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In Patients with Cushing's Disease and a Visible Tumor on MRI, IPSS does not Add to the Accuracy of Predicting Tumor Lateralization

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Introduction: There is controversy surrounding the value of bilateral inferior petrosal sinus sampling (BIPSS) for tumor lateralization in Cushing's disease (CD). We compare lateralization results between BIPSS and pituitary imaging against gold-standard surgical localization.

Methods: A retrospective chart review was conducted in patients with pathology-confirmed CD, visible tumor on MRI (with and without contrast), and who underwent BIPSS at our institution between 2003-2020. An inferior petrosal sinus to peripheral (IPS/P) prolactin ratio >1.8 was used to confirm appropriate IPS sampling. An inter-sinus ACTH gradient ratio greater than 1.4, adjusted for prolactin where available, was used to determine lateralization. In each case, the neurosurgeon performed a full pituitary gland exploration to avoid missing any tumors despite visible tumor on MRI. Descriptive statistics were used.

Results: Of 32 patients with CD, visible tumor on MRI, and BIPSS testing, 27 (84%) patients had technically successful bilateral IPSS catheterization and are the subjects of this study. All 27 of these patients had IPS/P ACTH ratio greater than 2 at baseline or 3 after CRH stimulation, consistent with CD, and all 27 lateralized. The median age at diagnosis was 42 years (range 21-69 years) and 85% were female (N=23). The median tumor size on MRI was 5 mm (range 3-8 mm). In 22/27 (81%) patients, the result of the IPSS lateralization was concordant with MRI findings. When MRI and BIPSS lateralization agreed, 21/22 (95%) were confirmed by surgical pathology. Of the 5 cases where MRI and BIPSS disagreed on laterality, the operative report was consistent with MRI lateralization in 3/5 cases, and bilateral disease in the remaining 2 cases. There were no cases where BIPSS lateralization was correct when MRI lateralization was incorrect. Overall, MRI correctly lateralized 26/27 cases (96%), whereas BIPSS correctly lateralized 23/27 (85%). In the subset of 13 patients with tumors measuring <6mm on MRI, MRI imaging lateralization was correct in all 13 (100%) cases and BIPSS lateralization was correct in 11/13 (85%). Adverse events associated with BIPSS were noted in 4 patients (15%) ranging from hematoma to headache. Among the 5 patients who did not have successful BIPSS cannulization, one experienced the adverse effect of transient severe headache. There were no serious complications. The surgeons performed bilateral sellar exploration in all cases regardless of BIPSS or MRI lateralization results.

Conclusion: When a tumor is visible on MRI, regardless of its size (≥ 3mm), BIPSS does not add to the accuracy of determining tumor lateralization. BIPSS may best be reserved for situations where the diagnosis of CD is in question. Further studies are required to determine the value of BIPSS in lateralizing the source of CD in patients without visible tumor.

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