Clinical Characteristics and Postoperative Outcomes in a Large Cohort of Patients with Prolactin Costaining Somatotroph Tumors

Kaasinath Balagurunath, BA[1]; Christopher S. Hong, MD[1]; Jakob V Gerstl, MBBS[1]; Ryan Chrenek, MD[1]; Sean Lyne, MD[1]; Noah L Nawabi, BS[1]; Rania A Mekary, PhD[2]; Timothy R. Smith, MD PhD[1]
[1]Brigham and Women's Hospital, [2]Massachusetts College of Pharmacy and Health Sciences

Introduction

Acromegaly is caused by lesions which are primarily growth hormone (GH) secreting, however a subset of tumors also stain positive for prolactin (PRL). Although previous studies have examined the incidence and histological characteristics of these lesions, little has been documented regarding the clinical/endocrinological characteristics and postoperative outcomes after transsphenoidal surgery (TSS).

In this preliminary study, we examined the clinical characteristics and postoperative outcomes in acromegaly patients with PRL positive lesions.

Methods and Materials

In this single institution, retrospective study, a large cohort of 156 acromegaly patients who had GH and PRL staining data available between 2008-2024 were examined. Radiological, surgical, clinical, and endocrinological characteristics at baseline and postoperatively were tracked. Pituitary adenoma size, location, and dimensions were determined using preoperative magnetic-resonance-imaging (MRI) and computerized-tomography (CT) imaging. T tests and chi-square tests were not performed due to the high type-1 error rate. A multivariate logistic regression model was created to determine whether PRL co-staining was predictive of postoperative complications, biochemical remission, or recurrence.

Results

Among the 156 patients with staining data available, 95 (60.9%) demonstrated PRL immunopositivity. The most common preoperative symptoms on presentation were headache (42.1% vs 39.3% in PRL+ vs PRL- patients respectively), acromegalic-bone changes (72.6% vs 78.7%), and tumor induced visual loss (21.1% vs 19.7% respectively). Preoperative demographics, as well as the rates of preoperative comorbidities and medication prescription were largely similar between groups.

Preoperatively, GH hypersecretion occurred in 84.8% of PRL+ and 83.3% of PRL- lesions. Unsurprisingly, rates of preoperative hyperprolactinemia were higher in the PRL+ group (26.4% vs 8.8% respectively). Hypogonadism and hypocortisolism were common in both groups (17.9% and 12.8% respectively, overall). Postoperatively, rates of GH hypersecretion were similar between groups (29.6% vs 26.2% in PRL+ vs PRL- respectively). Rates of hypoadrenalism were higher in the PRL+ group (116.3% vs 5.1%), and no other significant differences in postoperative endocrine dysfunction were noted.

Interestingly, rates of tumor adherence and parasellar location were higher in the PRL- group (16.4% vs 5.3%, and 9.1% vs 0% respectively). PRL+ lesions had higher MIB index scores (2.74 ± 2.4 vs 1.6 ± 0.9 respectively) and experienced higher rates of cystic features (20.2% vs 9.3%). Furthermore, the rates of p53, ACTH, and FSH immunopositivity were higher in the PRL+ group (68.7% vs 35.6%, 31.6% vs 13.1%, and 10.5% vs 1.7% respectively). All but two patients received endoscopic TSS, with nasal packing and fat grafting being the most common sellar reconstruction methods used. Postoperatively, the rates of gross total resection (84.2% vs 83.6%), biochemical remission (75.4% vs 75.5%), and recurrence (11.6% vs 6.6%) were largely similar.

Multivariate logistic regression demonstrated that PRL immunopositivity was not associated with a significantly increased risk of developing surgical complications (dysnatremia or CSF leak), a failure to achieve biochemical remission, or recurrence when adjusted for covariates.

Conclusions

Overall, despite distinct preoperative endocrinological and histological landscapes, PRL immunopositivity in acromegaly patients was not associated with worse postoperative outcomes. In the future, we aim to perform double staining to further classify PRL+ lesions as monomorphic or polymorphic lesions.

Preoperative Characteristics

		Prolactin+ (n=95)	Prolactin- (n=61)
Baseline Characteristics	Age	46.8 ± 15	48.8 ± 14
	Male Gender	41 (43.2%)	29 (47.5%)
	BMI	29.5 ± 5.9	29.3 ± 4
	Height (in)	67.6 ± 4.7	68 ± 4.1
	Weight (lbs)	193.9 ± 48.6	195.5 ± 48.6
Symptoms	Hypopituitarism	1 (1.1%)	3 (4.9%)
	Weight Gain	18 (18.9%)	12 (19.7%)
	Skin Changes	32 (33.7%)	23 (37.7%)
	Infection	1 (1.1%)	3 (4.9%)
	Skin Hyperpigmentation	3 (3.2%)	4 (6.6%)
	Depression	4 (4.2%)	2 (3.3%)
	Hypertrichosis	10 (10.5%)	5 (8.2%)
	Anxiety	4 (4.2%)	2 (3.3%)
	Cognitive Dysfunction	3 (3.2%)	1 (1.6%)
	Headache	40 (42.1%)	24 (39.3%)
	Tumor Induced Visual Loss	20 (21.1%)	12 (19.7%)
	Acromegalic Bone Changes	69 (72.6%)	48 (78.7%)
Comorbidities	Diabetes Mellitus	18 (18.9%)	9 (14.8%)
	Hypertension	40 (42.1%)	23 (37.7%)
	Coronary Artery Disease	2 (2.1%)	0 (0%)
	Stroke	0 (0%0	1 (1.6%)
	Hyperlipidemia	15 (15.8%)	12 (19.7%)
	Tobacco	3 (3.2%)	4 (6.6%)
	Obesity	14 (14.7%)	8 (13.1%)
Preoperative Medications	Synthroid	12 (12.6%)	10 (16.4%)
	Diabetes Mellitus Oral	14 (14.7%)	6 (9.8%)
	Insulin	4 (4.2%)	2 (3.3%)
	GH	0 (0%)	0 (0%)
	Testosterone	2 (2.1%)	3 (4.9%)
	Desmopressin	0 (0%)	1 (1.6%)
	HTN	28 (29.5%)	13 (21.3%)
	Beta Blocker	14 (14.7%)	9 (14.8%)
	Statins	17 (17.9%)	11 (18%)
	Cabergoline	4 (4.2%)	5 (8.2%)
	Somatostatin Analogues	9 (9.5%)	7 (11.5%)

Pre and Postoperative Labs

		Prolactin+ (n=95)	Prolactin- (n=61)
Preoperative	Hyponatremia	4 (4.3%)	1 (1.7%)
	Hypernatremia	1 (1.1%)	1 (1.7%)
	Hyperprolactinemia	23 (26.4%)	5 (8.8%)
	Hypoprolactinemia	4 (4.6%)	6 (11.5%)
	Hypocortisolism	11 (12.5%)	9 (16.1%)
	Hypercortisolism	7 (8%)	5 (8.9%)
	Hypothyroidism	16 (18%)	12 (20.7%)
	Hyperthyroidism	0 (0%)	0 (0%)
	Hypoadrenalism	7 (7.8%)	3 (5.2%)
	Hyperadrenalism	6 (6.7%)	2 (3.4%)
	Hypogonadism	0 (0%)	1 (1.8%)
	Low GH	0 (0%)	0 (0%)
	High GH	78 (84.8%)	50 (83.3%)
	Low ADH	3 (11.5%)	1 (4.8%)
	High ADH	0 (0%)	0 (0%)
Postoperative	Hyponatremia	27 (29.3%)	9 (15%)
	Hypernatremia	4 (4.3%)	3 (5%)
	Hyperprolactinemia	8 (8.8%)	2 (3.3%)
	Hypoprolactinemia	32 (35.2%)	17 (28.3%)
	Hypocortisolism	2 (2.2%)	2 (3.4%)
	Hypercortisolism	63 (69.2%)	32 (54.2%)
	Hypothyroidism	14 (15.6%)	6 (10.9%)
	Hyperthyroidism	0 (0%)	0 (0%)
	Hypoadrenalism	15 (16.3%)	3 (5.1%)
	Hyperadrenalism	2 (2.2%)	0 (0%)
	Hypogonadism	10 (17.2%)	6 (16.2%)
	Low GH	0 (0%)	0 (0%)
	High GH	28 (29.6%)	16 (26.2%)

Lesion and Surgical Characteristics

		Prolactin+ (n=95)	Prolactin- (n=61)
Lesion Characteristics	Adherent	5 (5.3%)	10 (16.4%)
	Invasive	11 (13.4%)	6 (10.9%)
	Suprasellar	28 (32.2%)	21 (38.2%)
	Maximum Diameter (cm)	1.4 ± 0.7	1.5 ± 0.8
	ABC/2 (cm^3)	2.3 ± 3.7	2.7 ± 3.3
	MIB Index	2.74 ± 2.4	1.6 ± 0.9
	Cystic	17 (20.2%)	5 (9.3%)
	Atypical	8 (8.9%)	1 (1.7%)
Surgical Approach	Microscopic Approach	6 (6.2%)	7 (11.5%)
	Endoscopic Approach	93 (97.9%)	61 (100%)
	Combined Approach	5 (5.3%)	7 (11.5%)
	Fat Graft	34 (35.8%)	25 (41%)
	Fascia	0 (0%)	0 (0%)
	Nasal Packing	43 (45.3%)	26 (42.6%)
	Lumbar Drain	1 (1.1%)	0 (0%)
	Nasoseptal Flap	1 (1.1%)	5 (8.2%)
	Intraoperative CSF Leak	24 (25.3%)	18 (29.5%)
IHC Staining	FSH+	10 (10.5%)	1 (1.7%)
	LH+	11 (11.6%)	2 (3.3%)
	GH+	95 (100%)	60 (98.4%)
	ACTH+	30 (31.6%)	8 (13.1%)
	TSH+	14 (14.7%)	4 (6.6%)
	p53+	46 (68.7%)	16 (35.6%)

Postoperative Course

		Prolactin+ (n=95)	Prolactin- (n=61)
Complications	SIADH	9 (9.5%)	2 (3.3%)
	Transient Diabetes Insipidus	9 (9.5%)	6 (9.8%)
	Permanent Diabetes Insipidus	1 (1.1%)	1 (1.6%)
	Postoperative CSF Leak	2 (2.1%)	0 (0%)
	Epistaxis	3 (3.2%)	4 (6.6%)
	ICA Injury	0 (0%)	0 (0%)
	Abscess	0 (0%)	0 (0%)
	Meningitis	2 (2.1%)	0 (0%)
	Site Infection	1 (1.1%)	0 (0%)
	Visual Deficit	0 (0%)	1 (1.6%)
	Hemorrhage	1 (1.1%)	1 (1.6%)
	Sinusitis	0 (0%)	0 (0%)
	Readmission Within 30 Days	8 (8.4%)	3 (5%)
	Reoperation Within 30 Days	2 (2.1%)	1 (1.6%)
Postoperative Course	Recurrence	11 (11.6%)	4 (6.6%)
	Gross Total Resection	80 (84.2%)	51 (83.6%)
	ICU Admission	7 (7.5%)	5 (8.2%)
	Biochemical Remission	51 (75.4%)	37 (75.5%)
Hormone Replacement	Dopamine Agonist	3 (3.2%)	4 (6.6%)
	Thyroid Hormone Replacement	15 (16%)	9 (14.8%)
	Testosterone Replacement	6 (6.4%)	5 (8.3%)
	Estrogen Replacement	0 (0%)	1 (1.6%)
	Cortisol Replacement	22 (23.4%)	7 (11.7%)
	Sandostatin	2 (2.1%)	0 (0%)
	Desmopressin	2 (2.2%)	2 (3.3%)

Multivariate Logistic Regression

	Odds Ratio	Lower Bound	Upper Bound
Any CSF Leak (n=44)*	0.93	0.43	2.02
Dysnatremia (n=28)**	1.2	0.5	3.2
Recurrence (n=15)***	1.9	0.6	6.1
Biochemical Remission (n=89)****	0.77	0.3	1.97

** Other covariates included suprasellar location and GTR*

*** Other covariates included GTR and suprasellar location*

**** Other covariates included GTR*

***** Other covariates included GTR, suprasellar location, preoperative maximum diameter, and preoperative GH hypersecretion*