

# Bilateral Inferior Petrosal Sinus Sampling in the Management of ACTH-dependent Cushing's Syndrome

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Clinicians are confronted with 2 major problems when managing patients with ACTH-dependent Cushing's syndrome. The first is to differentiate those with Cushing's disease (CD) from those with ectopic ACTH syndrome (EAS). The second is to localize the pituitary microadenoma in patients with a presumptive diagnosis of CD. The diagnostic accuracy of various biochemical tests is suboptimal in differentiating CD from EAS,<sup>1</sup> and bilateral petrosal sinus sampling (BIPSS) has become the most accurate procedure for this purpose.<sup>2</sup> Although earlier studies reported a diagnostic sensitivity and specificity approaching 100%,<sup>3</sup> many subsequent series have revealed some false-negative results.<sup>4</sup> Using a petrosal sinus-to-peripheral ACTH ratio  $>2.0$  in the basal state or a peak ratio  $>3.0$  after corticotropin-releasing hormone (CRH) stimulation, a false-negative rate up to 10% in patients with proven CD has been reported.<sup>4</sup>

False-negative results with BIPSS have been attributed to either technical problems or anomalous venous drainage.<sup>5</sup> Measurements of multiple pituitary hormones during BIPSS are proposed to serve as an index of pituitary venous effluent and thereby avoid misclassification. To avoid false-positive results, BIPSS should be performed after the confirmation of permanence of hypercortisolism and after thoracic and abdominal computed tomography (CT) scans have been systemically performed.<sup>6</sup>

In this issue of the journal, Lin et al report the results of BIPSS in the diagnosis of CD in Taipei Veterans General Hospital.<sup>7</sup> A total of 18 patients with CD were subjected to BIPSS and ovine CRH (oCRH) stimulation, including 4 patients who had previous

transsphenoidal surgery. The same diagnostic criteria were used for all patients. No technical failure was reported. One false-negative result was noted in a patient who had previous transsphenoidal surgery. The sensitivities of BIPSS for diagnosis of CD before and after oCRH stimulation were 89% and 94%, respectively. These results are comparable to those of other studies.

BIPSS has been used for lateralization of corticotroph microadenoma, thus guiding the surgeon during transsphenoidal surgery.<sup>6</sup> A combined analysis of reports published before 1998 showed that the diagnostic accuracy of simultaneous BIPSS for lateralization of corticotroph microadenoma was 78% (range, 50–100%).<sup>8</sup> However, in an Italian multicenter study, BIPSS was less reliable in identifying the adenoma site found at surgery than magnetic resonance imaging (MRI) or CT (65% *vs.* 75% and 79%, respectively).<sup>9</sup> Venous drainage pattern and catheter tip location are probably the primary limiting factors to correct localization.<sup>10</sup> In Lin et al's report, the sensitivities of lateralization by BIPSS were 53% and 59% before and after oCRH stimulation, respectively.<sup>7</sup> If the 4 patients who had previous transsphenoidal surgery were excluded, the sensitivities increased to 70% and 77%, respectively. So, their results are comparable to those in the literature.

BIPSS is not without complications, with thromboembolism and even lethal pulmonary embolism and cranial nerve (mainly 6<sup>th</sup>) paralysis having been reported. Based on this and the above noted limitations, BIPSS should be performed in patients with ACTH-dependent hypercortisolism in whom pituitary MRI is normal or equivocal.<sup>10</sup>

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