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Bilateral inferior petrosal sinus sampling is the most reliable test to differentiate Cushing's disease from ectopic adrenocorticotropic hormone (ACTH) production. Catheters, whether preshaped polyethylene or coaxial Tracker systems, are supple and atraumatic. Retrograde venograms are gentle procedures performed only to document catheter position at the time of sampling. And yet, as reported by Bonelli et al (page 306) in this issue of the *American Journal of Neuroradiology*, we continue to see the rare ischemic/hemorrhagic complication associated with this procedure. It is appropriate to report these rare complications to our colleagues; the question remains whether anything can be learned about their cause or prevention.

Historically, it is of interest to note that the first large reported series of patients who underwent petrosal sinus sampling were studied by a tip-deflecting catheter guidewire handle system (1). Using this method, a probing guidewire was never advanced beyond the tip of the 4-French sampling catheter, and the sampling site tended to be relatively proximal in the inferior petrosal system. No complications were encountered in 312 consecutive procedures, and the sensitivity for distinguishing Cushing's disease from ectopic ACTH-dependent hypercortisolism was 100% after corticotropin-releasing hormone (CRH) administration. Production of this catheter guidewire handle was discontinued in the late 1980s. Petrosal sinus sampling is currently performed with flexible catheters introduced over supple glidewires. Some groups routinely enter the petrosal system with only coaxial Tracker catheters, but both techniques involve probing for the inferior petrosal sinuses with guidewires over which the sampling catheter is subsequently positioned. Conversion to the use of finer wires and catheters permits more selective catheterization, but increases the risk of engaging small bridging veins that occasionally connect the inferior petrosal sinus with the brain stem. All reported ischemic/hemorrhagic complications of petrosal sinus sampling have occurred with such probing-wire catheters. One wonders whether more proximal sampling of the inferior petrosal sinuses might not lessen the risk of these ischemic/hemorrhagic complications with, in our experience, no loss of diagnostic sensitivity. Neurointerventionalists, however, are committed to performing more selective studies with highly refined catheter systems; some recommend routine sampling of the cavernous rather than petrosal sinuses, a technique we feel is unnecessary and risky (2).

In addition, we do not completely understand the anatomic basis for brain stem injury or hemorrhage during inferior petrosal sinus sampling. The most likely explanation is a variation occurs in the venous anatomy connecting the brain stem and the petrosal sinuses. Before the introduction of cross-sectional imaging, the veins of the posterior fossa were important diagnostic landmarks and were extensively studied. A number of small veins drain the posterior cerebellopontomedullary angle via one or more petrosal veins, but the anatomy is quite variable. A small venous channel originating in the region of the cerebellopontomedullary angle and crossing the subarachnoid space to connect with the inferior petrosal sinus has been described. Bridging veins also have been described between the transverse pontine vein, vein of the pontomedullary sulcus, and the lateral medullary vein with the inferior petrosal sinus. These small venous structures on the surface of the brain stem and bridging the subarachnoid space are never visible on retrograde venograms, but could potentially be engaged by the miniaturized wire-catheter systems currently used. Obturation of the veins by the catheter could lead to reversible edema followed by hemorrhagic infarction of the brain stem. Alternatively, the bridging venous structures in the subarachnoid space could be ruptured, leading to subarachnoid bleeding, as reported in the current case. And the forcible retrograde injection of contrast media, even through such microcatheters, could cause rupture and extravasation. Unfortunately, patients with such variant venous anatomy cannot be identified before petrosal sinus sampling, and one depends upon monitoring the patient's symptoms for early signs of brain stem dysfunction. We have reported two patients demonstrating reversible brain stem symptoms and suggesting that early venous hypertension is reversible if recognized (3). The early recognition of subarachnoid bleeding, as in the author's case, is a more challenging diagnosis. Such a patient would not show the symptoms of brain stem dysfunction such as slurred speech, hemifacial paresthesias, sensation of enlarged tongue, and perioral tingling that are often confused with anxiety and treated by increased sedation.

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Unlike these vague symptoms of brain stem dysfunction, the sign common to all reported cases and easily recognized by monitoring is the development of hypertension, often severe and erratic. Patients with Cushing's disease are mildly hypertensive and anxiety-related variations in pressure, particularly at the beginning of a sampling procedure, are not uncommon. Nonetheless, any patient developing labile hypertension during inferior petrosal sampling should be suspected of cerebellopontine dysfunction caused by catheter-induced venous hypertension. To treat such patients with antihypertensives or additional sedation entails the risk of converting a reversible into a permanent vascular complication. Close monitoring of blood pressure changes is particularly important in pediatric patients (15% of our series) undergoing sampling under general anesthesia because in these patients the symptoms of brain stem dysfunction cannot be elicited. With such guidelines, we have performed over 700 bilateral petrosal sinus samplings since our index case of brain stem injury (3), and have encountered no problems.

Does this mean that we must discontinue petrosal sampling in any patient developing hypertension during the procedure? The answer to this question is probably ''Yes,'' but fortunately, an alternative procedure of almost comparable sensitivity is available. We have recently reported that bilateral internal jugular vein sampling after the administration of CRH correctly distinguishes pituitary from ectopic ACTH syndromes in 85% of patients (4). Corticotropin-releasing hormone is essential, as sampling is positive only after its administration in more than half of the cases. A 4-French catheter introduced into both internal jugular veins under sonographic control and positioned at the angle of the mandible is practically a risk-free procedure. We have encountered several instances of positive jugular vein sampling in the presence of negative inferior petrosal sampling. These cases usually involve atrophic or plexiform inferior petrosal sinuses in one or both sides; precisely the anatomic circumstances that lead to prolonged catheterization procedures, and probably increase the risk of a cerebellopontine injury.

In summary, permanent neurologic injury from properly performed petrosal sinus sampling is a rare complication (one in 1200 cases, or 0.001% in our experience). But its prevention requires close monitoring during the procedure for symptoms of brain stem dysfunction, and a willingness to discontinue the study when signs or symptoms appear. Bilateral internal jugular vein sampling with CRH administration is an alternative, risk-free study of comparable sensitivity. Prolonged probing with wires and microcatheters may increase the risk of entering anomalous petrosal sinus-to-brain stem bridging veins, and thereby increase the risk of cerebellopontine injury or subarachnoid hemorrhage.

References

1. Oldfield EH, Doppman JL, Nieman LK, et al. **Petrosal sinus sampling with and without corticotropin-releasing hormone for the differential diagnosis of Cushing's syndrome.** *N Engl J Med* 1991;325:897–905
2. Doppman JL, Nieman LK, Chang R, Yanovski J, Cutler GB, Chrousos GP, Oldfield EH. **Selective venous sampling from the cavernous sinuses is not a more reliable technique than sampling from the inferior petrosal sampling in Cushing's syndrome.** *JCEM* 1995;80:2485–2489
3. Miller DL, Doppman JL, Peterman SB, Nieman LK, Oldfield EH, Chang R. **Neurologic complications of petrosal sinus sampling.** *Radiology* 1992;185:143–147
4. Doppman JL, Oldfield EH, Nieman LK. **Bilateral sampling of the internal jugular vein to distinguish between mechanisms of adrenocorticotrophic hormone-dependent Cushing syndrome.** *Ann Intern Med* 1998;128:33–36