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Corticotroph Macroadenomas with Extensions to Third Ventricle: Four Case Reports

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Background: Pathophysiology of corticotroph macroadenomas has not been elucidated. In this study, we present four cases of adrenocorticotropic hormone (ACTH)-secreting pituitary adenomas with extensions to the third ventricle (TV) and investigate their clinical and pathological characteristics. **Case 1:** A male in his seventies went to a hospital because of a fall. Upon performing computed tomography, a tumor was incidentally noted. Pituitary MRI revealed a macroadenoma with extension to TV. He presented with Cushingoid features (CF). His basal ACTH level was 112 pg/mL, and urinary free cortisol (UFC) was 129.1 μg/day. Cortisol was not suppressed in the 0.5 mg dexamethasone suppression test (0.5 mg DST). ACTH level increased in the corticotropin-releasing hormone (CRH) stimulation test and the desmopressin (DDAVP) stimulation test. He was diagnosed with Cushing's disease (CD), and endoscopic transsphenoidal surgery (ETSS) was performed. Pathological findings showed densely granulated corticotroph adenoma (DGCA). Somatostatin receptor type 5 (SSTR5) was negative, and ubiquitin-specific protease 8 (USP8) was not mutated. **Case 2:** A female in her fifties had a visual field defect and pigmentation of the face. MRI revealed a macroadenoma with extension to TV. She presented with CF. Her basal ACTH level was 57.9 pg/mL, and UFC was 259.7 μg/day. Cortisol was not suppressed in the 0.5 mg DST. ACTH level increased in the CRH test and the DDAVP test. She was diagnosed with CD. Pathological findings showed DGCA. SSTR5 was moderate positive, and USP8 was suspected to be mutated. **Case 3:** A female in her fifties had a throbbing headache. MRI showed a macroadenoma with extension to TV. She did not present with CF. Her basal ACTH level was 71.8 pg/mL, and UFC was 134.3 μg/day. Cortisol was not suppressed in the 0.5 mg DST. ACTH showed response to the CRH test and the DDAVP test. She was diagnosed with subclinical Cushing's disease (SCD) and sparsely granulated corticotroph adenoma (SGCA). SSTR5 was slightly positive, and USP8 was not mutated. **Case 4:** A male in his fifties had general malaise and polyuria. MRI showed a macroadenoma with extension to TV. He did not present with CF. His basal ACTH level was 179 pg/mL, and UFC was 187.4 μg/day. Cortisol was not suppressed in the 0.5 mg DST. ACTH did not show response to the CRH test and the DDAVP test. He was diagnosed with SCD, and the tumor had oncocytic changes. SSTR5 was negative, and USP8 was not mutated. **Conclusion:** The findings from these case reports suggest that phenotypes of CD and SCD are associated with the differences between SGCA and DGCA. Moreover, it is also suggested that USP8 mutations correlate with SSTR5 expression in macroadenomas that extend to the TV.

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