

Comparative Analysis of Mixed Gangliocytoma and Growth Hormone Pituitary Adenomas

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Abstract

Growth Hormone-secreting pituitary adenomas (GHPAs) clinically manifest with acromegaly due to hypersecretion of GH. In comparison, Mixed Gangliocytoma-Pituitary Adenomas (MGPA) are rare sellar tumors with manifestations mimicking functional pituitary adenomas. Most reported cases of MGPA are GH-secreting. The pathogenesis of this combination tumor is not well understood due to a paucity of data. We present our institutional experience in the surgical management and outcomes in GH-secreting MGPA and GHPAs.

Introduction

- Pituitary adenomas (PAs) are the most common tumors in the sellar region. Mixed or composite tumors usually consist of different cell populations of neuroendocrine origin, GHPAs being one of the most common.
- Mixed Gangliocytoma-pituitary adenomas (MGPA) are benign tumors with ganglionic and neuronal origins.
- MGPA have an incidence of 0.14-0.52% of all sellar tumors, more commonly presenting in women and a population with a median age of diagnosis of 45 years.^{1,2,3}
- As of 2022, only 174 cases of MGPA have been reported.⁴
- Few studies compare GHPAs and MGPA.
- MGPA are diagnosed exclusively post-operatively by immunohistochemical staining.⁵
- 6 patients with GH-secreting MGPA and compare their demographic and clinical information to patients with 41 GHPAs.

Methods and Materials

- Retrospective review of demographic and clinical data of adult patients with GHPAs and MGPA
 - All had an endoscopic endonasal transsphenoidal (EETA) operation from 2018 to 2024.
- Presenting symptoms compared were the three most common presenting symptoms in our cohort.
- Imaging included pre- and post-operative sellar magnetic resonance imaging (MRI)
- Analysis using maximum diameter measurements and a modified KNOSP grade ranging from 0-4.⁶
- Surgical complication rate (discharge summaries and readmission notes) was included.
- Follow-up period (months) is period from the surgical date to the most recent clinical follow-up at our institution.
- Categorical data was evaluated using a chi-square analysis and quantitative data using an independent samples t-test. The 2-tailed p-value for each variable can be visualized in *Table 1*.

Table 1: GHPA and MGPA Comparison of Patient Demographics and Clinical Courses

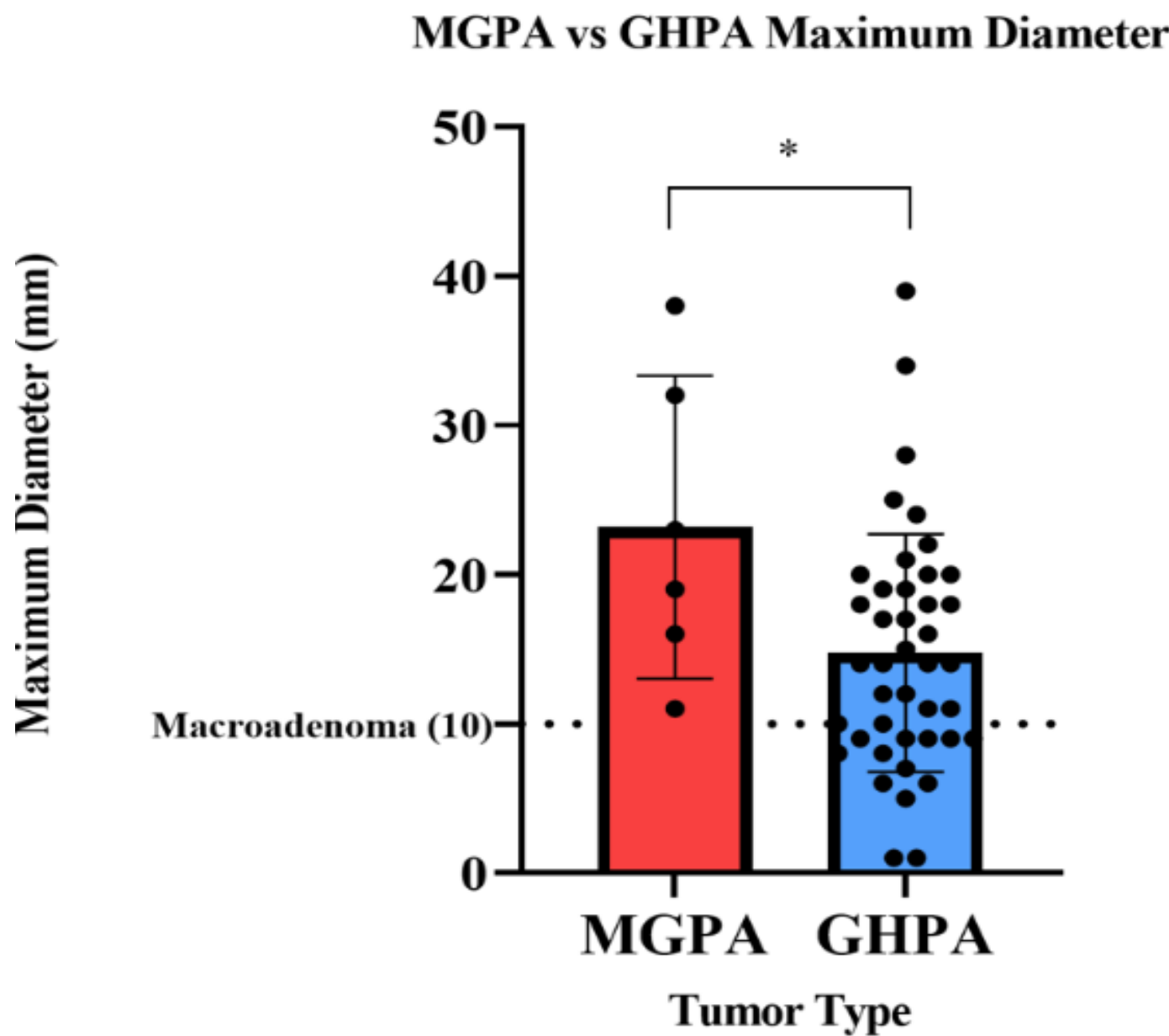
Characteristic	MGPA (n=6)	GHPA (n=41)	p-value
Sex			
Male [mean, %]	3 (50%)	20 (49%)	-
Female [mean, %]	3 (50%)	21 (51%)	-
Age			
Years of Age [mean, range]	47 (36-65)	49 (19-76)	0.809
Presenting symptoms			
Headaches [mean, %]	4 (67%)	18 (44%)	0.398
Acral Enlargement [mean, %]	3 (50%)	31 (76%)	0.326
Facial Changes [mean, %]	3 (50%)	10 (24%)	0.326
Preoperative Hormone Labs			
IGF-1 [mean, range]	587 (188-1,164)	610 (221-1,503)	0.488
GH [mean, range]	22 (0.2-62.4)	14 (1.6-51.3)	0.762
PRL [mean, range]	18 (5.4-42.2)	35 (0.3-231.0)	0.443
Cortisol [mean, range]	8 (7.0-8.9)	11 (2.6-22.4)	0.346
Imaging			
Maximum diameter in mm [mean, range]	23 (11-34)	15 (1-39)	0.034
KNOSP [mean, range]	2.1 (0-4)	1.1 (0-4)	0.227
Complications			
Number of complications [%]	17%	<1%	0.144
Postoperative Outcomes			
Follow-up period in months [mean, range]	19 (3-78)	34 (4-73)	0.493
Remission [total, %]	3 (50%)	19 (46%)	1.000
Recurrence [total, %]	0 (0%)	5 (12%)	1.000

All statistical comparisons between groups were performed using a chi-squared or independent, unpaired sample t-test. Raw totals, mean values, and percentages are indicated in each category under *Characteristics*.

Results

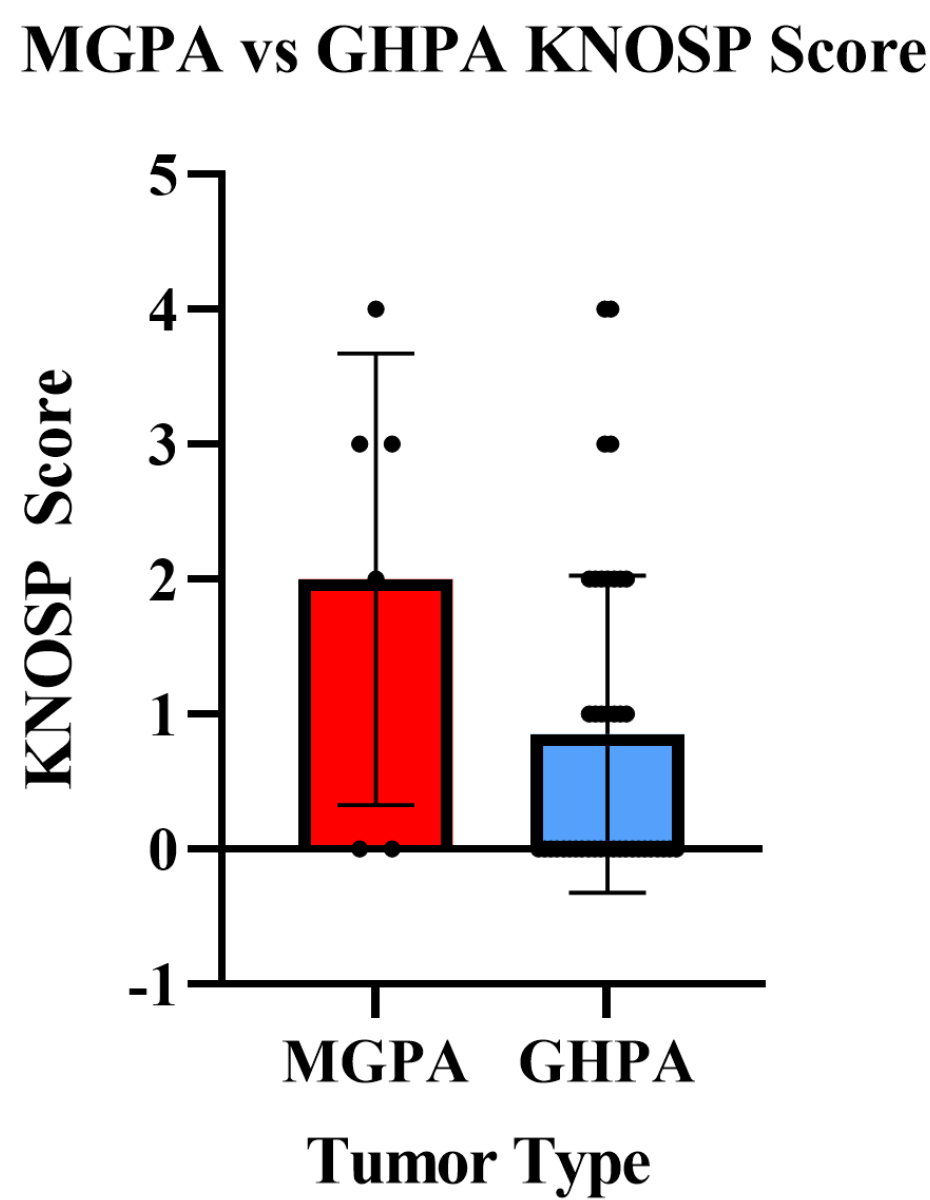
- Six MGPA patients (3 males, 3 females) and 41 GHPA patients (20 males, 21 females).
- Mean ages were 47 years (MGPA) and 49 years (GHPA).
- Common symptoms included headaches, acral enlargement, and facial changes.
- Tumor diameter and KNOSP score were both *larger in the MGPA group* compared to GHPA patients.
- Hormonal remission (IGF-1 normalization) was achieved in 50% of MGPA patients and 46% of GHPA patients.
- No MGPA patients experienced recurrence and 5 GHPA patients harbored tumor/hormonal recurrence with a mean follow-up of 34 months.

Figure 1: MGPA vs GHPA Maximum Tumor Diameter Comparison



All maximum diameter data are displayed in the data points on this graph. Point Y=10 (Macroadenoma (10)) represents the point at which all pituitary adenomas are considered a macroadenoma (diameter > 10 mm).

Figure 2: MGPA vs GHPA KNOSP Score Comparison

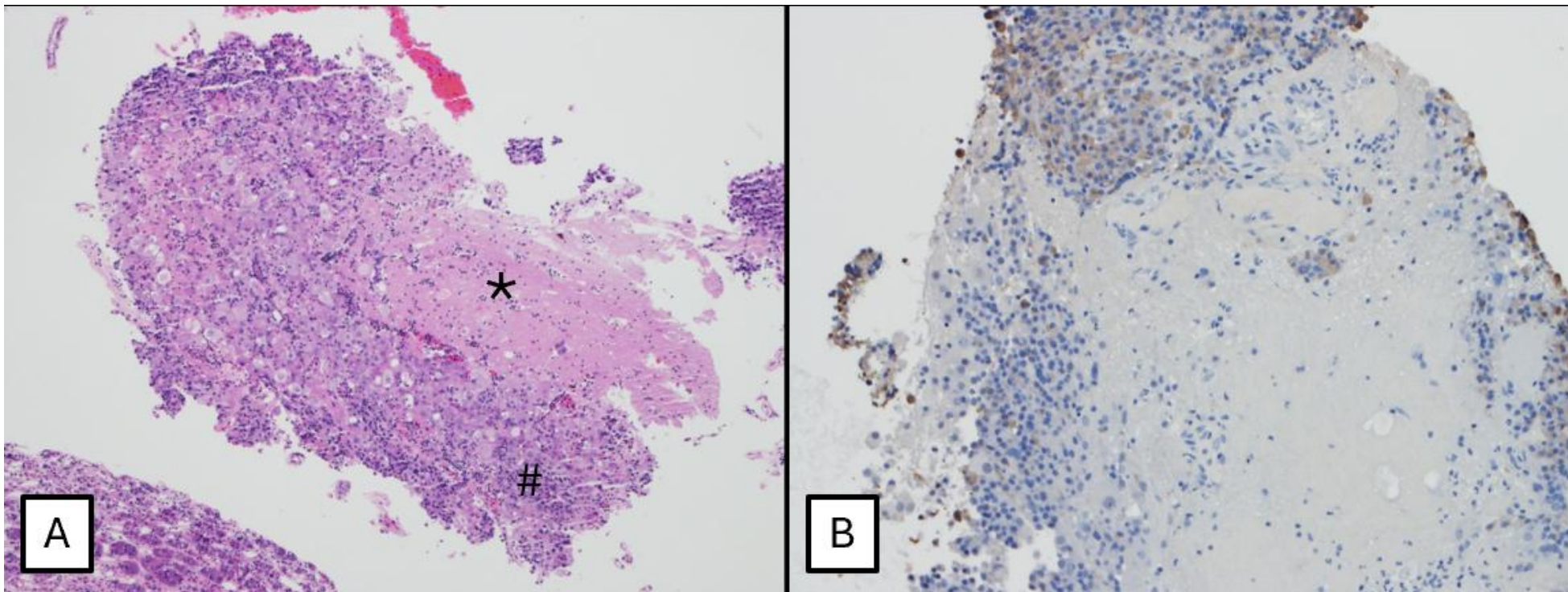


All KNOSP scores are displayed in the data points on this graph. KNOSPs are graded 0, 1, 2, 3, or 4 based on invasion on Coronal MR Sella. The inclusion of -1 on the y-axis is for visualization of the error bar.

Discussion

- MGPA have larger maximum diameters at presentation when compared to GHPAs (25mm vs. 15mm, p=0.034)
- All 6 patients with MGPA had macroadenomas while 27 (65%) of the GHPAs had macroadenomas.
- There was a trend of higher KNOSP scores in the MGPA group (p=0.227)
- Complications experienced by MGPA patients (17%) suggest that surgical intervention may incur more risk postoperatively.
- Recurrence was found in 12% of GHPA patients and 0% in MGPA patients,
- Longer follow-up time seen in GHPA patients (34 months) compared to MGPA patients (19 months).

Figure 3: Mixed Gangliocytoma – Sparsely Granulated Somatotroph Tumor



A) Hematoxylin and eosin (H&E)-stain of a Mixed Gangliocytoma - consisting of mostly eosinophilic Gangliocytoma component (*) with many ganglion cells with neuropil and a small patchy component of the Sparsely Granulated Somatotroph Tumor B) Pituitary adenoma cells immunostained for growth hormone (GH), demonstrating patchy staining of tumor cells positive for this hormone

Conclusions

We present our institution's experience in managing patients with MGPA and compare this rare pituitary adenoma subtype to GHPAs. Pre-operative presentation and hormone panels displayed no differences between cohorts. However, MGPA had larger tumors and greater cavernous sinus invasion compared to GHPAs. EETA was safe and effective in both groups, with similar remission rates. Limitations of our study include the retrospective design of the review, the small sample size and short follow-up time for MGPA patients.

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