LETTER TO EDITOR

Report of Bilateral Inferior Petrosal Sinus Sampling in Iran

Dear Editor

The differential diagnosis of ACTH-dependent Cushing syndrome is a challenging issue for clinical endocrinologists.

MRI is commonly used to diagnose Cushing disease and remains the obvious technique to identify pituitary microadenomas in a noninvasive manner but it has proved to be problematic in some cases.

Bilateral inferior petrosal sinus sampling (BIPSS), despite being invasive, is established as a highly accurate diagnostic procedure in distinguishing pituitary from ectopic sources of ACTH.[1,2,3] The management options for Cushing syndrome have been changed due to this procedure dramatically.

It is one of the most sensitive and specific tests, both in the correct diagnosis and in the precise lateralization of tumors in patients with Cushing disease.

In addition, BIPSS can serve as a guide to avoid unnecessary pituitary surgery in a significant number of patients with nonfunctional microadenomas.

A 36-year-old male patient was referred to our clinic in Shariati Hospital with a 2-year history of obesity, edema, acne, alopecia and hypertention.

After some evaluations such as biochemical tests and hormonal studies, the patient met the criteria for proving Cushing disease, but his MRI could not identify the site of the adenoma precisely. So, he was selected for the BIPSS procedure.

BIPSS was performed on April 24, 2007 and because it was the first experience of this procedure in Iran, it was valuable to be informed.

The results are reflected in Table 1 and 2:

Transsphenoidal surgery (TSS) was performed on May 12, 2007. Taking into account the patient with a left side microadenoma shown at TSS examination, the BIPSS ACTH ratio was not in agreement with the side recorded by the neurosurgeon. The pathology results also confirmed adenoma. The plasma cortisol was measured twice, three days and one month after the operation and the levels reported were 5μg/dl and 0.55μg/dl, respectively. Then the patient was treated with prednisolone.

The existence of a significant ACTH gradient between venous samples from the inferior petrosal sinuses (IPS) and the periphery (p) is considered diagnostic of pituitary–dependent Cushing syndrome,

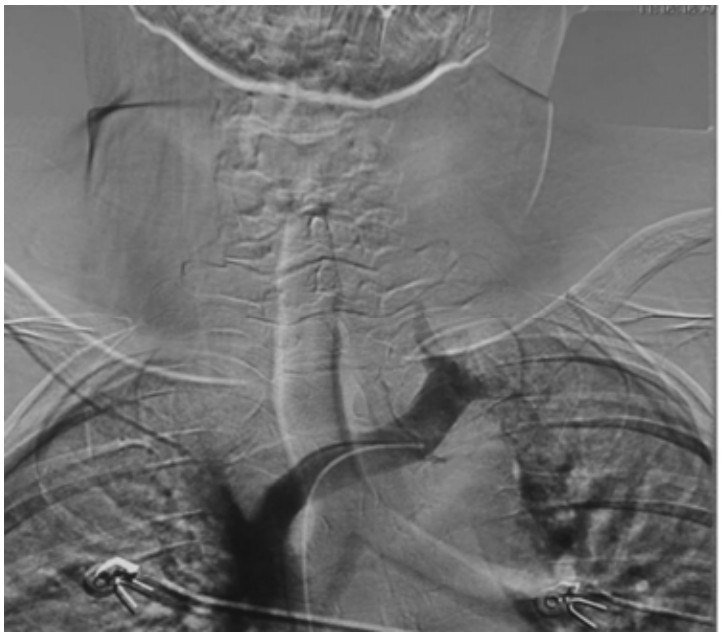

Fig. 1. Catheter in the left brachiocephalic vein

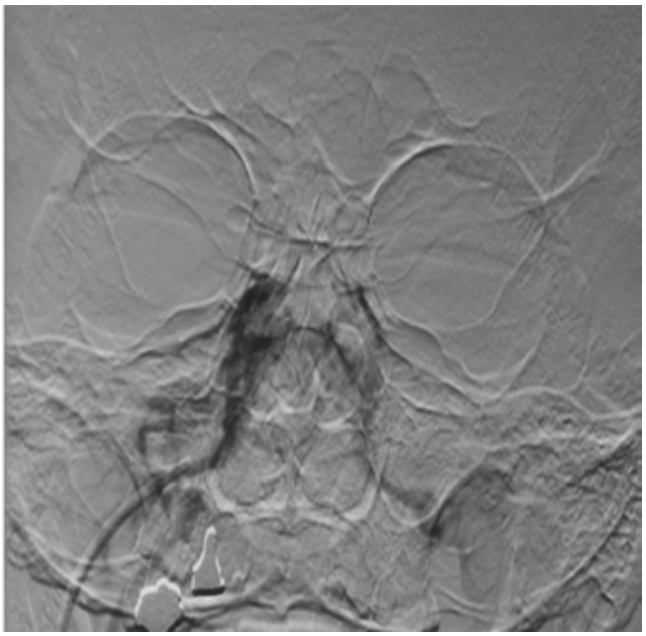

Fig. 2. Catheter in the right inferior.

Table 1. Patient ACTH Values During IPSS Test Following Intravenous Injection of AVP

	Side	Minute	pg/ml
ACTH	Right	-10	1016
		0	862
		+2	1568
		+5	810
		+10	721
	Left	-10	199
		0	226
		+2	653
		+5	441
		+10	269
	Peripheral	-10	97
		0	109
		+2	106
		+5	122
		+10	110

Table 2. Central to Peripheral ACTH Ratio During IPSS

Side	Minute	Ratio	
		Rt	Lt
C/P	-10	10.47	2.05
	0	7.9	2.07
	+2	14.79	6.16
	+5	6.63	3.61
	+10	6.5	2.44
R/L	-10	5.1	
	0	3.8	
	+2	2.4	
	+5	1.8	
	+10	2.6	

whereas its absence suggests ectopic ACTH secretion.[4,5]

In this procedure, a catheter was placed in the orifice of each of the right and left inferior petrosal sinuses via a femoral vein approach.

Blood samples for ACTH assay were obtained simultaneously from both sides of the inferior petrosal sinus and from a peripheral vein before and 3, 5 and 10 minutes after argenin vasopressor (AVP) was given as a bolus injection.

ACTH concentrations in the bilateral sampling and in the periphery were calculated for central to peripheral (C/P) ratio for each set of samples.

A C/P ratio higher than 2 at basely or higher than 3 after corticotropin releasing hormone (CRH) injection is considered to indicate a pituitary origin of ACTH secretion.[6] In our patient the C/P ratio showed that this level was higher than 3 before and after injection, and it was diagnostic. It is important to know that a difference in the gradient between the right and left sinuses of 1.4 predicts the site of the lesion with 68% accuracy before and 71% accuracy after CRH injection in a series of more than 200 patients.[7]

In our patient, the right to left incidence flow was higher in the right side, but interestingly the operative findings of the neurosurgeon were not in agreement with this ratio, because the adenoma was observed in the left side of the pituitary gland. Therefore, BIPSS could confirm the pituitary source of ACTH but could not correctly lateralize the tumor in our case.

False negative results occur in 5-10% of patients with Cushing's disease who do not have a peripheral plasma ACTH or cortisol response to CRH.[8]

False positive results occur in patients with ectopic ACTH syndrome or adrenal tumor, in whom an increase in peripheral plasma ACTH in response to CRH, due to incomplete suppression of pituitary ACTH secretion takes place.[9]

In conclusion, BIPSS together with MRI should be used as a diagnostic approach for patients in whom other diagnostic tests have not been able to localize the adenoma. Patients should be considered on a case-by-case basis, taking into account both radiological and biological findings to minimize the risk of patient misclassification and mismanagement.

In this patient, we also observed that the results of lateralization by IPSS sampling do not remove the need for a thorough TSS examination of the sella turcica contents.

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