

**Conflicting Inferior Petrosal Sinus Sampling (IPSS) and Pituitary MRI in a Patient with Cushing's Disease Co-existent with a Rathke's Cleft Cyst**

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Inferior petrosal sinus sampling (IPSS) aids in the differential diagnosis of ACTH-dependent Cushing's syndrome with a diagnostic accuracy of nearing 100%. It may also help in predicting the side of a corticotroph adenoma with an accuracy of 70-80%. In the case presented below we show how this test was conflicted by a pituitary MRI.

A 40-year-old Caucasian male presented to our Centre with a 4-year history suggestive of Cushing's syndrome. Clinically, he had hypertension, supra-clavicular fat pads, centripetal obesity, acne, proximal myopathy, with intact visual fields and no ocular palsy. The Cushing's workup gave urinary free cortisols of 2484 nmol/24hrs and 3879 nmol/24hrs (0-560), midnight serum cortisols of 602 nmol/L and 736 nmol/L, a 0900h ACTH of 58.9 ng/L (0-46). His potassium was 3.2 mmol/L (3.5-5.0). A low dose dexamethasone suppression (LDDST) test failed to suppress, with a 48-hour cortisol of 737 nmol/L. A high dose dexamethasone suppression test (HDDST) showed no suppression, with a 48-hour cortisol of 722 nmol/L. A CRH test at the outset of the workup resulted in a rise of the cortisol from 722 nmol/L to 1287 nmol/L (i.e., >20% rise) and a rise of ACTH from 44 ng/L to 151 ng/L (i.e., >50% rise), suggesting Cushing's disease. A pituitary MRI done by the referring hospital was reported as normal. The review of the scans by our neuro-radiologist suggested a left-sided pituitary lesion. With a positive CRH test but a non-suppressed HDDST, we proceeded to an IPSS which confirmed Cushing's disease (central/peripheral ACTH >3) and lateralized to the right inferior petrosal sinus (a right/left ratio of >1250/197). As the pituitary MRI suggested left-sided disease, and the IPSS suggested it to be on the contralateral side, it was decided to proceed to a dynamic pituitary MRI immediately pre-operatively. This again suggested a left-sided microadenoma, and the patient underwent a trans-sphenoidal adenectomy (TSA) in 2007. Intra-operatively, the neurosurgeon saw a yellowish-green abnormality on the left side and thought it to be a Rathke's cleft cyst and performed a partial pituitary resection; the right side was explored and found to be normal. 9am cortisols post-operatively were raised at 660 and 648, suggesting a biochemical non-cure. Histology confirmed a Rathke's cleft cyst but did not identify a pituitary adenoma or ACTH hyperplasia. There was, however, Crooke's hyaline change consistent with exposure to high cortisol levels. The patient underwent a repeat TSA a fortnight later, with a complete hypophysectomy. The post-operative 9am cortisol of 47 nmol/L suggested biochemical cure and the histology identified an adenoma staining strongly positive to ACTH. At 6-weeks his 0900h cortisol was <6 nmol/L. A 3-month follow-up pituitary MRI reported an empty sella and no residual tumour.

This case reports one of the few reported cases of co-existence of a Rathke's cleft cyst with a corticotroph adenoma. The indications of IPSS and potential pitfalls in the diagnostic work-up of Cushing's syndrome are discussed.