Letter to the Editor from Lukas Andereggen: "Pitfalls in Performing and Interpreting Inferior Petrosal Sinus Sampling: Personal Experience and Literature Review"

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To the editor

We read with great interest the article by Perlman et al. (1) reporting important pitfalls in the performance of inferior petrosal sinus sampling (IPSS). The case-based review not only helps correctly interpret the results of IPSS, but also resonates well with the ongoing difficulties encountered when assessing patients with hypercortisolism. Correct identification of adenomas in Cushing's syndrome (CS) remains a difficult task, highlighting the need to offer strategies to avoid misleading interpretations of IPSS results. While IPSS is highly sensitive and specific in distinguishing ectopic adrenocorticotropic hormone (ACTH) syndrome (EAS) from Cushing's disease (CD), correct prediction of the adenoma side remains difficult. This continues to be the case when prolactin-adjusted intersinus ACTH gradients are used to confirm adequacy of IPS cannulation, (2) or in the use of a PET-CT to better identify the source of ACTH in CS. (3) So far, various explanations for the poor accuracy in lateralization of IPSS have been reported. From our own experience, we found the following points critical for correct identification of the adenoma side:

1) It is crucial to enable meticulous classification of the venous outflow pattern. Besides the classical patterns described Shiu et al.,(4) awareness of infrequent anatomical variants is crucial to avoid sampling errors and ensure correct interpretation of the IPSS results. For a better understanding of the venous anatomy, knowledge of the morphologic variations observed by 3D rotational venography can be helpful.(5) In case of unsuccessful IPS cannulation, the drainage type should be documented using an internal carotid artery injection, with assessment of the dominant veins draining from the cavernous sinus on the contralateral side,(6) in order to avoid misleading results.

2) We emphasize that the position of the catheter tip should be checked before, during and after the venous sinus petrosal sampling, even in the case of concomitant prolactin measurement, to ensure adequate IPS venous efflux. Also, we emphasize the use of super-selective catheterization—namely, any catheter displacement or hindering of the venous outflow that may result in false positive or negative results both before and after oCRH stimulation.(7)

3) The venous outflow symmetry may influence the prediction of the adenoma side. It is conceivable that a hypoplastic or plexiform IPS may lead to misleading intersinus gradients, with asymmetric outflow patterns resulting in asymmetry of ACTH

measurements. While we could not find evidence that IPS asymmetry diminished the prediction of the adenoma side,(6) the influence of a dominant pattern has to be considered.

4) Despite careful evaluation of the IPS results, surgeons may still be faced with failed intraoperative adenoma visualization. Under these circumstances, two-thirds gland resection or hemi-hypophysectomy has been proposed on the side indicated by IPSS, with a subsequent risk of hypopituitarism. We noted that when limiting the approach to the lateral one-third in these cases instead, low new endocrinopathies could be attained, yet long-term remission rates were modest.(8)

Interdisciplinary multimodal therapies probably offer the best chances for long-term cure in this extremely challenging disorder among hormone-secreting pituitary tumors.

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