Preface

Updates and Highlights in Pituitary Medicine

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Pituitary diseases are relatively rare and often manifest with pleomorphic and vague clinical features commonly overlapping with those of other, more common diseases. As a result, pituitary diseases are often overlooked by health care providers, leading to missed or late diagnosis and increased burden of illness on patients, physicians, and the health care system. Moreover, misinterpretation of disease status and inappropriate treatment are frequent and can lead to increased morbidity and mortality in this unique subgroup of patients.

When filtered by the terms “pituitary gland,” “pituitary adenoma,” or “pituitary tumor,” more than 5000 publications have been documented in PubMed since 2008, the year in which the last special issue of Pituitary Disorders (edited by Dr Ariel Barkan) was published in Endocrinology and Metabolism Clinics of North America, quite a plethora for such a rare set of diseases. Indeed, significant progress in our understanding of pituitary tumor pathophysiology, diagnosis, and treatment has occurred over the last 6 years.

Several important pathways in the pathogenesis of pituitary tumors have been unraveled. The role of cyclin E and EGFR signaling in pituitary adenoma formation and progression was elucidated, leading to new clinical trials with relevant inhibitors. Multiple germline mutations or deletions in the aryl hydrocarbon receptor interacting protein gene were shown to be involved in the pathogenesis of familial isolated pituitary adenomas and pituitary adenoma, gigantism, and apoplexy in young patients. Novel IgG4-related hypophysitis and secondary hypophysitis due to treatment with anticytotoxic T-lymphocyte antigen-4 antibodies have been described. Traumatic brain injury and pituitary apoplexy have been increasingly recognized as important causes of hypopituitarism.
In the diagnostic field, a much-needed new clinicopathologic classification of pituitary adenomas has been proposed, integrating tumor immunohistochemical type, size, and degree of invasion in addition to proliferation markers. GH and IGF-I assays, despite being essential for the diagnosis and follow-up of acromegaly and GH deficiency, remain a challenge because of significant variations caused by the use of different assay methods. An ongoing global effort to standardize this measurement process is underway. Furthermore, our ability to diagnose and follow-up on the recurrence of ACTH-secreting pituitary adenomas has improved with the implementation of the late night salivary cortisol test and the addition of prolactin measurements, along with cortisol and ACTH obtained during the inferior petrosal sinus sampling test. Mass spectrometry has replaced immunoassays in some laboratories and its performance profile in accurately and reproducibly measuring hormone levels is being assessed.

New pharmacotherapy for Cushing disease had been approved, including the multiligand somatostatin receptor pasireotide (SOM230, Signifor) and the glucocorticoid receptor antagonist mifepristone (Korlym). Several additional compounds, like the 11β-hydroxylase LCI699 and the cyclin E inhibitor roscovitine, are currently in clinical trials in patients with Cushing disease. Pasireotide, in both its short-acting and its long-acting formulas, has also been tested in advanced clinical trials for the treatment of acromegaly. Dopamine agonist treatment remains the mainstay approach for the treatment of prolactinomas and is occasionally used for the treatment of other pituitary tumors. Although a possible involvement of cabergoline in the development of heart valve disease had been demonstrated in a patient with Parkinson disease treated with high doses of the drug, clear evidence that this side effect occurs in patients with pituitary adenoma treated with the lower doses has not yet been demonstrated.

The surgical management of pituitary adenomas, with the expansion of the endoscopic endonasal approach, allows removal of invasive tumors previously considered nonresectable. Radiation, especially stereotactic radiation, could play a different role in the management paradigm. Highly aggressive pituitary adenomas and carcinomas are still a considerable therapeutic challenge; however, multidisciplinary endocrinology, neuro-oncology, and radiology approaches using chemotherapeutic agents and irradiation may be advantageous.

With better diagnosis and treatment of pituitary diseases and increased success rates of fertility treatments, more women with pituitary disease are able to conceive and proceed with pregnancy. Better understanding and proper management of pituitary dysfunction in pregnancy are therefore essential and new best-practice modalities are evolving. The recognition that fragility fractures are a frequent complication of pituitary disease has led to increased awareness and better treatment of bone diseases in patients with pituitary hormonal abnormalities.

Of great importance is the consideration of quality-of-life issues when managing a patient with a pituitary disease; there is clear evidence now that residual morbidity and decreased quality of life could persist despite endocrine control or even cure of pituitary dysfunction. The current issue on Pituitary Disorders of the Endocrinology and Metabolism Clinics of North America is unique in focusing on important updates and highlights in pituitary disease, beyond common knowledge. The articles are concise, clear, and written by internationally leading experts in the field who emphasize the contemporary state-of-the-art knowledge in the field. It is hoped that you will find this issue helpful in the management of patients with pituitary diseases.

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