

Editorial

Spinal cord tumor research

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One of the basic fundamental principles of modern-day medicine has been the application of scientific knowledge to clinical practice. In this era, the pursuit of evidence-based bench-to-bedside medicine is of critical importance. If we do not have a clear and correct understanding of the characteristics of a given disease including the natural history, pathobiology, or treatment modalities, clinicians and researchers are unable to effectively deal with the condition or advance knowledge in the area. Such is the case when dealing with spinal cord tumors, given their rarity, the relative lack of research in this area, and the profound impact that these lesions have on patients.

Given the unique challenges inherent to studying spinal cord tumors, the National Institutes of Health's Office of Rare Diseases in coordination with the National Cancer Institute and the National Institute of Neurological Disorders and Stroke sponsored a multidisciplinary workshop to discuss the current status of research and therapeutic strategies related to these uncommon but clinically important neoplasms. In this issue of *Journal of Neurosurgery Spine*, Claus et al.¹ summarized the proceedings and recommendations of this important meeting. As succinctly pointed out by Claus et al., the relative rarity of spinal cord tumors is a relative impediment to undertaking controlled trials. Spinal cord neoplasms represent 0.5% of newly diagnosed tumors, and only 5–12% of all tumors of the central nervous system.^{6,10,11} According to the Central Brain Tumor Registry of the United States, the 1-, 5-, and 10-year survival rates following diagnosis of a primary malignant spinal cord tumor were 85, 71, and 64%, respectively.⁸ Could this be improved? One hopes that, with the implementation of recommendations of the workshop, significant advances in this field will occur.

In 1887, Sir Victor Horsley performed the first resection of an intradural neoplasm in which the resection was successful, but the patient died.³ In 1925, the first large series of primary spinal cord tumor resection was published by Charles Elsberg.² Over the past several decades, there have been remarkable advances in imaging, microsurgical techniques, radiotherapeutic approaches, and chemotherapy. However, our knowledge related to the etiopathogenesis and optimal management of certain lesions including high-grade intramedullary spinal cord tumors remains unclear. The future will certainly lie in collaborative, multidisciplinary research efforts. Indeed, early successes have been seen in this regard. For example, the collation of information across nationwide databases has elucidated further issues with spinal cord tumor surgery on a large scale, as reported recently in a Stanford study.⁷

In their workshop report, Claus et al. emphasized the importance of collaborative research efforts. As they pointed out, "Extension of a collaborative network to include the laboratories of neurobiologists, stem cell biologists, and cancer biologists would similarly accelerate the pace of basic science research and the discovery of effective new treatments for spinal cord tumors." It would be natural that with such an open and collaborative approach, the domino effect will open many new doors.

From the epidemiological standpoint, a better understanding of the risk factors associated with spinal cord tumors based on larger scale studies will allow us to identify patient groups at higher risks and implement preventive measures, screening, and intervention programs. The economics of such exercises certainly will benefit humankind, as evidenced by the many successful programs for other tumors such as colorectal, breast, and upper gastrointestinal tract.

With the sharing of centralized and pooled registries, pathologists are able to access mass amounts of gross and histological data and conduct tumor boards on a nationwide or even international basis. A small center suddenly finds its database increased exponentially, and the potential for information explosion is unimaginable.

The extension of tumor boards beyond clinicians to include paraclinical experts will ensure keener and more close-knit cooperation among surgeons, oncologists, pa-

thologists, and radiotherapists as clinical, imaging, and intraoperative details are better correlated so that each one does not practice in isolation.

It is encouraging to note how the workshop participants freely shared their knowledge and updated one another on spinal cord tumorigenesis models,⁵ theories, and advances, as well as experiments based on animal studies with the application of cutting-edge technology.

Let us not forget the general public's contribution in this concerted effort either. Patient advocacy groups^{4,9} were noted to have been included in the workshop's pipeline, as this struggle is not just the physician's or the patient's own struggle. It is everybody's struggle.

One of the key outputs of the National Institutes of Health Office of Rare Diseases, National Cancer Institute, and the National Institute of Neurological Disorders collaborative workshop on spinal cord tumors is a series of key recommendations. These include the following: 1) establishment of a population-based public registry for spinal cord tumors; 2) central pathological review of collections of spinal cord tumors to develop improved classifications; 3) collaborative clinical trials networks; and 4) improved preclinical research into spinal cord tumors including the development of animal models and the identification and study of spinal cord progenitor cells.

We applaud the organizers and participants of this unique workshop on spinal cord tumors and eagerly await the implementation of the workshop recommendations.

References

- Claus EB, Abdel-Wahab M, Burger PC, Engelhard HH, Ellison DW, Gaiano N, Gutmann DH, et al: Defining future directions in spinal cord tumor research. Proceedings from the National Institutes of Health workshop. *J Neurosurg Spine* **12**:117–121, 2010
- Cramer FJ: Charles Albert Elsberg 1871–1948. *Surg Neurol* **4**: 1–3, 1975
- Gowers WR, Horsley V: A case of tumour of the spinal cord. Removal; recovery. *Medico-Chirurgical transactions*. **Vol 71**:377, 1888
- Malia's CORD Foundation: <http://www.cordfoundation.org/malia> [Accessed October 14, 2009]
- Mavinkurve G, Pradilla G, Legnani FG, Tyler BM, Bagley CA, Brem H, et al: A novel intramedullary spinal cord tumor model: functional, radiological, and histopathological characterization. *J Neurosurg Spine* **3**:142–148, 2005
- Newton HB, Newton CL, Gatens C, Herbert R, Pack R: Spinal cord tumors: review of etiology, diagnosis and multi-disciplinary approach to treatment. *Cancer Pract* **3**:207–218, 1995
- Patil CG, Patil TS, Lad SP, Boakye M: Complications and outcomes after spinal cord tumor resection in the United States from 1993 to 2002. *Spinal Cord* **46**:375–379, 2008
- Schellinger KA, Propp JM, Villano JL, McCarthy BJ: Descriptive epidemiology of primary spinal cord tumors. *J Neurooncol* **87**:173–179, 2008
- Spinal Cord Tumor Association, Inc.: <http://www.spinalcordtumor.homestead.com> [Accessed October 14, 2009]
- Stieber VW, Tatter SB, Shaffrey ME, Shaw EG: Primary spinal tumors, in Schiff D, O'Neill BP (eds): *Principles and Practice of Neuro-Oncology*. New York: McGraw Hill Publishers, 2005, pp 501–533
- Tihan T, Chi JH, McCormick PC, Ames CP, Parsa AT: Pathologic and epidemiologic findings of intramedullary spinal cord tumors. *Neurosurg Clin N Am* **17**: 7–11, 2006

Response

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On behalf of the researchers, clinicians, and patient advocates involved in spinal cord tumor research, we thank Drs. Fehlings and Chua for their kind commentary and enthusiastic support of our efforts. As highlighted in their editorial, the study of rare diseases is indeed difficult and necessitates a collaborative cross-disciplinary approach involving a diverse number of scientific specialties and patient groups. A fundamental first step is the development of a population-based spinal cord database already underway through the Central Brain Tumor Registry of the United States. Second, initiatives using Internet resources have been developed to identify patients for clinical studies as well as to disseminate accurate information about these uncommon tumor types. To further accelerate research in this important underserved area, we recommended in the meeting summary the construction of a large-scale registry complete with detailed clinical and epidemiological data. Moreover, this annotated tumor registry should be linked to a repository containing uniformly collected and processed biological specimens. While this endeavor represents a complex task on many levels, it is absolutely necessary to galvanize research aimed at identifying risk factors relevant to clinical outcomes for this group of patients. In addition, we strongly advocate the development of an interdisciplinary collaborative research consortium to define specific research goals and to ensure that clinical, biological, and genomic data collected from these rare tumors be uniform and readily compared. This is particularly germane to spinal cord tumors in which results from numerous national and international centers will need to be pooled to obtain sufficient statistical power to identify environmental and genetic risk factors as well as gene-gene and gene-environment interactions. Inclusion of persons of diverse ethnic and racial groups must also be considered. The strength of this approach for cancers of the CNS was recently highlighted by the publication of the first two genome-wide association studies of glioma,^{1,2} an effort that involved collaboration within the United States as well as from Europe and Israel. We look forward to facilitating similar successes for tumors of the spinal cord. (DOI: 10.3171/2009.8.SPINE09608)

References

- Shete S, Hosking FJ, Robertson LB, Dobbins SE, Sanson M, Malmer B et al: Genome-wide association study identifies five susceptibility loci for glioma. *Nat Genet* **41**:899–904, 2009
- Wrensch M, Jenkins RB, Chang JS, Yeh RF, Xiao Y, Decker PA et al: Variants in the *CDKN2B* and *RTEL1* regions are associated with high-grade glioma susceptibility. *Nat Genet* **41**: 905–908, 2009