EDITORIAL



The growing importance of neuro-oncology for neurologists

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Historically, the basis for the current concept of neurooncology was summarized in two major books: "Cancer and the nervous system" [1] and "Neurological complications of cancer" [2].

Both books are valuable resources to connect the effects of cancer on the nervous system, not only by direct but also remote effects such as paraneoplastic disease, metabolic diseases, and infections. Therapy at the time of the book publications was an important aspect, but the dimension of the toxicity and side effects, in particular for the peripheral nerve CIPN [3], emerged later. This also relates to other toxicities such as in RT therapy and the new and amazing spectrum of immune therapies.

In the past decades, neuro-oncology became an established part of neurology and has strong multidisciplinary and multi professional links. The initial content of neurooncology—primary brain tumors—has received much research attention and many groups worldwide use several approaches to improve the fate of patients with primary brain tumors. The field has moved from classical pathology based surgery and conventional chemo and RT to immune and genetic therapies and molecular based approaches and is energetically and perpetually moving forward. However, primary brain tumors are only a small spectrum of neuro-oncology.

The number of cancer patients is increasing globally, as well documented by the WHO [4]. The reasons are manifold, including the increase of non-communicable diseases, environment, and, above all, the aging population. Cancer therapies are based on surgery, RT, chemotherapy, and increasingly on immune interventions. These new possibilities have changed the fate of cancer patients in many countries of the world where medicine and oncology is affordable. Nevertheless, globally the situation in low and middle income countries remains unresolved and the issues of access and equity are disconcerting.

For example, the basic histological investigations of tumor material, which are not available in low income countries, as pathology services are non existent [5], which hampers diagnosis, treatment, and prognosis.

Statistically, the neurological number of complications seems small in given entities such as brain metastases (10%) and toxic complications (20-40%) [6–8]; however, given the large number of cancer patients, this affects many patients. According to Globocan [9], the global incidence of cancer is 19.3 million cancer cases a year, and 10 million cancer deaths occur. Extrapolated form the incidence, this would be 2 million people with brain metastases and 8 million people with toxic complications a year.

The number for the global cancer prevalence varies between 0.4% and 5%, but an estimate is 1.3% [10] of the world population of 8 billion people, meaning 62 million people have cancer in some stage worldwide. The modest estimates of 10% for brain metastases and 40% for toxicity indicate that 6.2 million people would have brain metastasis and 24 million would have neurological sequelae of treatment toxicity (Fig. 1)

This number compares with the prevalence of stroke (101.5 million, 2019), epilepsy (50 million), Parkinson's disease (10 million), and MS (2.8 million) and makes cancer and the effects on the nervous system the third largest priority after epilepsy. The neurooncologist must be knowledgeable of the neurological functions at all levels and the characteristics of different pathomechanims.

The success in cancer therapies has been based on solid investigations, studies and experience, and for many entities, powerful therapeutic protocols are available. Immune therapies and molecular targeted therapies have proven effective and can change tumor progression and in some cases even heal the patient.

The tools used at present are surgery, radiotherapy, conventional chemotherapy, immune modulators, immunotherapies, and cellular therapies with a fast pace of development. These efficient therapies prolong the life of the patient but

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Fig. 1 Cancer: Global incidence and prevalence, estimated number of brain metastases and toxic complications



also take their toll in the development of neurotoxicity, which can be dose limiting. Increasingly, targeted therapies are used for some tumors [11], thus increasing the spectrum of immune therapy [12].

Neoplastic involvement is a serious complication in cancer patients and involves not only the brain and spinal cord [13] but can also rarely involve the peripheral nervous system [14].

The toxic effects of radiation therapy are well established [15], and increasingly late effects such as SMART syndrome [16] or other entities have appeared. Two important aspects are the observation of radiation fibrosis syndrome (RTF) [17] and possible effects of RT on the skeletal muscle.

The peripheral nerves are often affected by toxic neuropathies, a condition termed chemotherapy induced neuropathy (CIPN), which is usually a cumulative dose effect. In addition, there are also acute side effects (oxalipaltin), "coasting," and late effects complicating the course of neurotoxicity. Although the clinical manifestations of CIPN are similar, the different chemotherapeutic drugs have diverse pathogenic modes. Despite many efforts for prevention and treatment, presently no prevention and only symptomatic therapies are available [18].

Rare but significant neuropathies occur in conjunction with hematological diseases such as myeloma and Waldenstroems disease. Several types of neuropathies can be distinguished that also require specific and diverse therapies [19].

Although rare, the phenomenon of paraneoplastic diseases in both the central and peripheral nervous system deserves much attention, and indeed the immunological pathways of PNS are considered as an important source to explore the interactions of cancer and the nervous system [20].

The neurologist, in particular as a consultant, is exposed to the cancer patient presenting with neurological signs and symptoms, which can be the presenting sign of cancer, or appear in the course. Metastasis such as neoplastic effects can occur during the whole disease trajectory and may also be the cause of severe handicap and death. However, given the side effects of therapies and other potential causes such as paraneoplastic, metabolic, immune effects, and infections, the distinction of the cause in the individual cases by the neurologists is important, as interventions differ considerably.

The presentation of neurological side effects ranges from acute effects, delayed and cumulative effects, and late effects. The immune therapies, in particular the immune checkpoint inhibitors, have opened a new spectrum of side effects, which induce immune mediated syndromes, such as encephalopathies/encephalitis [21] myopathies, myasthenia, and neuropathies after irregular and unpredictable time intervals.

Symptomatic therapies are important as therapy for seizures and pain, for example, cancer pain, as this severely impacts the patient's life and reduces QoL. It is important for neurologists to be included in tumor boards and pain conferences, as often the type, quality, and other characteristics help to distinguish the syndromes and are useful in the interdisciplinary pain concept [22].

Last but not least, neuro-onco-rehabilitation is emerging. Two decades ago the term cancer rehabilitation was unknown, and given the fate of the patients, only symptomatic therapies and, reluctantly, neurorehabilitation could be prescribed. This has dramatically changed in some European countries, where cancer rehabilitation, integration, and, in particular, therapy for neurological complications of the CNS [23] and PNS [24] are treated, and many patients can resume a normal life.

This topical collection presents a few important neurological aspects in cancer care and is not complete. Nevertheless, it is intended to raise awareness through articles written by highly qualified specialists, who upon invitation completed peer reviewed articles on important topics. This awareness should be helpful to attract attention and create even more awareness.

As the NEUS has provided this outstanding platform for the topics, we hope to attract additional articles on the issues of cancer and neurology. NEUS is a journal for clinical neurologists, and the invitation drives in this direction.

Declarations

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Conflict of interest The author declares he has no conflict of interest.

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