



Update in Endocrine Pathology

Özgür METE^{1,2,3}

¹Department of Pathology, University Health Network, TORONTO, ONTARIO, CANADA,

²Department of Laboratory Medicine and Pathobiology, University of Toronto, ONTARIO, CANADA

³Endocrine Oncology Site Group, Princess Margaret Cancer Centre, TORONTO, ONTARIO, CANADA

UPDATE IN ENDOCRINE PATHOLOGY

Over the past decades, endocrine pathology has emerged as a distinct clinical subspecialty in the field of surgical pathology. Endocrine pathologists play an essential role in the management of patients with endocrine disorders arising from pineal, hypothalamus, pituitary, parathyroid, thyroid, adrenal, paraganglia, pancreas, gastrointestinal tract, lung, thymus, and urogenital system. Recent advancements made in translational endocrine research utilizing molecular testing has significantly improved our understanding of the pathogenesis of endocrine neoplasms and simultaneously led to the development of modern practices that integrate diagnostic, predictive, and prognostic biomarkers. In this special issue of the Turkish Journal of Pathology, several experts have been invited to provide an update on the expanding knowledge of endocrine disorders.

Pituitary adenomas are common neuroendocrine tumors, found in approximately 20% of the general population (1-3). The diagnosis of pituitary adenoma alone or demonstration of hormone products in a pituitary adenoma is no longer sufficient for the management of these patients. Accurate subtyping of pituitary adenomas in conjunction with some biomarkers is crucial (1-4). The distinct behaviour of a select group of pituitary adenomas in specific clinical settings is discussed by Mete and coworkers.

Pathologists are often faced with the question of how to distinguish a malignancy during the preoperative assessment of thyroid nodules. The overall rate of malignancy in thyroid nodules is as high as 15% (5-6). In this special issue, challenges and pitfalls associated with the cytological evaluation of thyroid nodules are discussed by Schmitt and coworkers.

Papillary thyroid carcinoma is the most common endocrine malignancy. Several variants of papillary thyroid carcinoma have been described based on the size, architecture, cytology, nature of the tumor boundaries, stromal features,

additional components, or a combination of these features (7-9). In this special issue, the histopathologic and clinical features of common histological variants of papillary thyroid carcinoma are summarized by Serpil Dizbay Sak.

The distinction of dedifferentiation is of clinical significance. While the diagnosis of anaplastic (undifferentiated) thyroid carcinoma is generally made after excluding other undifferentiated malignant neoplasms using immunohistochemical tools, the diagnosis of poorly differentiated thyroid carcinoma is often rendered morphologically (7,10,11). Recent advances in our understanding of the histologic, immunohistochemical, and molecular characteristics of poorly differentiated and anaplastic thyroid carcinoma are summarized by Sobrinho-Simões and coworkers.

Medullary thyroid carcinoma originates from parafollicular C-cells and represents fewer than 10% of all thyroid cancers (12-14). In this special issue, the morphological and molecular features of C-cell disease are discussed by Baloch and LiVolsi by reviewing diagnostic pitfalls as well as the latest American Thyroid Association guidelines for management of patients with medullary thyroid carcinoma (15).

Clinicopathological correlates of primary hyperparathyroidism include parathyroid adenoma (80-85%), hyperplasia (10-15%) and carcinoma (<1-5%) (16). Advances in molecular pathology have shed light to the pathogenesis of parathyroid neoplasms and resulted in the development of new biomarkers (17, 18). The review submitted by Duan and Mete provides an update on the current knowledge of parathyroid carcinoma by highlighting diagnostic pitfalls as well as its exciting changes in the practice of endocrine oncology.

Adrenal cortical carcinoma is now recognized as a heterogeneous disease with various molecular background and prognostic features unmatched with morphological features in most cases (9, 19-21). The reticulin algorithm

introduced by Volante and colleagues provided a simplified and reliable approach to distinguish malignancy (22, 23). Transcriptome studies of adrenal cortical carcinomas showed that the diagnosis of malignancy can be rendered by using molecular techniques. Moreover, they also highlighted two distinct molecular subgroups depending on the behavior of adrenal cortical carcinoma (“poor” versus “improved” survival outcome) (19, 20). The various aspects of adrenal cortical carcinoma are discussed by Papotti and coworkers.

The last decade has provided significant progress in the field of neuroendocrine disease. The discoveries of genetic susceptibility in up to 40% of paraganglioma and pheochromocytoma led to the development of genotype-phenotype correlations as well as standardized synoptic reporting to advance the medical care (24-28). In this special issue, advances in paraganglioma and pheochromocytoma are reviewed by Alfred Lam.

The nomenclature for gastro-entero-pancreatic (GEP) neuroendocrine tumors (NETs) has been an area of controversy in medicine. Many terms have been applied to what we now call as neuroendocrine tumor or neuroendocrine carcinoma. The 2010 WHO classification of GEP-NETs introduced a histologic grading system based on the proliferation rate (mitotic count and Ki67 labeling index) (29). On the other hand, the 7th edition of the AJCC/UICC staging scheme provided for the first time a site specific and grade dependant staging for GEP-NETs. While the field of GEP-NETs is still evolving to optimize diagnosis and management, the colorful aspect of GEP-NETs are discussed by La Rosa and coworkers.

The morphologic, immunohistochemical, and molecular features of neuroendocrine tumors of the gynecological tract along with other endocrine tumors in the gynecological tract are discussed in the review submitted by Kefeli and Usubutun.

The manifestations of endocrine disorders may also present with dermatological diseases. As a consequence, awareness of the skin manifestations of endocrine disorders alert physicians to further initiate a comprehensive endocrine workup. A brief review of skin lesions associated with endocrine disorders is summarized by Cuyan Demirkesen.

In addition to paraneoplastic syndromes leading to clinical or biochemical endocrine disorders, growing evidence expanded the link between inherited endocrine tumour syndromes (30-32) and genitourinary disorders. The review submitted by Özlük and Kılıçaslan discusses comprehensive aspects of this association.

Over the past few years, important milestones in the understanding of metabolic syndrome and type 2 diabetes mellitus have been achieved (33-35). Chronic low grade inflammation in adipose tissue is now known to play a key role in obesity and insulin resistance. As a result, adipose tissue is currently recognized as an active immune organ regulating energy metabolism. Winer and coworkers summarized the expanding knowledge on the pathology of innate and adaptive immune cells in obese adipose tissue by emphasising various immunological mechanisms leading to obesity-related insulin resistance.

Progress in the cellular and molecular biology led to increased usage of molecular biologic techniques in modern practices. The review article submitted by Serinsoz Linke and Guler Tezel summarizes an update of genetic changes observed in different endocrine system pathologies and their diagnostic, therapeutic and prognostic values.

As the field of endocrine pathology continues to evolve on a daily basis, the authors of this special issue provided timely updates for diagnostic pathologists and treating physicians in multidisciplinary endocrine oncology teams.

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