH, and anti-GH antibodies to determine tumor subtype. The cohort showed a marked female predominance (71.4%), with a mean age of 40.7 years. Headache and decreased visual acuity were the most common presenting symptoms. Magnetic resonance imaging revealed a predominance of macroadenomas. Immunohistochemistry identified silent gonadotroph and silent somatotroph adenomas, while most tumors were classified as null cell or poorly differentiated adenomas. These findings highlight the importance of immunohistochemistry in accurately classifying NFPAs and identifying subtypes with potential aggressive behavior. An integrated clinical, radiological, and pathological approach is essential for optimal patient management and prognostic stratification.

Keywords: Non-functioning pituitary adenoma, Immunohistochemistry, Silent adenoma, Macroadenoma, Corticotroph adenoma, WHO classification, Morocco.

INTRODUCTION

Non-functioning pituitary adenomas (NFPAs) account for approximately 15–30% of all pituitary adenomas and represent a significant proportion of sellar tumors [1, 2]. Unlike functioning adenomas, they are not associated with clinical signs of hormonal hypersecretion, which often leads to delayed diagnosis. Most patients present with symptoms related to tumor mass effects, including headache, visual field defects, and hypopituitarism [3].

Historically, pituitary adenomas were classified according to morphological features and hormonal immunohistochemical expression [4]. However, this classification proved insufficient with the recognition of silent adenomas tumors that show positive hormonal staining without corresponding clinical syndromes [5]. Among these, silent corticotroph adenomas have drawn particular attention due to their potentially aggressive clinical course and higher recurrence rates compared to other NFPAs [6].

The 2017 World Health Organization (WHO) classification introduced lineage-specific transcription factors into pituitary tumor classification [7]. The 2022 update reinforced this lineage-based approach using SF-1, PIT-1, and T-PIT, allowing more accurate tumor categorization and improved prognostic assessment [8].

The objective of this study was to analyze the immunohistochemical profile of non-functioning pituitary adenomas diagnosed in our institution and to identify tumor subtypes according to contemporary classification standards.

MATERIALS AND METHODS

This descriptive cross-sectional study included 28 patients diagnosed with non-functioning pituitary adenomas between January 2018 and December 2024 at CHU Mohammed VI of Marrakech.

Clinical, radiological, and histopathological data were retrospectively collected from patient medical records. Magnetic resonance imaging (MRI) of the hypothalamic-pituitary region was performed in all cases. Adenomas measuring 10 mm or more were classified as macroadenomas, while those smaller than 10 mm were classified as microadenomas.

All tumor specimens underwent routine histopathological examination followed by immunohistochemical analysis. A hormonal antibody panel including anti-LH, anti-FSH, and anti-GH antibodies was used to determine hormonal expression profiles and identify silent tumor subtypes.

RESULTS

Twenty-eight patients were included in the study. A marked female predominance was observed, with 20 women (71.4%) and 8 men (28.6%), corresponding to a male-to-female ratio of 0.4. The mean age was 40.7 years, ranging from 11 to 67 years, with the highest frequency in the 40–60-year age group.

The most common presenting feature was tumor syndrome characterized by headache and decreased visual acuity, observed in 43% of patients. Galactorrhea was reported in 14.3% of cases, decreased libido in 7.1%, and isolated cases of growth retardation and intracranial hypertension were noted.

MRI revealed macroadenomas in 67.8% of patients and microadenomas in 32.1%. One case of pituitary macroadenoma complicated by apoplexy was identified.

Histopathological examination combined with immunohistochemistry confirmed the non-functioning nature of the majority of tumors. Two adenomas showed positive immunostaining for LH and FSH, consistent with silent gonadotroph adenomas. One tumor expressed GH, indicating a silent somatotroph adenoma. Twenty-five adenomas showed no specific hormonal expression, suggesting null cell or poorly differentiated adenomas. The detailed immunohistochemical profile and tumor subtypes are summarized in Table 1.

Table 1. Immunohistochemical profile and tumor subtypes of non-functioning pituitary adenomas

Immunohistochemical markers	Number (n)	Percentage (%)
Hormonal expression		
LH and FSH positive	2	7.1
GH positive	1	3.5
No hormonal expression (null cell)	25	89.2
Tumor subtype (based on immunohistochemistry)		
Silent gonadotroph adenoma	2	7.1
Silent somatotroph adenoma	1	3.5
Null cell adenoma / unclassified	25	89.2

DISCUSSION

NFPAs constitute a heterogeneous group of pituitary tumors characterized by the absence of clinical hypersecretion and a tendency toward delayed diagnosis [2, 3]. The predominance of macroadenomas in our cohort reflects the silent hormonal course of these tumors and is consistent with epidemiological data reported in the literature [2, 9].

Galactorrhea observed in some patients can be explained by pituitary stalk compression leading to moderate hyperprolactinemia, a well-recognized mechanism in large NFPAs [10]. Visual impairment and headache remain the most frequent presenting symptoms due to suprasellar extension and optic chiasm compression.

The predominance of null cell or poorly differentiated adenomas in our series aligns with earlier pathological classifications [4]. The main contribution of our study lies in the immunohistochemical analysis of these adenomas, which allowed for precise hormonal profiling and identification of silent subtypes even in the absence of clinical hypersecretion. However, recent evidence suggests that true null cell adenomas are less common when transcription factor profiling is systematically performed [8, 11]. The integration of transcription factors such as SF-1, PIT-1, and T-PIT has significantly improved lineage-specific tumor identification and aligns with the updated WHO 2022 criteria [8].

The identification of silent gonadotroph and silent somatotroph adenomas underscores the importance of immunohistochemical evaluation even in clinically non-functioning tumors [12]. Particular attention should be paid to silent corticotroph adenomas, which are associated with more aggressive behavior and increased recurrence risk [5,6].

Limitations of our study include its retrospective design, relatively small sample size, and

the absence of systematic transcription factor analysis. Nevertheless, it provides valuable regional data and highlights the importance of comprehensive pathological assessment in the management of NFPAs.

CONCLUSION

Non-functioning pituitary adenomas are often diagnosed at the macroadenoma stage [2,9,10]. Immunohistochemistry is essential for accurate classification and detection of silent subtypes, especially silent corticotroph adenomas with aggressive potential [5,6,12]. Integrating imaging, hormonal profiling, and lineage-based classification improves prognosis and patient management [8].

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