ILLUSTRATIVE CASE OF PROLACTINONA LOCALIZATION BY INFERIOR PETROSAL SINUS SAMPLING

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Abstract

Inferior petrosal sinus sampling (IPSS) may be a useful endovascular diagnostic procedure to distinguish between ectopic ACTH production and central ACTH-dependent Cushing's Disease, whereby the inferior petrosal sinus is selectively catheterized to provide values of ACTH secreted from each side of the pituitary gland at the site of direct venous outflow of the gland. The utility of IPSS to localize secreting adenomas outside of the Cushing Disease population is uncommonly reported, with few reports detailing its use in prolactinomas. In this study, inferior petrosal sinus sampling (IPSS), an important technique utilized in the work-up of select Cushing Disease patients, was performed in a patient with hyperprolactinemia and two pituitary lesions. The objective of this study was to describe the novel diagnostic utility of IPSS in a case of hyperprolactinoma with bilateral pituitary lesions by IPSS.

Introduction

Medical management has been traditionally considered the primary initial management in the treatment of prolactinomas. However, a more recent Consensus Statement by the Pituitary Society on the diagnosis and management of prolactin-secreting pituitary adenomas suggests a role surgical resection for well-circumscribed (Knosp 0 and 1) prolactinomas when accomplished by an expert pituitary neurosurgeon.[1]

However, the appropriate identification and resection of secreting pituitary adenomas becomes challenging in the setting of multiple adenomas; representing a unique and nuanced entity for surgical treatment, ranging in prevalence from 0.9%-5.4%.[2-4] Prolactin-staining tumors were the most frequently identified in patients with multiple adenomas in a large series of post-mortem specimens[3], and histopathologic specimen of resected tumors.[3,4]

Inferior petrosal sinus sampling (IPSS) is a useful endovascular diagnostic procedure to distinguish between ectopic adrenocorticotropic hormone (ACTH) production and pituitary Cushing Disease. In this technique, the inferior petrosal sinuses are selectively catheterized to obtain baseline and stimulated ACTH levels from each side of the pituitary gland at the site of direct venous outflow. Measurement of, and adjustment to, simultaneously collected prolactin levels can improve diagnostic accuracy. The utility of IPSS outside of the differential diagnosis of ACTH-dependent hypercortisolism is uncommonly reported. In this study, IPSS was performed in a patient with hyperprolactinemia and two pituitary lesions.

Methods and Materials

This is the case of a 37-year-old female who presented with 6 months of amenorrhea and headaches. Blood work obtained by her primary care provider revealed an elevated prolactin of 172.9 ng/mL. Her other lab work was unremarkable including an ACTH of 37.4 pg/mL and TSH of 1.4 uIU/mL, and her beta-HCG was negative. She was referred to an endocrinologist and had repeat blood work and sellar MR imaging performed. Her repeat prolactin following dilution was 99.6 ng/mL and her MRI scan demonstrated two distinct pituitary lesions – a larger right sided lesion measuring 8 mm and a left sided lesion measuring 5 mm, without optic nerve compression (**Figure 1**). The remainder of her hormone panel demonstrated an IGF-1 of 108 ng/mL, ACTH of 104 pg/mL (reference 7.2-63.3), serum cortisol (8:07 am collection) of 17.9 mcg/dL, TSH of 1.895 uIU/mL, free T4 of 0.85 ng/dL, and total T3 of 139 ng/dL . Despite cabergoline treatment, her prolactin remained elevated at 89.9 ng/mL; her IGF-1, serum am cortisol, TSH and free T4 were within normal limits. Given the medical refractoriness of her tumor(s) to medical therapy, surgical options were discussed with the patient.

Time	Prolactin (ng/ml)			Prolactin ratio			ACTH (pg/ml)			ACTH ratio			PRL/ACTH ratio		ACTH-Adjusted PRL ratio
	P	R-IPS	L-IPS	R-IPS/P	L-IPS/P	R/L IPS	P	R-IPS	L-IPS	R-IPS/P	L-IPS/P	R/L IPS	R	L	R/L
Baseline	121.1	482.0	179.9	4.0	1.5	2.7	35	59	86	1.7	2.5	0.7	8.2	2.1	3.9
10'	123.1	490.9	130.1	4.0	1.1	3.8	31	46	79	1.5	2.5	0.6	10.7	1.6	6.5
20'	118.7	324.7	128.5	2.7	1.1	2.5	24	32	52	1.3	2.2	0.6	10.1	2.5	4.1

Table 1. Simultaneous bilateral inferior petrosal sinus sampling in comparison to peripheral prolactin and ACTH .

Results

Baseline simultaneous samples for prolactin were obtained from bilateral catheters and at one, ten, and twenty minutes following catheterization. Peripheral blood from the femoral sheath was collected at the same time points for comparison **(Figure 2).** Based on the usefulness of prolactin to confirm adequate inferior petrosal sinus efflux when IPSS is performed for Cushings disease, ACTH was collected simultaneously with prolactin samples in our patient to be used an in internal control. **Table 1** demonstrates the biochemical data including the prolactin and ACTH levels, the prolactin and ACTH (IPS to peripheral) ratios, the PRL/ACTH ratios, and the ACTH-adjusted prolactin ratios. The patient proceeded with right sided adenoma resection.

Her intraoperative prolactin level was 130.6 ng/mL. Her prolactin nadir was 1.5 ng/mL on POD#1 and her prolactin level on POD#6 was 4.4 ng/mL. Histopathological analysis confirmed a pituitary adenoma which was immunohistochemically positive for prolactin (**Figure 3**).

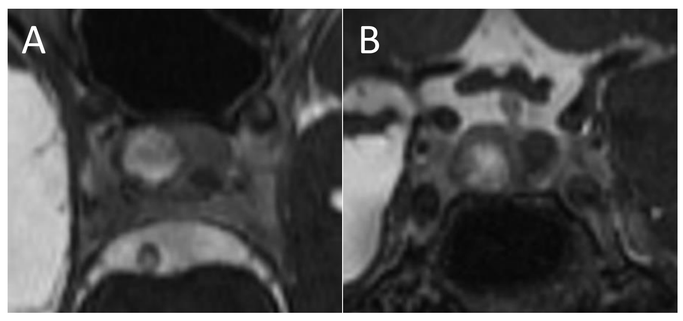

Figure 1. Preoperative imaging demonstrating bilateral pituitary lesions. A. Axial post-contrast constructive interference steady state (CISS) imaging. B. Coronal post-contrast constructive interference steady state (CISS) imaging.

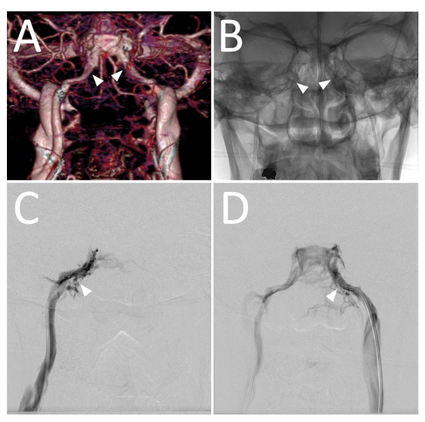

Figure 2. Inferior petrosal sinus sampling. A. 3D angiography showing location of bilateral inferior petrosal sinuses. B. Un-subtracted selective catheter angiography of bilateral inferior petrosal sinuses. C. Right inferior petrosal sinus injection. D. Digital subtracted angiography of selected left inferior petrosal sinus injection with contralateral filling and venous efflux to the pterygoid plexus.
*White arrows note the tips of the catheters in the IPS.

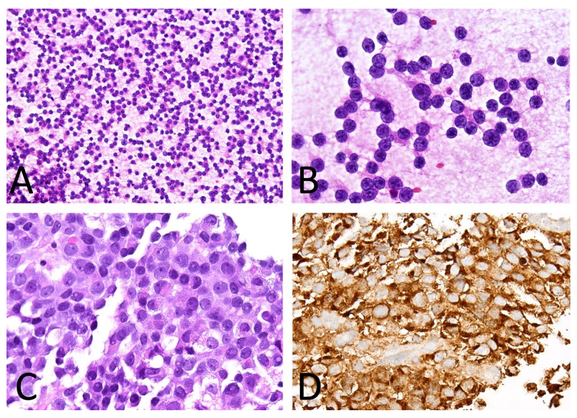

Figure 3. Photomicrographs of prolactin-secreting adenoma specimen. A. 10x magnification smear. B. 40x magnification smear. C. Hematoxylin and eosin staining. D. Immunohistochemical staining for prolactin.

Discussion

Inferior petrosal sinus sampling (IPSS) may be a useful endovascular diagnostic procedure traditionally employed to distinguish between ectopic ACTH production and central ACTH-dependent Cushing's Disease, whereby the inferior petrosal sinus is selectively catheterized to provide values of ACTH secreted from each side of the pituitary gland at the site of direct venous outflow of the gland. Prolactin is collected in these cases as an internal control to the adjusted ACTH level, in order to differentiate Cushing's Disease from ectopic ACTH syndrome. The utility of IPSS to localize secreting adenomas outside of the Cushing's Disease population is uncommonly reported, with few reports detailing its use in prolactinomas. We report the application of IPSS in a patient with hyperprolactinemia and bilateral pituitary tumors. This technique may be helpful in prolactinoma patients with multiple sellar masses.

Conclusions

We report the application of IPSS in a patient with hyperprolactinemia and bilateral pituitary tumors. This technique may be helpful in prolactinoma patients with multiple sellar masses.

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