Exploring the Relationship Between Serum Markers, Immunohistochemistry Markers, and Clinical Outcomes Following Endoscopic Endonasal Resection of Pituitary Neuroendocrine Tumors: Insights From a Single-Center Experience in Latin America

Edgar G Ordonez-Rubiano[1,2], MD, PHD(c), Martin Pinzon, MD,[1,2] Laura F Bonilla-Mendoza,[1] MD, Julian D Barraza-Diaz,[1] MD,Luis E Umana-Laiton,[1] MD, MSc, Oscar F Zorro-Guio,[1] MD, Javier G Patiño-Gomez,[1] MD

1. Fundacion Universitaria de Ciencias de la Salud, 2. Fundación Santa Fe de Bogotá,

Introduction

Pituitary neuroendocrine tumors (PitNETs) are a heterogeneous group of tumors that originate from the pituitary gland, representing up to 10-15% of all intracranial neoplasms and making them the third most common brain tumor. These tumors vary significantly in their biological behavior, ranging from indolent lesions to aggressive, invasive forms capable of causing significant morbidity through hormone overproduction or mass effects.

This study aims to evaluate the correlation between clinical presentation, serum markers, and immunohistochemistry markers, as well as their impact on patients' clinical outcomes in individuals diagnosed with PitNETs. By elucidating these relationships, we aim to provide insights that may enhance treatment planning and prognostication for patients suffering from these complex tumors.

Methods and Materials

This study is a retrospective cohort analysis conducted at Hospital de San José, Bogotá, Colombia. Patients diagnosed with PitNETs who underwent surgical resection between January 2015 and October 2023. were included in the study. Inclusion criteria were: (1) confirmed histopathological diagnosis of PitNET, (2) availability of complete preoperative serum hormone levels, and (3) accessible immunohistochemical analysis results. Patients without complete clinical, biochemical, or histopathological data were excluded from the study.

Data were collected from electronic medical records and included demographic details (age, sex), clinical presentation (e.g., visual disturbances, hormonal hypersecretion syndromes), preoperative serum hormone levels (e.g., prolactin, growth hormone), and immunohistochemical markers from resected tissue samples. Data regarding tumor size, invasiveness (as assessed by MRI), and recurrence were also collected.

Serum hormone levels were measured at the time of initial clinical presentation, before any surgical or medical intervention. Hormones of interest included prolactin, growth hormone (GH), adrenocorticotropic hormone (ACTH), and others based on clinical suspicion. Hormonal assays were performed using immunoassay techniques (e.g., ELISA), with values compared to standard reference ranges to determine hypersecretion or deficiency.

Immunohistochemical analysis was conducted on paraffin-embedded tumor tissue following surgical resection. Hormone-specific markers (e.g., prolactin, GH, ACTH) were assessed using standard immunohistochemical staining techniques. Expression levels were semi-quantitatively scored based on staining intensity and percentage of positive cells.

Descriptive statistics were used to summarize patient demographics and clinical characteristics. The Spearman correlation coefficient was used to assess the relationship between preoperative serum hormone levels and immunohistochemical marker expression. A p-value of <0.05 was considered statistically significant.

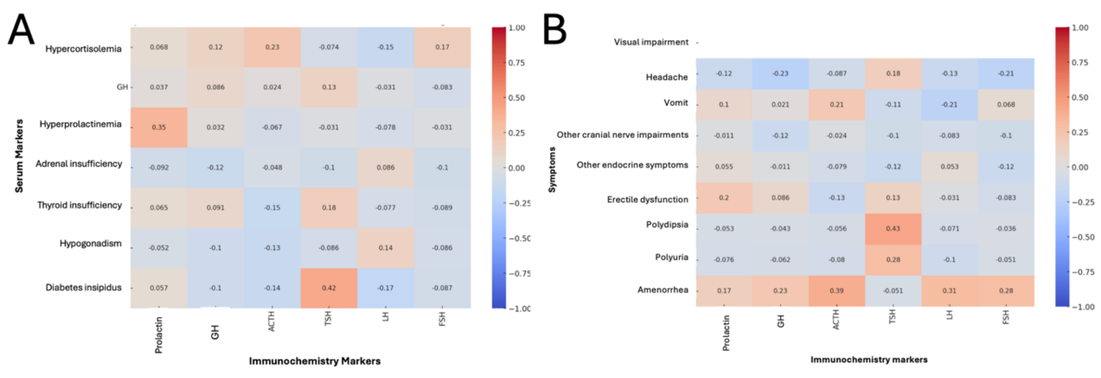

Figure 2. ROC curves. The logistic regression model demonstrated an area under the curve (AUC) of 0.6 for headache, 0.8 for endocrine symptoms, 0.7 for vomiting, 0.9 for other cranial nerve impairment, and 0.75 for erectile dysfunction..

Results

A total of 65 patients with PitNETs and complete data available were included. 31 (47.69%) were females. With an average age of 54.48 ± 11.49. All patients (100%) presented with altered visual function, 47 (72.30%) with headaches, 29 (44.61%) with clinical hypothyroidism, and 7 (10.77%) with other cranial nerve impairments. Spearman correlation coefficients demonstrated that serum gonadal dysfunction had a strong correlation with the presence of erectile dysfunction in males (0.62), and diabetes insipidus (DI) had a moderate correlation with polydipsia (0.40). Other serum abnormalities had weak or very weak correlations with the rest of the symptoms. Correlation coefficients between the positivity of histological markers and symptoms demonstrated a moderate positive correlation between histologically positive prolactin (0.17) and positive ACTH (0.39) and amenorrhea, a weak positive correlation between histological positive luteinizing hormone and amenorrhea (0.31) and polyuria (0.28). Correlation coefficients between the positivity of histological markers and serum markers demonstrated a moderate positive correlation between histologically positive prolactin and hyperprolactinemia (0.35), a weak positive correlation between growth hormone (0.12), follicle-stimulating hormone (0.1), and ACTH (0.23) with hypercortisolemia. Also, a weak positive correlation between the positivity of thyroid-stimulating hormone (TSH) with hypothyroidism (0.18) and a moderate positive correlation between the positivity of TSH and DI (0.42). The logistic regression model demonstrated an area under the curve (AUC) of 0.6 for headache, 0.8 for endocrine symptoms, 0.7 for vomiting, 0.9 for other cranial nerve impairment, and 0.75 for erectile dysfunction.

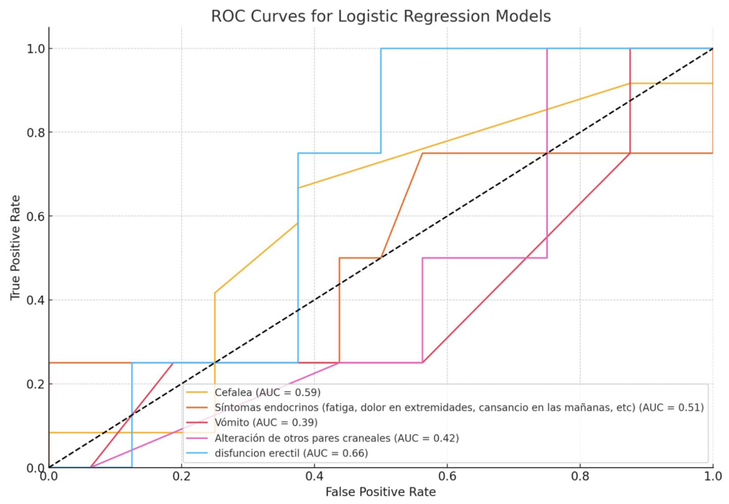

Figure 2. ROC curves. The logistic regression model demonstrated an area under the curve (AUC) of 0.6 for headache, 0.8 for endocrine symptoms, 0.7 for vomiting, 0.9 for other cranial nerve impairment, and 0.75 for erectile dysfunction..

Discussion

The moderate correlations observed between prolactin, ACTH, and symptoms such as amenorrhea indicate that certain hormonal markers can serve as indicators of specific clinical manifestations. However, the weak correlations between other hormones and symptoms suggest that there are other factors at play that influence clinical outcomes. These findings underscore the complexity of PitNETs, where hormonal secretion and tumor behavior are influenced by a multitude of factors beyond the markers measured in this study. The AUC values derived from the logistic regression analysis also provide insight into the predictive capacity of the model for various symptoms. For instance, while the model showed good to excellent predictive power for endocrine symptoms (AUC of 0.8) and cranial nerve deficits (AUC of 0.9), it was less reliable for other symptoms such as headache (AUC of 0.6) and vomiting (AUC of 0.7). This variability suggests that different symptoms may be driven by different underlying mechanisms, which may not be fully captured by the current set of markers. Future studies should consider incorporating additional biomarkers or imaging data to improve predictive accuracy.

Conclusions

Correlations between immunochemistry markers and symptoms are generally weak. Amenorrhea shows moderate positive correlations with several markers (Prolactin, ACTH, LH, FSH). Other symptoms have weaker correlations, indicating that histological markers alone may not be sufficient to explain variations in symptoms. On the other hand, correlations between serum markers and histological markers are mostly weak, suggesting that serum markers have a limited relationship with histological markers. Larger series are necessary to make stronger correlation studies.

Contact

Edgar G Ordóñez-Rubiano
Department of Neurosurgery
Fundación Universitaria de Ciencias de la Salud
Hospital de San José
Bogotá, Colombia
egordonez@fucsalud.edu.co
+57-300-643-9837

References

1. Chin SO. Epidemiology of Functioning Pituitary Adenomas. Endocrinol Metab. 2020;35(2):237-242. https://doi.org/10.3803/EnM.2020.35.2.237
2. Dumitriu-Stan RI, Burcea IF, Salmen T, Poiana C. Prognostic Models in Growth-Hormone- and Prolactin-Secreting Pituitary Neuroendocrine Tumors: A Systematic Review. Diagnostics 2023, 13, 2118. https://doi.org/10.3390/diagnostics13122118
3. Asa SL, Casar-Borota O, Chanson P, et al. From pituitary adenoma to pituitary neuroendocrine tumor (PitNET): an International Pituitary Pathology Club proposal. Endocr Relat Cancer. 2017;24(4):C5-C8. https://doi.org/10.1530/ERC-17-0004
4. Rindi G, Klimstra DS, Abedi-Ardekani B, et al. A common classification framework for neuroendocrine neoplasms: an International Agency for Research on Cancer (IARC) and World Health Organization (WHO) expert consensus proposal. Mod Pathol. 2018;31(12):1770-1786. https://doi.org/10.1530/ERC-17-0004
5. Casar-Borota O, Burman P, Lopes MB. The 2022 WHO classification of tumors of the pituitary gland: An update on aggressive and metastatic pituitary neuroendocrine tumors. Brain Pathol. Published online September 1, 2024. https://doi.org/10.1111/bpa.13302