Multi-modal Diagnosis and Treatment of Neuroendocrine Tumors – Complexity as a Model for Interdisciplinary Cooperation

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Neuroendocrine tumors (NETs) pose a very heterogeneous group and can vary dramatically in their clinical appearance and prognosis depending on origin, functional activity, and biological behavior. The spectrum ranges from benign, highly-differentiated neuroendocrine tumors – with an excellent prognosis – all the way to poorly-differentiated neuroendocrine carcinomas similar in biology and prognosis to small cell lung carcinomas. NETs are considered to be an infrequent tumorous disease, although the prevalence is not low if one takes into account the recently recalculated incidence rate of 30 to 50 cases per million individuals in the population and the partially excellent prognosis. For Thuringia this adds up to an estimated prevalence of several hundred patients with disease caused by a neuroendocrine tumor.

The clinical heterogeneity of NETs requires close interdisciplinary cooperation between conservative and surgical disciplines. First contact is often made at the gastroenterologist or visceral surgeon; in terms of the functional NETs at the internist or endocrinologist, also. The inclusion of nuclear medicine, pathology, oncology, along with diagnostic and therapeutic radiology is necessary for further care and they are to be supplemented by pulmonology, cardiology/cardiac surgery, and neurosurgery. It could be shown that the prognosis for NET patients depends on productive interdisciplinary cooperation. Here, the choice of the right therapy is just as crucial as the avoidance of therapies that are ineffective and not of importance to the prognosis (such as lymphadenectomy in the case of distant metastases which determine the prognosis or chemotherapies for NETs of the midgut).

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The prognosis for NET patients can vary widely and depends primarily on an exact pathological analysis. In his overview, PD Dr. Martin Anlauf presents the pathological principles of classification and categorization of the NETs which play an important role in determining patient prognosis. The newly discovered precursor lesions of NETs and the genetic basis of multiple endocrine neoplasia syndrome (MEN) are also covered. The newly established TNM system for NETs of the gastrointestinal tract making standardization of the stage categories possible for the first time is also presented.

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Neuroendocrine tumors of the lung are the second most common tumor entity after those of the gastro-entero-pancreatic (GEP) system. They can be accompanied by functional syndromes, such as carcinoid syndrome which is distinguished by diarrhea and paroxysmal facial redness, and (more seldom) bronchial asthma. Yussuf Sayeg and Adjunct Professor of Medicine Dr. Reiner Bonnet present the diagnostic and therapeutic particulars of this rare lung tumor.

A comprehensive and exact diagnosis at the beginning and during the course of the disease is absolutely necessary for specific treatment. A combination of a diagnostic screening tool with slice-imaging methods is recommended. Positron emission tomography combined with x-ray computed tomography offers excellent possibilities for this. Receptor PET/CT using Gallium-68-labeled somatostatin analogs fulfills both requirements in one test procedure. Endosonography as a diagnostic procedure is also of critical importance for NETs of the foregut. An overview of proven and new methods for efficient diagnosis of NETs is presented by PD Dr. Dieter Hörsch and Prof. Dr. R.P. Baum.

There is a wide range of possibilities for treating neuroendocrine tumors; however, targeted therapy is crucial. Dr. Patricia Grabowski and Prof. Dr. Richard P. Baum give an overview of the conservative treatment options (biotherapy, chemotherapy, and peptide receptor radionuclide therapy) balanced between individual therapy and reliable knowledge. Of significant importance in terms of this is, again, close interdisciplinary cooperation.

Aside from rare exceptions, complete surgical resection of the NETs offers the only possibility of curation; endoscopic removal does also in cases of very early tumor manifestations in the gastrointestinal tract. This is the case for at least nearly half of new cases. The success of the resection must, however, be followed up on after pathological risk stratification. Preventive surgery also plays an important role concerning genetically inheritable syndromes. PD Dr. Merten Hommann and Dr. Daniel Kämmerer go into the details of onco-surgical therapy of NETs.

With NETs, hepatic metastasis is usually decisive regarding prognosis. As a result, particular emphasis lays here on tumor control in the liver through local ablative measures which are presented by Dr. Alexander Petrovitch. Through sequential or repetitive use of transcatheter arterial chemoembolization (TACE), transcutaneous radiofrequency thermal ablation (RFTA), portal vein embolization, and selective internal radiotherapy (SIRT),

local tumor control can often be achieved and, as a result, a stable disease progression.

An entire arsenal of diagnostic and therapeutic possibilities is available at specialized centers to patients with neuroendocrine tumors. This diversity, however, should not hide the fact that very little well-founded data exist on NETs. On the one hand, this is certainly to blame on the rarity of these tumors. However, centers specializing in these tumor entities will not be able to avoid the requirement – valid for other oncological centers – to include more than 10% of patients in studies. We fulfill this basic principle by regularly collecting prospective data on our patients and recruiting them into multiple prospective, randomized, placebo-controlled phase III studies. We are also establishing a case-controlled cohort study for conservative, local ablative, and palliative surgical procedures in order to collect reliable comparative data for these treatment options as well. In doing this, the objective is to be able in a few years to make specific recommendations regarding the diverse therapy options available on the basis of well-founded and reliable knowledge.

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