Silent corticotroph adenoma

Silent corticotroph adenomas (SCAs) are clinically nonfunctioning pituitary adenomas (NFPAs) with positive staining for corticotropin (ACTH) by immunohistochemistry. Whether SCAs behave more aggressively than NFPAs without ACTH immunoreactivity (ACTH negative) remains controversial.

To compare characteristics and outcomes of SCAs with ACTH-negative NFPAs and to identify predictors of aggressive outcome. Primary composite endpoint included the first of any of the following events: progression, recurrence, or death.

Retrospective cohorts included 33 SCAs followed for 42.5 months (median) (range, 6.7-179.0 months) and 126 ACTH-negative patients followed for 42 months (range, 6-142 months). SCA were younger (mean ± SD; 49.6 ± 14.1) than ACTH-negative patients (55.6 ± 12.8, P = .02). Tumor diameter was similar (2.8 ± 1.0 cm); cavernous sinus invasion was present in 45.5% of SCAs and 30.2% of ACTH-negative NFPAs (P = .09). Postoperative tumor residual was detected in 53.1% of SCAs and 49.6% of ACTH-negative patients. Radiation was administered in 40.6% of SCAs at 16 months (range, 3-149 months) and 33.3% of ACTH-negative patients at 13 months (range, 3-94) postoperatively. Progression of residual tumor occurred in 24.2% of SCAs and 11.1% of ACTH-negative patients (P = .08); recurrence was similar (6.0% SCAs vs 5.5% ACTH-negative patients). Cumulative event-free survival rates were not significantly different between the 2 groups (P = .3). Age, sex, tumor size, cavernous sinus invasion, or SCA subtypes were not associated with outcome.

SCA patients were younger, but exhibited similar postoperative tumor regrowth rates as ACTH-negative macroadenomas while using a similar adjuvant radiation protocol. Long-term follow-up is warranted because predictors of regrowth are currently lacking.

The 2017 World Health Organization classification of tumors of the pituitary gland, in addition to hormone immunohistochemistry, recognizes the role of other immunohistochemical markers including but not limited to pituitary transcription factors. Recognizing this novel approach, the fourth edition of the WHO classification has abandoned the concept of “a hormone-producing pituitary adenoma” and adopted a pituitary adenohypophyseal cell lineage designation of the adenomas with subsequent categorization of histological variants according to hormone content and specific histological and immunohistochemical features. This new classification does not require a routine ultrastructural examination of these tumors. The new definition of the Null cell adenoma requires the demonstration of immunonegativity for pituitary transcription factors and adenohypophyseal hormones Moreover, the term of atypical pituitary adenoma is no longer recommended. In addition to the accurate tumor subtyping, assessment of the tumor proliferative potential by mitotic count and Ki-67 index, and other clinical parameters such as tumor invasion, is strongly recommended in individual cases for consideration of clinically aggressive adenomas. This classification also recognizes some subtypes of pituitary neuroendocrine tumors as “high-risk pituitary adenomas” due to the clinical aggressive behavior; these include the sparsely granulated somatotroph adenoma, the lactotroph adenoma in men, the Crooke's cell adenoma, the silent corticotroph adenoma, and the newly introduced plurihormonal Pit-1-positive adenoma (previously known as silent subtype III pituitary adenoma). An additional novel aspect of the new WHO classification was also the definition of the spectrum of thyroid transcription factor-1 expressing pituitary tumors of the posterior lobe as representing a morphological spectrum of a single nosological entity. These tumors include the pituiocyta, the spindle cell oncocytoma, the granular cell tumor of the neurohypophysis, and the sellar ependymoma.
Total surgical resection for silent pituitary corticotroph adenoma (SCA) is often challenging as these tumors frequently invade a cavernous sinus. Early remnant tumor intervention is justified, because untreated residual pituitary tumors regrow when patients were followed up for a long time. Prophylactic radiotherapy is not warranted for completely resected SCAs as tumor recurrence is uncommon.

