Neuroendocrine Tumors: A Multidisciplinary Approach

Volume Editors

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51 figures, 26 in color, and 27 tables, 2015
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Preface

Over 100 years ago the term carcinoid ('Karzinoide Tumoren des Dünndarmes', Siegfried Oberndorfer) entered the medical literature to describe a rare and peculiar type of epithelial neoplasm, apparently restricted to the intestine, characterized by a solid, trabecular or nested (organoid rather than glandular) histology and a less aggressive biological behavior [1]. Since then a large body of literature has expanded the concept of carcinoid, defining a wide spectrum of peculiar tumors, potentially affecting all organs and apparatuses, sharing common biological properties (i.e. signs of neuroendocrine, NE, differentiation), while presenting pathognomonic epidemiological, hormonal, pathological, radiological and, above all, clinical features and outcomes [2–7].

The more generalist term neuroendocrine neoplasm (NEN) was recommended in the latest WHO classification [4]. In the field of gastroenteropancreatic tumors, only two entities are now recognized, NE tumor and NE carcinoma, subclassified according to tumor grade and stage [4], although the acronym NET (neuroendocrine tumor) still remains the most popular in the medical community (the WHO classification itself recognizes NEN and NET as synonyms). This is not the case for pulmonary NETs, which still maintain the original nomenclature of the single different entities described over the years, including typical and atypical carcinoids, as well as small and large cell (NE) carcinomas [8], while the use of terms applied to the single tumor entities in the past (i.e. malignant carcinoid or well-differentiated neuroendocrine carcinoma) are discouraged for being potentially confusing.

Despite the extensive multidisciplinary studies on these rare tumors, several management (i.e. diagnostic work-up and the therapeutic strategies) controversies and gray areas still exist. Several impediments were identified 6 years ago at a National Cancer Institute summit in the USA, which have hampered or slowed down the development of valid solutions for NET care [9]. These include the poor understanding of NE cell and tumor biology and tumorigenesis mechanisms, the heterogeneous application of pathological classifications (including grading and staging), the incomplete knowledge of specific therapeutic targets as well as of complications and side effects in terms of morbidity and mortality, the limited availability of in vitro and in vivo models for research, and the paucity of relevant prognostic and predictive factors in NETs. Solutions to some of these impediments have begun to emerge and progress...
has been made in recent years. Nevertheless, the above difficulties support the opportunity of gathering experts from different fields of the involved medical disciplines and from centers of excellence for the cure of NETs to update the current knowledge on diagnosis and treatment, to highlight the most relevant controversial issues and, above all, to offer tentative or established answers.

The reason for undertaking such an adventure in the field of NET/NENs is primarily linked to the increasing evidence that these tumors are not as rare as they have been considered so far [9–12]. In addition, because of their widespread occurrence in the body, their partial biological and clinical similarities, and their unpredictable behavior, it seems that an organic and uniform approach to these diseases is necessary. This does not mean to interfere with the various specialists, in terms of their competence or entitlement to manage single affected patients, but rather to offer the chance of comparing the various diagnostic and therapeutic strategies for the management of NETs arising from the different organs, and realizing an advantage from it (indeed, irrespective of the site of origin and clinical background, these tumors share many biological properties and features).

**General Design of the Current Volume**

The current volume has been designed around four main areas of interest, with the aim of presenting the most important achievements in the management of NETs. Gastroenteropancreatic NETs will form the core of the volume, but pulmonary and thymic counterparts will also be discussed.

In the first interest area, NE tumors will be approached with regard to the clinical syndromes and symptoms that characterize this tumor type, and also to the relevant role of laboratory medicine for their definition. The chapters dedicated to imaging procedures will help to clarify the major controversies in NET recognition by computed tomography, ultrasonography and nuclear medicine imaging, as well as endoscopic techniques. In the following chapters, the pathology and genetics of NETs will be discussed, with an update on the major controversies related to NET nomenclature, classification, genetic, epigenetic, immunological and gene-expression profiles. Finally, a large part of the volume will be devoted to NET treatment.

Surgery represents the gold-standard approach for patient cure, and should be performed whenever possible. The various (traditional and new) currently available surgical approaches will be presented, concluding with a chapter dedicated to organ transplantation and debulking procedures, both of which are part of the surgical strategy for NETs management.

The volume will close with a session dedicated to currently available medical treatments (i.e. targeted, symptomatic and chemotherapy) for the various types of NETs, followed by radionuclear therapy modalities and, finally, new perspectives and novel biotherapy and immunotherapy options.
Rigorous classification, timely diagnosis and a high standard of surgical and medical treatment are mandatory to achieve the best results at the right time in patients affected by NETs. We hope this volume will be a valid tool for the broader scientific community dealing with the diagnosis and management of NETs.

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References
