

and DM2 in combination with biochemical testing and presence of bilateral adrenal adenomas was suggestive of CS secondary to PBMAH. On her evaluation for recurrent kidney stones she had a PTH of 107.2 pg/mL (15-65 pg/mL), and a calcium of 10.8 mg/dL (8.3-10.5 mg/dL). She was diagnosed with primary hyperparathyroidism. Imaging studies found a 1.1 cm ectopic parathyroid adenoma situated at the aortic pulmonary window. Surgical evaluation was performed and surgery was not offered given the precarious location of the parathyroid tumor. She had a known history of four meningiomas, two of which were resected and two considered unresectable. PBMAH in presence of all her other medical comorbidities prompted genetic evaluation for the patient. Analysis revealed a heterozygous ARMC5 mutation. Given the familial pattern of inheritance associated with ARMC5 mutations, patient's daughter also underwent genetic testing. Daughter tested positive for the mutation as well. Patient was offered surgical and medical therapy options for her PBMAH. She is currently being evaluated for an unilateral adrenalectomy.

Discussion: The pathophysiology of CS from PBMAH remains poorly understood leading to an insidious delay in diagnosis and treatment. Inactivating ARMC5 mutations of familial origins are known genetic triggers for development of PBMAH. ARMC5 is also a proposed tumor suppressor gene whose proteins are found in endocrine tissues all over body. Mutation of ARMC5 gene potentially can lead to multi-glandular tumor syndromes. Screening PBMAH patients and their family members for ARMC5 mutations may lead to earlier CS diagnosis/treatment times as well as better understanding of the gene's neoplastic potential.

References: Faucz, Fabio R., et al. "Macronodular Adrenal Hyperplasia Due to Mutations in an Armadillo Repeat Containing 5 (ARMC5) Gene: A Clinical and Genetic Investigation." *The Journal of Clinical Endocrinology & Metabolism*, vol. 99, 2014.

Tumor Biology

TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

Characterization of Transcription Factor Immunostaining and Null Cell Adenoma Status in Hormone Negative Pituitary Adenomas

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Introduction: Since the 2017 W.H.O. classification of pituitary adenomas redefined null cell adenomas (NCAs) as negative for all adenohypophyseal hormones and the transcription factors (TFs) SF-1, PIT-1, and T-PIT, limited data exist characterizing these tumors¹. We characterize NCAs in comparison to hormone negative adenomas (HNAs), which demonstrate negative hormone immunostaining in the context of positive TF immunoreactivity.

Methods: Retrospective review of 22 patients with HNAs between 2011-2019. Samples were stained for PIT-1

and SF-1. Negative ACTH staining served as a proxy for T-PIT given demonstrated prior concordance of these stains². Demographics, tumor characteristics, preoperative symptoms, and postoperative outcomes were assessed.

Results: Fifteen samples (68%) stained negative for both PIT-1 and SF-1 and were classified as NCAs. Seven were positive for SF-1 (n=3), PIT-1 (n=3), or both (n=1) and were classified as HNAs. NCA patients were predominantly female (80%), while those with HNAs were predominantly male (57%). All tumors were macroadenomas, with mean maximal tumor diameter of 28mm in NCAs vs 23mm in HNAs (p=0.2705). NCAs were more likely to demonstrate suprasellar invasion (100% vs. 71%, p=0.0325), and although not statistically significant, cavernous sinus invasion (53% vs. 43%, p=0.6695), and higher MIB-1 proliferative index (2.271 vs. 1.971, p=0.733). The most common preoperative symptoms were headache (73% NCA, 71% HNA) and vision loss (53%, 40%). Postoperative improvements in headache (60% NCA, 71% HNA) and vision (53%, 50%) were comparable. Sixty-four percent of NCAs underwent gross total resection vs. 43% of HNAs (p=.3712). There were no recurrences or progressions in either group over 24mo. Few comparisons reached significance, potentially due to limited sample size.

Conclusion: A majority of HNAs demonstrated negative TF immunostaining and met criteria for NCAs. NCAs may be more common in females and demonstrate more suprasellar invasion than HNAs, but otherwise, do not vary significantly. TF staining may be of limited clinical utility in identifying high-risk pathology, however future studies with larger cohorts are warranted.

References:

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- Nishioka H, Inoshita N, Mete O, Asa SL, Hayashi K, Takeshita A, Fukuhara N, Yamaguchi-Okadad M, Takeuchi Y, Yamada S (2015) The Complementary Role of Transcription Factors in the Accurate Diagnosis of Clinically Nonfunctioning Pituitary Adenomas. *Endocr Pathol* 26(4):249-55.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Hypercalcemia - Is This Sarcoidosis, Hyperparathyroidism, or Both?

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Hypercalcemia (HC) is a common clinical problem. Among all causes of HC, primary hyperparathyroidism (HPT) and malignancy are the most common, accounting for >90 % of cases. We present a case of HC in a patient attributed to long-standing history of Sarcoidosis (SC) and later found