BACKGROUND AND INCIDENCE

- ACTH-dependent Cushing’s disease (CD) is a condition characterized by pituitary hypersecretion of ACTH, leading to adrenal cortisol upregulation.
- Along with cushingoid features, hypercortisolism also has long-term complications, notably metabolic syndrome, cardiovascular disease, and osteoporosis.
- The incidence of CD is approximately 1-2 cases per million.
- ACTH can be secreted by pituitary microadenomas and macroadenomas, and in some cases, ectopic sources.
- Here, we report a case that describes ACTH-dependent CD caused by a pituitary microadenoma in a patient with a history of planum sphenoidale meningioma.

CASE DESCRIPTION

- 48-year-old female with a past medical history of planum sphenoidale meningioma s/p transsphenoidal partial resection, central hypothyroidism on levothyroxine, and hypogonadotropic hypogonadism presented with worsening truncal obesity and prediabetes.
- The physical exam was remarkable for obesity and hyperpigmentation of knuckles.
- Labs are shown below. Prolactin, TSH, and HGH levels were normal.

| AM Cortisol | 27.2 mcg/dL |
| ACTH | 18.8 mcg/dL |
| PM Salivary Cortisol | 0.154 ug/dL |
| Post Low Dose | 8.5 mcg/dL |
| Dexamethasone Suppression Test | 2.0 mcg/dL |

Figure 1: MRI pituitary showing hypo-enhancing areas on both sides of pituitary in this case representing pituitary microadenomas

Figure 2: Sellar region surgical pathology. Neats of neuroendocrine pituitary cells in a fibrous stroma in 10x (left) and 40x (right)

Figure 3: Sellar region surgical pathology. Immunohistochemical stains positive for synaptophysin (left), chromogranin (middle), and keratin CAM 5.2 (right). Negative for GFRAP.

- Since the cortisol was not suppressed by low dose dexamethasone test, but was suppressed by high dose, this indicates a pituitary source.
- MRI of the pituitary was performed to locate the potential source and was significant for hypo-enhancing lesions suspicious for bilateral synchronous pituitary microadenomas (9x5 mm right and 4x4 mm left). Shown in Fig. 1.
- PET [F-fluorodeoxyglucose] scan was done and showed hypermetabolic meningioma corresponding to the findings of the pituitary MRI and confirmed no other abnormal focal radiotracer uptake.
- Non-functioning pituitary tumors are common, hence, to confirm the pituitary source of ACTH prior to surgery, she underwent inferior petrosal sinus sampling (IPSS). This revealed a significantly elevated ACTH secretion from the right microadenoma.
- Transsphenoidal resection of pituitary tumor was performed.
- After pituitary resection, her cortisol levels were undetectable.
- She was then started on hydrocortisone for presumed adrenal insufficiency post pituitary lesion resection.
- No signs of diabetes insipidus were shown after surgery.

Discussion

- Simultaneous occurrence of pituitary adenoma and meningioma without a history of radiotherapy is extremely rare, with only 49 cases described before 2019. Even more rare, is an ACTH secreting pituitary adenoma consisting with a meningioma.
- IPSS procedure was performed after MRI in this case to get even more accurate localization of the source before surgical excision, as it is the best test to differentiate pituitary from ectopic ACTH-dependent Cushing’s.
- In approximately 1 out of 3 patients, remission is not achieved with surgical excision alone.
- For this reason, patients need post-operative monitoring and secondary medications to control their symptoms.

REFERENCES

- Phenotype-Genotype Association Analysis of ACTH-Secreting Pituitary Adenomas and Its Molecular Link to Patient Osteoporosis - PAMC (nih.gov)
- The role of bilateral inferior petrosal sinus sampling in determining the preoperative localization of ACTH secreting pituitary microadenomas in Cushing's disease: Experience of a tertiary pituitary center. 18th International Conference of the Endocrine Society: Trends in Endocrinology and Metabolism - ESM (esm.org)