Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

Atypical Teratoid Rhabdoid Tumor of the Sellar Region: An Unusual Cause of Hypopituitarism
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Background: Atypical teratoid/rhabdoid (AT/RT) tumor of the sellar region is an extremely rare malignant tumor in adults. To date, there are no definitive guidelines for optimal treatment and the prognosis of this tumor is poor. The pituitary insufficiency was rarely mentioned in previous literature and might be overlooked.

Clinical case: A 43 years old female presented to our clinic with severe periorbital pain. The magnetic resonance imaging of the brain revealed a 1.5x1.5x 3 cm sellar mass which showed inhomogeneous enhancement after gadolinium administration. Hormonal work up showed 8AM cortisol of 1.86 mcg/dL, free T4 1.0 (0.8–1.8 ng/dL), TSH 0.05 (0.3 - 4.1 uIU/ml), FSH 6.0 (1.6–9.3 IU/L), LH 1.8 (2.4–9.3 IU/L), estradiol <18.35 (80–790 pmole/L), IGF-1 96.6 (50.6–263.7 ng/mL), prolactin 56.6 ng/mL.

She underwent transphenoidal surgery with tumor removal. The pathological result showed a mixture of pleomorphic spindle cell, oval shape tumor and poorly differentiated cell. The tumor was negative for INI1 (SMARCBI) compatible with AT/RT WHO grade IV. She developed panhypopituitarism after surgery. She received 6 courses of 5950 cGy/25 fractions cranial irradiation and 6 courses of ifosfamide, cisplatin and etoposide. She completed the treatment regimen without significant toxicity. She continued hormonal replacement for panhypopituitarism and is still being followed at our clinic for 4 years without tumor progression or other complications.

In previously reported cases, all of the sellar AT/RT were female with a median age of 45 years old (range 20–61). The clinical presentations are rapidly enlarged sellar mass with compressive symptoms to the adjacent structures. The radiological findings of sellar AT/RT are non-specific. The diagnosis is based on histopathological findings. Presence of rhabdoid cells on histopathology and polyphenotypic immunopositivity for epithelial, mesenchymal, and neuroectodermal markers along with loss of expression of SMARCBI/INI1 help in establishing a diagnosis of AT/RT.

Currently, there are no definitive guidelines for optimal treatment. Multimodality treatment consisted of surgery, radiation and chemotherapy are the mainstays of treatment of the AT/RT. Of the 16 adults reported in the literature, 9 patients survived more than 12 months resulted in 47% of one-year survival rate. To our knowledge, this case is the sellar AT/RT with the longest survival to date.

Conclusion: AT/RT is one of the most aggressive tumors in the sellar area. Due to its aggressiveness, hypopituitarism is anticipated. Our patient had postoperative secondary adrenal insufficiency, secondary hypothyroid and hypogonadotropic hypogonadism. Apart from multimodality treatment required for tumor control, pituitary hormones should be evaluated preoperatively to prevent perioperative mortality and long-term improvement in the quality of life.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL GLUCOSE METABOLISM AND DIABETES

A Framework for Understanding and Managing ‘The Diabetes Syndrome’: A Unified Pathophysiologic Approaching the Context of the Beta-Cell Classification of Diabetes
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We have previously presented a proposal for a new, beta-cell centric classification of diabetes based on a consilience of genetic, metabolic, and clinical research that have accrued since the current classification was instituted. It recognizes that the beta-cell is THE core defect in all patients with diabetes. Differences in the genetics (and epigenetics), insulin resistance, environment and inflammation/immune characteristics resulting in the damage to the beta-cell in each individual will determine the phenotypic presentation of hyperglycemia and allow for a patient-centric, precision-medicine therapeutic approach, part of which we labeled ‘the Egregious Eleven’.

We now recognize the same pathophysiologic mechanisms that account for damage to the beta-cells govern the susceptibility of the cells involved in the complications and other conditions ‘tied to’ diabetes to damage by the abnormal metabolic environment that typifies beta-cell dysfunction and ‘fuel excess’. This abnormal metabolic environment is typified by oxidative stress which alters metabolic pathways (a la Brownlee’s Hypothesis model), alterations in gene expression, epigenetics, and inflammation. This allows us to understand the varied risk of developing complications of diabetes, including malignancies, dementia, NASH, psoriasis with similar levels of glycemic control; how non-glycemic effects of some medications for diabetes result in marked complication risk modification; and the value treating co-morbidities of diabetes in modifying complication risk.

Principles we outlined in using ‘the Egregious Eleven’ model- use agents that preserve beta-cell function, treat with least number of agents that treat most number of mechanisms of hyperglycemia- can be extended to use those agents, in combination, that also engender weight loss, decrease CV outcomes and have real or potential benefits in cancers related to diabetes, dementia risk, NASH, psoriasis. This approach allows for a more accurate assessment of each patient’s disease and effecting true precision medicine.

Schwartz, S, et al, Diabetes Care 2016, 39:179–186. Schwartz SS, et al Trends Endocrinol Metab. 2017;28(9):645–655.

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ADVANCES IN NEUROENDOCRINOLOGY

Estradiol Changes Angiotensin II-Induced ERK1/2 Phosphorylation by Different Pathways in the Hypothalamus and Lamina Terminalis
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