

Center for Neuro-Oncology in Turin (Italy)

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Abstract

The Center for Neuro-Oncology of the University Hospital in Turin is hosted by the Division of Neuro-Oncology/Neurology and coordinates the Multidisciplinary Brain Tumor Board (MTB; which includes neuro-oncologists, neurosurgeons, neuroradiologists, neuropathologists, medical and radiation oncologists, and hematologists). The MTB guarantees the continuity of care from diagnosis to the end of life support. The Division of Neuro-Oncology/Neurology has an in- and outpatient clinic. In addition to daily clinical practice, major activities consist of clinical trials, translational studies, and teaching. This neurology-centered model of brain tumor care is similar to other brain tumor centers in the United States and Europe.

Keywords

Center for Neuro-Oncology, neuro-oncology, neurology, clinical trials, multidisciplinary brain tumor model, research, teaching, rare brain tumors

Introduction

The annual age-adjusted incidence rate of primary malignant brain and other central nervous system (CNS) tumors in the United States is 7.15 per 100,000 population, while the annual age-adjusted incidence rate of nonmalignant brain and other CNS tumors (including pituitary tumors) is 15.49 per 100,000 population (CBTRUS Statistical Report on 2010–2014).¹ Overall, the incidence of primary brain tumors over time is stable, but there is an increase in frequency of glioblastomas (GBMs) and primary CNS lymphomas (PCNSLs) in the elderly population (>65–70 years). Conversely, there has been a significant increase in the incidence of secondary brain tumors (brain and leptomeningeal metastases), which now are 7- to 10-fold primary malignant brain tumors.²

Total costs for neurological diseases have been recently analyzed and published in *Acta Neurologica Scandinavica*.³ Brain tumors, while being less prevalent compared to other major neurological diseases (stroke, dementia, multiple sclerosis, epilepsy), represent the second cause of costs (estimated around €21,000/year/person) following only multiple sclerosis. Major health costs are represented by neuroimaging investigations, neurosurgical techniques, radiation facilities, antineoplastic drugs, repeated hospitalization for complications, and end-of-life care. Social costs are extremely important as well, due

to physical and cognitive impairment of patients, leading to a reduction of working capabilities, and a need for continuous assistance, involving family caregivers and social assistants.

Definition and history of neuro-oncology

According to the Bylaws of the Section of Neuro-Oncology of the American Academy of Neurology, neuro-oncology is an independent discipline, which includes the management of primary and secondary CNS tumors, nonmetastatic disorders of the nervous system directly or indirectly related to systemic cancer, and neurological complications of antineoplastic treatments.

Neuro-oncology was born in the 1970s (originally in the United States, and thereafter in Europe) within the

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specialties of neurology and neurosurgery. For the first two decades of the discipline's development, neurologists became the oncologists as well as neurologists for patients with brain tumors, being active in the development and administration of chemotherapy regimens in addition to applying their understanding of diseases within the nervous system.

Over the last three decades, there has been an explosive growth of interest in neuro-oncology (from every related field). In particular, specialists from the field of radiation oncology and medical oncology began to turn their attention to cancer of the nervous system, joining neurologists and neurosurgeons in the setting of daily clinical practice, active academic research, and scientific societies (Society for Neuro-Oncology (SNO) in the United States and European Association for Neuro-Oncology (EANO) in Europe).

The increasing complexity of management of brain tumor patients has led to the development of brain tumor centers (centers for neuro-oncology), which are comprehensive clinical and research entities capable of providing all aspects of care through multi-professional involvement to brain tumor patients and family.^{4,5}

Center for Neuro-Oncology, Turin

Organization and clinical activities

The Center for Neuro-Oncology in Turin was developed as an entity recognized by the Health System of the Regione Piemonte/Valle d'Aosta (approximately four million inhabitants) in 2005 and is located in the University Hospital called "City of Health and Science" in Turin. From an administrative and organizational point of view, it is hosted by the Division of Neuro-Oncology/Neurology, which acts as the coordinator of the Multidisciplinary Brain Tumor Board (MTB) to guarantee the continuity of care (diagnosis, specific treatments, supportive and palliative care) for primary and secondary brain tumors. The MTB involves, in addition to full-time neuro-oncologists, dedicated physicians from the Division of Neurosurgery, Radiation Oncology, Neuroradiology, Neuropathology, Medical Oncology (for secondary brain tumors), Hematology (for PCNSLs), Palliative Care Medicine, and a specialized nurse. Available in-house technologies include advanced magnetic resonance imaging, positron emission tomography imaging, neuronavigation, intraoperative mapping, fluorescence-guided and awake surgery, radiosurgical equipment (Linac-based), and intensity-modulated radiotherapy.

The MTB meets weekly (Thursday afternoon), and all new and recurrent brain tumors are presented with clinical data, imaging studies, and actual pathology. The treatment options are discussed and a consensus opinion should be reached. After each case discussion, patients and family are informed of management decisions, including pros and cons of the different options, to obtain an informed consent. A written report is developed, and all reports are placed in

an electronic database, that will contain all information regarding treatments and follow-up.

The clinical activity of the Division of Neuro-Oncology/Neurology is performed both in an inpatient and outpatient setting. Hospitalization in "dedicated beds" is reserved for patients presenting with acute symptoms needing treatment and diagnostic workup before surgery, patients undergoing highly complex medical therapies (i.e. high-dose methotrexate for PCNSL, intrathecal chemotherapy for neoplastic meningitis), patients with hematotoxicity grade IV following chemotherapy, or patients in the advanced phase of disease needing symptoms control and organization of hospice access. The outpatient clinic includes several activities that are described in Table 1. In terms of volumes of activity, about 1500 patients/year have access to the Center to define diagnosis or treatment, and about 500 are treated at the Center for Neuro-Oncology with medical treatments and follow-up (about 300 gliomas; 40 atypical malignant/recurrent meningiomas; 20 PCNSLs; 40 rare brain tumors, such as medulloblastomas and ependymomas; and 60 brain/leptomeningeal metastases). The Center for Neuro-Oncology represents the hub of the Neuro-Oncology Network of the Regione Piemonte-Valle d'Aosta, which comprises six other hospitals with neurosurgical and oncological facilities. Patients requiring standard treatments (for instance radiotherapy and temozolomide in high-grade gliomas) are treated at local institutions, while they are referred to the Center for Neuro-Oncology in Turin for complex treatments, clinical trial inclusion, or second opinions. The Center for Neuro-Oncology has guidelines for all major tumor types, which are also shared at the regional level, and are updated every 2 years (or even earlier in case of breakthrough advances).

About 30% of patients come from Italian regions outside Piemonte and Valle d'Aosta. The Center for Neuro-Oncology is a Referral Center for Rare Brain Tumors within the Italian Network of Rare Cancers, and has been recently recognized as a Center of Expertise for Brain Tumors of the European Network for Rare Solid Tumors of the Adult (so-called EURACAN).

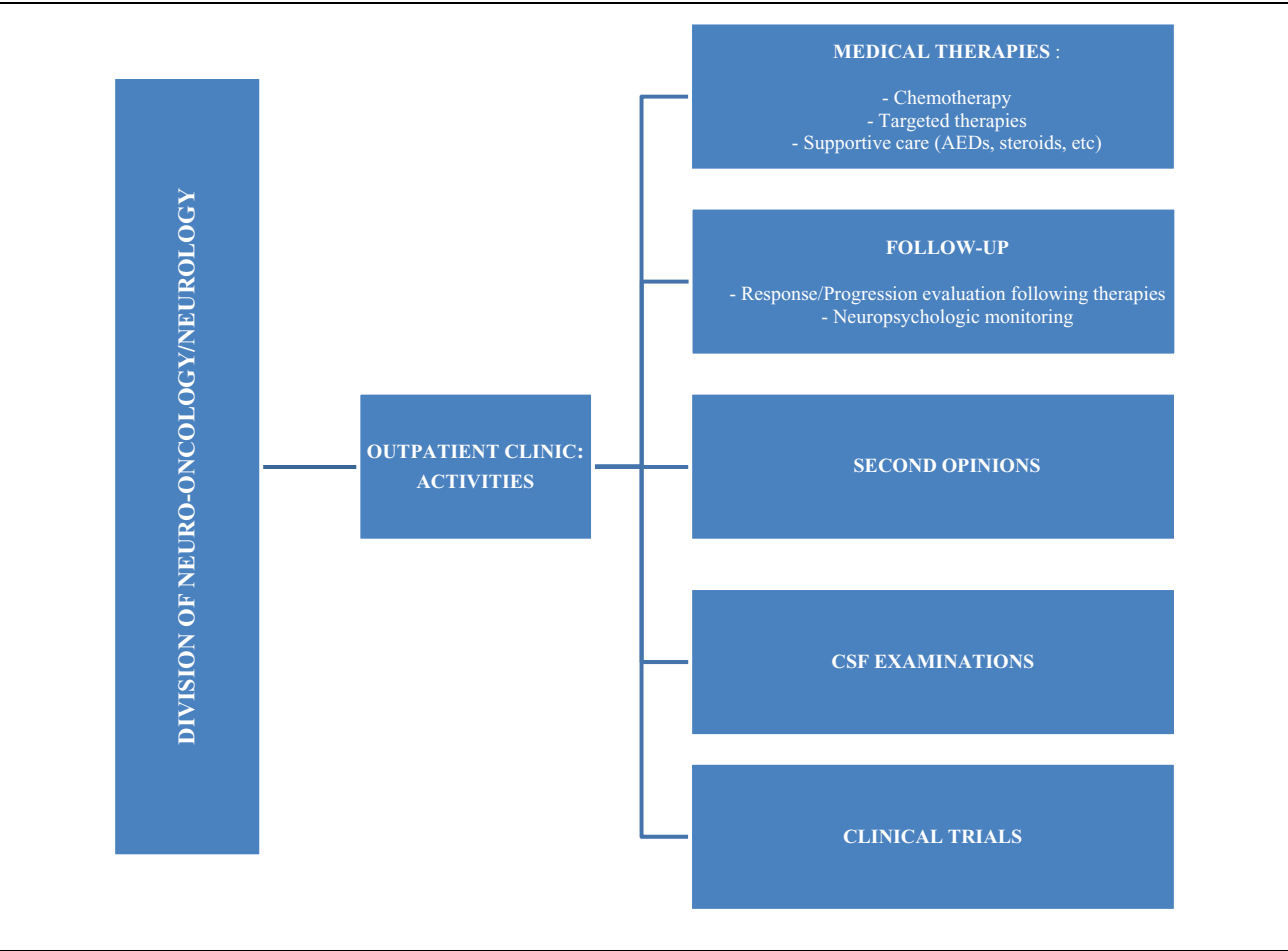
The staff of the Center for Neuro-Oncology comprises the Head of the Division of Neuro-Oncology/Neurology, three board-certificated neurologists, one PhD in neuroscience, one neuropsychologist, one data manager, one administrative employee, and one specialized nurse for the outpatient clinic. Residents in neurology and neurosurgery rotate in the in- and outpatient clinic.

The Center for Neuro-Oncology regularly hosts post-residency physicians (neurologists, neurosurgeons, radiation oncologists, medical oncologists) from both national and international institutions for training in medical neuro-oncology.

Research/clinical trials

Several clinical trials (national and international, phase II or III) are ongoing: new molecular treatment for GBMs

Table 1. Outpatient clinic activities.



(checkpoint inhibitors and proteasome inhibitors), medulloblastomas (Sonic hedgehog inhibitors), PCNSL (rituximab and ibrutinib), and brain metastases and neoplastic meningitis (human epidermal growth factor receptor2+ inhibitor neratinib); preoperative chemotherapy in low-grade gliomas; antiepileptic drugs (lacosamide and perampanel). New research programs have been recently developed, in particular, monitoring of epileptic seizures by MR-spectroscopy for isocitrate dehydrogenase (IDH1), glutamate, and GABA, and liquid biopsy of CSF for GBM and CNS/leptomeningeal metastases.

The Center for Neuro-Oncology is a member of the European Organization for Research and Treatment of Cancer (EORTC) Brain Tumor Group (BTG) and of the Collaborative Ependymoma Research Network (CERN), with the Coordinating Center at MD Anderson Cancer Center (Houston).

The scientific activity is documented by papers published in international journals with high impact factor (i.e. *Journal of Clinical Oncology*, *Lancet*, *Lancet Oncology*, *Lancet Hematology*, *Neuro-Oncology*, *Annals of Oncology*, *Neurosurgery*, etc.).

Teaching

Physicians of the Center for Neuro-Oncology have appointments as faculty members to teach neuro-oncology in the Residency Programs of Neurology, Neurosurgery, Radiology, Radiation and Medical Oncology at the University of Turin and Milan.

Since 2005, the Center for Neuro-Oncology organizes Annual “Updates in Neuro-Oncology” as a CME event.

Discussion

The model of the Center for Neuro-Oncology in Turin is an example of a multidisciplinary management of brain tumors centered on neurologists/neuro-oncologists. It is similar to other comprehensive brain tumor centers in the United States, such as those of Dana–Farber Cancer Center/Massachusetts General Hospital (Harvard Medical School) in Boston, Memorial Sloan-Kettering Cancer Center in New York, and MD Anderson Cancer Center in Houston. This model is similar to the brain tumor centers in Zurich, Heidelberg, and Paris as well. One of the advantages of this

model is to guarantee a continuity of care from diagnosis to palliation in the end of life by the same team of specialists (neuro-oncologists) within a multi-professional tumor board. In terms of scientific activity it offers a unique opportunity to develop clinical and translational studies on the interactions at different levels (molecular, neurophysiologic, and neuroimaging) between a brain tumor and the normal brain tissue.

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Declaration of conflicting interests

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