

Preface

Complexity of Patient Care in Neuroendocrine Tumors of the Digestive Tract

Neuroendocrine tumors (NETs) have emerged as paradigm tumors for which multidisciplinary care is required. NETs are known as rare tumors. However, the increasing incidence of NET renders it likely that physicians caring for cancers may have either already faced or may be certainly exposed during their career to the challenging issues of discussing the case of a patient with NET. During the last 5 years, several novel therapeutic options have emerged for NET, profoundly challenging practices that had been previously set for decades. This moving field has generated some confusion, leading to novel treatment algorithms to guide medical decisions. To either better understand or handle the multidisciplinary approaches that are required for optimizing the care of NET patients, physicians are now looking for references from experts and comprehensive reviews summarizing the current knowledge on treatments of patients with NET.

NETs are fascinating multifaceted diseases that can primarily localize in many organs with various presentations. Few patients may present with symptomatic tumors at diagnosis due to endocrine secretions and/or bulky tumor masses. In some instances, emergency care may even be required to speedup diagnosis and therapy. More frequently, NETs are diagnosed at late stages due to the lack of symptoms and the relative indolence of the disease, even in the presence of multiple metastases. Therefore, the vast majority of patients with NET may present at diagnosis with advanced primary and already developed metastasis, the liver being the primary site of digestive NET dissemination. Although only a small number of patients may undergo surgical resection, surgery remains the only curative approach and shall therefore be discussed along with other options even in the presence of metastases. Since most patients will develop multiple non-operable liver metastases early on during the natural history of their disease, curative surgery is often impossible and instead debulking liver-resection and liver-directed therapy, such as chemoembolization of radiofrequency ablation, may have palliative benefits for patients with liver-dominant metastases. Interestingly, NET cells often express somatostatin receptors that can control hormonal secretions and stimulate tumor proliferation. Somatostatin analogs, inhibiting somatostatin

receptor functions, are often prescribed to relieve symptoms resulting from hormonal hypersecretion in functioning tumors such as diarrheas and flushing episodes. Recently, data also demonstrated that somatostatin analogs could also delay tumor progression in selected patients with carcinoid tumors, although this demonstration has not yet been fully demonstrated for patients with pancreatic NETs (PNETs). Taking advantage of the presence of somatostatin receptors at the surface of cancer cells, somatostatin analogs loaded with radionucleotides have been used to selectively target cancer cells and deliver metabolic radiotherapy to disseminated NET metastases. Based on large retrospective clinical experiences, Peptide Receptor Radionucleotide Therapy (PRRT) is now frequently proposed to patients with advanced NET. Although evidences suggest activity of PRRT in NET, the overall benefit and long-term safety of this therapeutic approach remains to be validated prospectively. For patients with advanced NET, chemotherapy has been an important part in the history of treatment for NET. Chemotherapy was the first treatment option demonstrating significant benefits, delaying tumor progression, controlling symptoms, and in some circumstances improving overall survival. While midgut carcinoid tumors showed poor sensitivity to chemotherapy, PNETs have been acknowledged to be more sensitive to chemotherapy. Chemotherapy, such as streptozocin, either combined with doxorubicin or fluorouracil, has been the only systemic treatment approved for many years in advanced PNETs, though the magnitude of benefit has been often challenged in recent publications. Temozolomide, an oral methylating chemotherapy with mechanisms of action similar to DTIC, has been evaluated in retrospective series. Temozolomide demonstrated evidence of activity, possibly related to the lack of methyl guanine transferase expression, the enzyme that repairs DNA insults caused by temozolomide. More recently, large prospective trials using sunitinib and everolimus demonstrated that progression of PNET could be delayed using small molecules targeting cell signaling. Inhibition of mTOR using everolimus may cause inhibition of cancer cell proliferation and can alter metabolic function of NET cancer cell, delaying tumor progression in advanced well-differentiated tumors. In addition, sunitinib, inhibiting NET angiogenesis at the level of endothelial cells and pericytes was also shown to delay tumor progression in well-differentiated PNET. These two drugs have been recently approved in advanced PNET and now offer more opportunities in the NET armamentarium to delay progression. While treatment options have progressed, imaging techniques and endoscopy have also gained in precision allowing earlier diagnosis, better sensitivity in the detection of metastases, and more efficient criteria for evaluating drug efficacy. Considering the multiple treatment options in PNET, strategies are now required to optimize the sequential use of somatostatin analogs, PRRT, chemotherapy, and targeted therapies in patients with advanced PNETs that are not amenable to curative surgery. Another important issue in the care of patients with NET shall also consider how quality of life could be impacted by treatment decisions.

The multiple options for treatment of patients with NET require multidisciplinary approaches and discussions from experts from various specialties to select

the best treatment choice for each individual case. Multidisciplinary boards developed in expert centers are aiming to encompass the various needs for care of patients with NET and should be promoted, eventually using networking through teleconferences in centers that cannot develop expertise in all the domains. In this book, we have aimed to keep the spirit of multidisciplinary board meetings, asking experts to deliver chapters where readers may find data to make their own opinions. Authors have been selected from centers of expertise for NET in Europe and in the United States. Authors have been requested to provide updated information about current knowledge for various aspects of treatment of patients with NET. We expect that readers will find inspiring ideas and information that may help them to better understand options and optimize the care of patients with NET.

Eric Raymond
Sandrine Faivre
Philippe Ruszniewski

Management of Neuroendocrine Tumors of the
Pancreas and Digestive Tract
From Surgery to Targeted Therapies: A Multidisciplinary
Approach

Raymond, E.; Faivre, S.; Ruszniewski, P. (Eds.)

2014, X, 236 p. 30 illus., 24 illus. in color., Hardcover

ISBN: 978-2-8178-0429-3