Multifaceted presentation of the GH-positive PIT-1 lineage Pituitary Tumors: Literature review and Representative Cases

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Abstract

Growth Hormone pituitary adenomas (GHPAs) compose around 10% of all pituitary adenomas, classically causing acromegaly when clinically functional. In this report, we review and discuss three patients presenting with varying subsets of GHPAs: Clinically silent GHPAs, mammosomatotrophs (MSPA), and mixed cell growth hormone (GH) and prolactin (PRL) adenomas. Distinguishing between subtypes is crucial for customizing postoperative care, as treatment options vary depending on the tumor cell populations identified through transcription factors and immunohistochemical staining.

Introduction

- Pituitary Adenomas (PA) are benign tumors that develop in the anterior pituitary gland.
- Growth Hormone-secreting pituitary adenomas (GHPAs) are a subtype of PAs that often causes acromegaly, characterized by acral enlargement, facial changes, hypertension, and other comorbidities; these are diagnosed biochemically based on IGF-1 levels and growth hormone (GH) suppression to glucose.[1]
- Not all GHPAs are clinically active; some can present as Non-Functional pituitary adenomas (NFPAs) with headaches, visual disorders, and often signs of hyperprolactinemia due to the stalk effect.[2]
- Mammosomatotroph adenomas (MSPAs) are rare bihormonal adenomas that produce both GH and PRL, secrete both hormones from the same cell, and are associated with less favorable outcomes than pure GH adenomas.[3,4,5]
- Mixed GH-PRL tumors secrete GH and PRL from two distinct cell populations.[6] These are also considered more clinically aggressive than pure GH-adenomas. They and are classified by a 30% difference in cell type. [5,7]

Methods and Materials

We present three cases treated at our institution with the following tumor types: Silent GHPA, MSPA, and Mixed GH-PRL adenoma respectively in a retrospective review.

Table 1: Patient Preoperative Characteristics

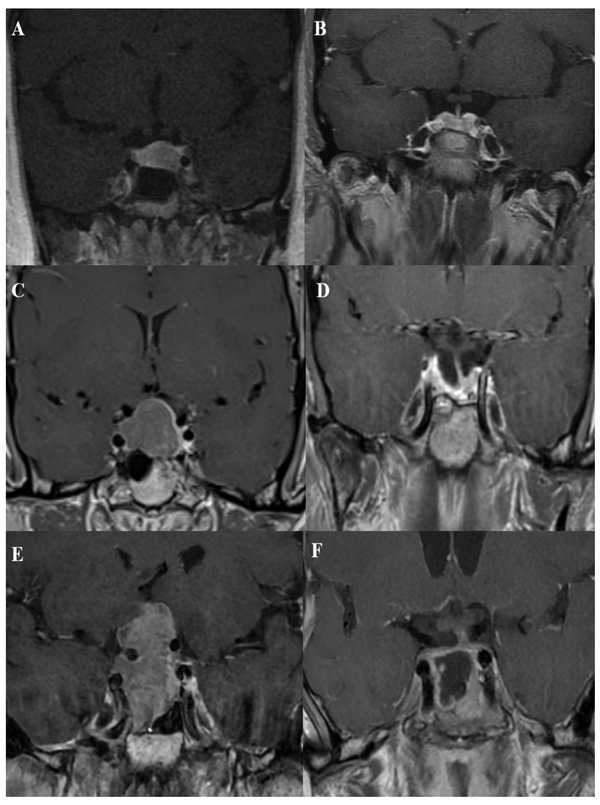
	Age, Sex	Presenting Symptoms	Tumor Size (cm)	Knosp Categories	Hormone Levels
NFPA	37, F	Chronic headache, change in teeth spacing	1.1 x 1.1 x 0.6	1	PRL: 15.6 ng/mL IGF-1: 162 ng/mL (z-score: 0.1) GH: 1.33 ng/mL
MSPA	40, F	Secondary amenorrhea, increased finger size, skin tags	2.4 x 1.9 x 1.5	2	PRL: 5.0 ng/mL* IGF-1: 400 ng/mL (z-score: 3.2) GH: 6.06 ng/mL
Mixed GH-PRL	62, M	Blurred and peripheral vision loss, increased emotionality	2.8 x 2.9 x 3.7	3	PRL: 1,609 ng/mL IGF-1: 483 ng/mL (z-score: 4.2) GH: 2.11 ng/mL

NFPA= Silent, non-functional PA; MSPA= Mammosomatotrophs. Tumor size is reported as length x width x height. KNOSP score indicates the extent of invasion into the cavernous sinus.
*normalized with cabergoline

Results

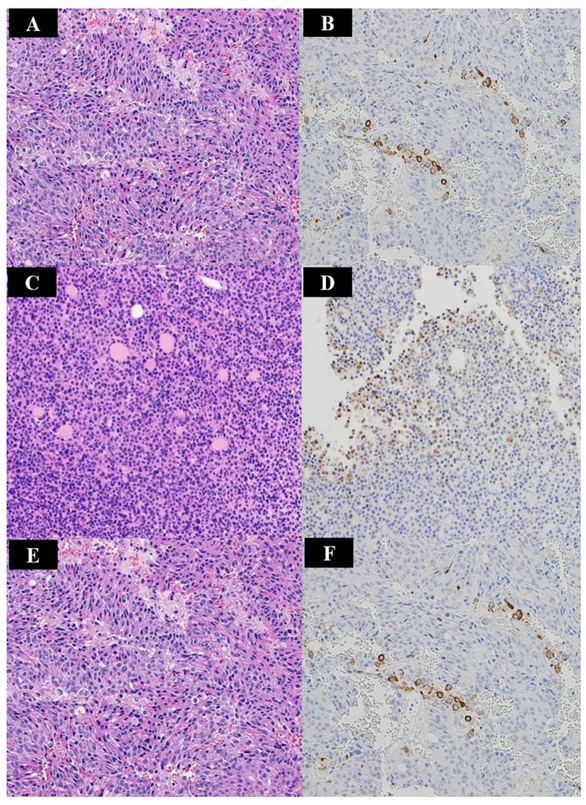
- All patients presented with a symptomatic pituitary adenoma.
- Elevated IGF-1 and PRL levels were noted in the hormone-secreting cases The NFPA case resolved with no residual symptoms following EEA intervention
- The MSPA case's symptoms resolved as the patient achieved hormonal remission with no residual tumor seen on postoperative MRI
- The Mixed-cell GH-PRL case's IGF-1 level normalized months following EEA resection. PRL improved postoperatively, then normalized after cabergoline was added.

Figure 1



GHPA- A&B
MSPA – C&D
Mixed GH-PRL PA – E&F

Figure 2



GHPA- A&B
MSPA – C&D
Mixed GH-PRL PA – E&F

Discussion

- GHPA subtypes have significant variability in symptoms and clinical presentation.
- In our literature review, MSPAs had smaller diameters compared to mixed GH-PRL PAs. Additionally, mixed GH-PRL PA's had more significant hyperprolactinemia and were less likely to achieve remission via EEA resection.[8,9,10,11,12]
- Headaches resolved in the silent GHPA patient following surgery.
- Biochemical remission was achieved for the MSPA case.
- Cabergoline led to PRL biochemical control in the Mixed GH-PRL when EEA resection did not resolve PRL elevation.
- All three patients had a favorable postoperative course at our institution.

Conclusions

- Understanding the pathophysiology of less frequent types of GHPA is required for individualized management and patient counseling
- Management of mixed or MSPA GHPAs often entails both surgical and medical treatment
- All patients with PA should have IGF-1 and PRL levels measured postoperatively
- Endocrinological evaluation and multidisciplinary collaboration are essential for GHPA management.

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References

1. Mehta GU, Lonser RR. Management of hormone-secreting pituitary adenomas. Neuro-oncology. June 1, 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5464431/.
2. Drummond JB. Non-functioning pituitary adenomas. Endotext [Internet]. October 12, 2022. https://www.ncbi.nlm.nih.gov/books/NBK534880/.
3. Jiang S, Chen X, Wu Y, Wang R, Bao X. An update on silent corticotroph adenomas: Diagnosis, mechanisms, clinical features, and Management. Cancers. December 6, 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8656508/.
4. Al-Brahim NYY, Asa SL. My approach to pathology of the pituitary gland. Journal of clinical pathology. December 2006. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1860551/.
5. Rick J., Jahangiri A., Flanigan P.M., Chandra A., Kunwar S., Blevins L., Aghi M.K. Growth hormone and prolactin-staining tumors causing acromegaly: A retrospective review of clinical presentations and surgical outcomes. *J. Neurosurg.* 2019;131:147–153. doi: 10.3171/2018.4.JNS18230.
6. Araujo-Castro M, Marazuela M, Puig-Domingo M, Biagetti B. Prolactin and growth hormone signaling and Interlink focused on the MAMMOSOMATOTROPH Paradigm: A comprehensive review of the literature. International journal of molecular sciences. September 12, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10531307/.
7. Sandret L, Maison P, Chanson P. Place of cabergoline in acromegaly: A meta-analysis. OUP Academic. May, 2011. https://academic.oup.com/jcem/article/96/5/1327/2833476.
8. Starke RM, Raper DMS, Payne SC, Vance ML, Oldfield EH, Jane JA. Endoscopic vs microsurgical transsphenoidal surgery for acromegaly: outcomes in a concurrent series of patients using modern criteria for remission. *J Clin Endocrinol Metab*. 2013;**98**(8):3190–3198.
9. Shih RY, Schroeder JW, Koeller KK. Primary tumors of the pituitary gland: Radiologic-pathologic correlation. *RadioGraphics*. 2021;41(7):2029-2046. doi:10.1148/rg.2021200203
10. Sharma R, Kopchick JJ, Puri V, Sharma VM. Effect of growth hormone on insulin signaling. Molecular and cellular endocrinology. December 1, 2020. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7606590/.
11. Dhaneshwar S, Shandily S, Tiwari V. Growth hormone excess: Implications and management. Endocrine, metabolic & immune disorders drug targets. 2023. https://pubmed.ncbi.nlm.nih.gov/36237164/.
12. Drummond J, Roncaroli F, Grossman AB, Korbonits M. Clinical and pathological aspects of silent pituitary adenomas. The Journal of clinical endocrinology and metabolism. July 1, 2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6517166/.