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A Contemporary Review of the Treatment of Medullary Thyroid Carcinoma in the Era of New Drug Therapies **233**

Carolyn D. Seib, Thomas C. Beck, and Electron Kebebew

Medullary thyroid cancer (MTC) is a rare neuroendocrine tumor that can be sporadic or inherited and is often associated with mutations in the RET (Rearranged during Transfection) oncogene. The primary treatment for MTC is surgical resection of all suspected disease, but recent advances in targeted therapies for MTC, including the selective RET inhibitors selpercatinib and pralsetinib, have led to changes in the management of patients with locally advanced, metastatic, or recurrent MTC. In this article, we review updates on the evaluation and management of patients with MTC, focusing on new and emerging therapies that are likely to improve patient outcomes.

A Nomogram for Relapse/Death and Contemplating Adjuvant Therapy for Parathyroid Carcinoma **251**

Angelica M. Silva-Figueroa

Parathyroid carcinoma (PC) is a rare endocrine malignancy with an increased incidence in the last decade. There is no reliable prognostic staging system for PC. Several hosts, tumors, and tumor microenvironment factors have been negatively correlated with survival in the last decade. Surgical resection with negative margins is still the standard of treatment in PC. Chemo and radiotherapy have no proven beneficial effect. A new promising approach with molecular profiling could lead to adjuvant therapies.

Parathyroid Cancer: Updates and Postoperative Surveillance Imaging **271**

May Thwin and Radu Mihai

Imaging after definitive surgical management of parathyroid carcinoma remains a poorly defined area, and at present, there are no standard guidelines to direct care, which should be individualized and patient-oriented. The current role of imaging is largely reserved for patients who demonstrate biochemical or clinical evidence to suggest disease recurrence, and in these patients, imaging is directed at identifying the culprit site of disease to direct further surgery. There is no established role for "routine" or "surveillance" imaging in those patients with sporadic who do not display signs of disease recurrence.

Adrenocortical Carcinoma: Role of Adjuvant and Neoadjuvant Therapy 279

Lisa Kenney and Marybeth Hughes

Adjuvant and neoadjuvant chemotherapy in the treatment of adrenocortical carcinoma (ACC) is limited by few existing trials, most of which are retrospective. The drug mitotane has been used for the treatment of ACC, although existing guidelines only support its use in high risk of recurrence. The first phase 3 trial involving systemic chemotherapy for ACC supports the use of etoposide, doxorubicin, cisplatin, and mitotane for combination therapy. No significant breakthrough has been discovered thus far in of targeted and immunotherapies. Neoadjuvant chemotherapy is only used to allow for complete surgical resection because complete excision is the definitive treatment of ACC.

Succinate Dehydrogenase Mutations as Familial Pheochromocytoma Syndromes 289

Michael S. Lui, Uriel Clemente-Gutierrez, Catherine M. Skefos, and Nancy D. Perrier

It is recognized that a large portion of pheochromocytoma and paraganglioma cases will have an underlying germline mutation, supporting the recommendation for universal genetic testing in all patients with PPGLs. A mutation in succinate dehydrogenase subunit B is associated with increased rates of developing synchronous and/or metachronous metastatic disease. Patients identified with this mutation require meticulous preoperative evaluation, a personalized surgical plan to minimize the risk of recurrence and tumor spread, and lifelong surveillance.

Genetic Testing for Adrenal Tumors—What the Contemporary Surgeon Should Know 303

Maria F. Bates and Meredith J. Sorensen

Surgical diseases of the adrenal gland include pheochromocytoma/paraganglioma, primary hyperaldosteronism, Cushing syndrome, and adrenocortical carcinoma. These conditions may be associated with familial syndromes, and genetic testing is available and recommended in most. Adrenal surgeons should be familiar with these syndromes and know when to consider referral for genetic counseling and genetic testing. Identification of patients with familial syndromes allows for the detection and screening of associated syndromic neoplasms, guides surgical planning and operative approach, influences recurrence and malignancy risk assessment, aids in the development of a postoperative surveillance plan, and determines the need for screening family members.

Multiple Endocrine Neoplasia Type 1 Syndrome Pancreatic Neuroendocrine Tumor Genotype/Phenotype: Is There Any Advance on Predicting or Preventing? 315

Bhavishya Ramamoorthy and Naris Nilubol

Multiple endocrine neoplasia type 1 syndrome (MEN1) is a disease caused by mutations in the MEN1 tumor suppressor gene leading to hyperparathyroidism, pituitary adenomas, and entero-pancreatic neuroendocrine tumors. Pancreatic neuroendocrine tumors (PNETs) are a major cause of mortality in patients with MEN1. Identification of consistent genotype–phenotype correlations has remained elusive, but MEN1 mutations in

exons 2, 9, and 10 may be associated with metastatic PNETs; patients with these mutations may benefit from more intensive surveillance and aggressive treatment. In addition, epigenetic differences between MEN1-associated PNETs and sporadic PNETs are beginning to emerge, but further investigation is required to establish clear phenotypic associations.

Minimally Invasive Pancreatectomy: Robotic and Laparoscopic Developments **327**

Seth J. Concors, Matthew H.G. Katz, and Naruhiko Ikoma

Minimally invasive pancreatectomy is increasingly used. Although offering potential advantages over open approaches, minimally invasive pancreatectomy has many challenges to maintain high-quality of oncologic resection. Multiple patient and surgical factors should be considered in planning laparoscopic or robotic resection, including the learning curve required to produce proficiency. For pancreaticoduodenectomy, distal pancreatectomy, and other pancreatic resections, a safe, margin-negative resection remains the goal. National and societal guidelines for the adoption of minimally invasive pancreatectomy are ongoing and will continue to be important as these techniques are further adopted.

Status of Surveillance and Nonsurgical Therapy for Small Nonfunctioning Pancreatic Neuroendocrine Tumors **343**

Dirk-Jan van Beek, Anna Vera D. Verschuur, Lodewijk A.A. Brosens, Gerlof D. Valk, Carolina R.C. Pieterman, and Menno R. Vriens

Pancreatic neuroendocrine tumors (PNETs) occur in < 1/100,000 patients and most are nonfunctioning (NF). Approximately 5% occur as part of multiple endocrine neoplasia type 1. Anatomic and molecular imaging have a pivotal role in the diagnosis, staging and active surveillance. Surgery is generally recommended for nonfunctional pancreatic neuroendocrine tumors (NF-PNETs) >2 cm to prevent metastases. For tumors $\leq$2 cm, active surveillance is a viable alternative. Tumor size and grade are important factors to guide management. Assessment of death domain-associated protein 6/alpha-thalassemia/mental retardation X-linked and alternative lengthening of telomeres are promising novel prognostic markers. This review summarizes the status of surveillance and nonsurgical management for small NF-PNETs, including factors that can guide management.

Lobectomy or Total Thyroidectomy—Where Is the Pendulum now for Differentiated Thyroid Cancer? **373**

Oliver J. Fackelmayer and William B. Inabnet III

Thyroid surgery remains an essential treatment of thyroid cancer. The historical one-size-fits-all approach to differentiated (papillary and follicular) thyroid carcinoma of total thyroidectomy with central lymph node dissection has been shown to be overtreatment with associated risk of perioperative complications including nerve palsy and hypoparathyroidism. Furthermore, thyroid lobectomy may obviate life-long thyroid hormone replacement. Low-risk thyroid cancers have a low risk of recurrence and those that do recur can be salvaged with reoperation without compromising prognosis. Perioperative risk stratification for recurrence and death greatly influence the need for total thyroidectomy.

A Nod to the Nodes: An Overview of the Role of Central Neck Dissection in the Management of Papillary Thyroid Carcinoma **383**

Robert Mechera, Isabella Maréchal-Ross, Stan B. Sidhu, Peter Campbell, and Mark S. Sywak

Lymph node metastasis in thyroid cancer is common and associated with an increased risk of locoregional recurrence (LRR). Although therapeutic central neck dissection is well established, prophylactic central node dissection (pCND) for microscopic occult nodal involvement is controversial and recommendations are based on low-level evidence. The potential benefits of pCND such as reducing LRR and re-operation, refining staging, and improving surveillance are enthusiastically debated and the decision to perform pCND must be weighed up against the increased risks of complications.