Diffuse Low-Grade Gliomas in Adults

Hugues Duffau
Editor

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Natural History, Interaction with the Brain, and New Individualized Therapeutic Strategies

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Editor
Hugues Duffau, MD, PhD
Doctor Honoris Causa
Department of Neurosurgery
Gui de Chauliac Hospital
INSERM 1051
Institute for Neurosciences of
Montpellier
Montpellier University Medical Center
Montpellier
France

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Foreword

When it is all said and done, this will be the definitive source on diffuse low-grade gliomas and will serve as a comprehensive textbook for all clinicians and health-care providers who take care of patients with this disorder. What makes this book so unusual is the individualized personal approach to this problem on a patient-by-patient basis. In other words, one size does not fit all when it comes to diffuse low-grade gliomas. The approach the authors have taken in defining this entity and the options for management are quite unique and innovative, to say the least. We have come full circle in the way in which we approach this disease from a "wait-and-see" attitude to a more proactive individualized treatment regime based upon the dynamics of the lesion as seen preoperatively and the individualized approach to surgery and therapy which has influenced the outcome of this disease over the past decade.

The book is organized in a very logical and informative fashion, starting off with several chapters on epidemiology and pathological classification. There has been a significant evolution of our thought processes on the gliomagenesis of these lesions as well as its molecular profile, and therefore to truly understand how best to manage a patient with a diffuse low-grade glioma, one has to know the distinct patterns that exist in molecular classification for each patient. In other words, it is simply not acceptable anymore to classify a tumor based on histology without knowing the genotypic expression profile of the tumor. Further depth is developed in chapters devoted to the cellular origin of this lesion and the possible relationship this tumor has with stem cells or progenitors from different regions of the brain. While some of the chapters involving genomics do overlap, I particularly enjoyed reading the different ways in which this information is expressed and interpreted. Other particularly useful contributions include the role of proteomic classification, including a bioinformatic approach linking classification to outcome, as well as chapters involving cell cultures and animal models. To date, there have been very few cell cultures established for low-grade gliomas and, for that matter, appropriate animal models. However, it is clear that xenografts do exist, as do genetically engineered mouse models based upon certain types of phenotypic backgrounds. Overall, I found the basic science components of this textbook to be extraordinarily revealing, very thorough, and quite easy to read and apply to a given patient's tumor.

The clinical aspects of this entity are further evolved in chapters on imaging, clinical presentation, and quality of life issues. The imaging is particularly valuable in that all aspects are covered, from anatomical imaging with

MRI to physiological imaging involving MRI and metabolic imaging with PET scanning. All of this information is woven together in subsequent chapters that develop predictive models based upon growth rates and invasion along white matter tracts to understand what the natural history of this disease will be likely to demonstrate. A particularly important contribution is that by Dr. Soffietti who explains in great detail various prognostic factors that influence the natural history and therefore define the risk of the disease as it affects the patient. This is done in such a way that incorporates all of the molecular biology, imaging, and clinical factors to enable the clinician to predict outcome and progression for a given patient's diffuse low-grade glioma.

Subsequent contributions apply to the functional assessment of various brain regions involved with these types of tumors. We all realize that language and cognition are so important to understand in terms of deciding how best to manage a patient and what to expect with the treatment strategy that we select for that given individual. Thus, bringing together some of the functional imaging modalities that we have, such as fMRI and MEG along with connectivity maps, allows us to be able to predict how language and cognition could be affected with surgery as well as various treatment options.

Clearly, surgery remains the most important treatment modality for this lesion, and thus, the chapters by Duffau and colleagues on surgery and functional considerations are extremely valuable in terms of planning any operative procedure with a lesion of this type. Dr. Duffau has one of the greatest experiences in the world in operating on diffuse low-grade gliomas, and he explains in great detail how to consider not only the anatomy but the function as mapped intraoperatively and how this influences the outcome of the patient. Great insight is given to how stimulation mapping can be used to decrease permanent deficits, making surgery for some of these complicated lesions quite safe. As he states so nicely, the surgeon has to adapt the surgical strategy to the anatomy and function of the brain done under awake conditions to maximize the extent of resection while minimizing morbidity. Another chapter is devoted to the oncological considerations of extensive resections and how important this is in not only affecting progression free survival but overall survival and malignant transformation.

Following surgery, adjuvant modalities are necessary in certain circumstances when residual disease remains. Excellent contributions are made in the areas of chemotherapy and radiation and how and when some of these modalities should be used. Several innovative strategies are also described, such as the use of chemotherapy performed preoperatively to reduce the volume of the mass, thus making so-called inoperable lesions quite operable. In fact, even patients with gliomatosis may become surgical candidates if they respond appropriately to chemotherapy. In addition, in the postoperative setting, one has to consider the use of functional rehabilitation as a means to improve the outcome of the patient and expedite relearning of functions that may be temporarily lost or compromised. This brings into consideration the concept of neuroplasticity and reorganization, which we know exists and, through a number of writings from Dr. Duffau, has shown all of us that areas thought to be functional can lose their functionality over time with chronically based lesions in so-called eloquent areas.

When reading this textbook, one cannot ignore the fact that we as clinicians must find new endpoints and look at different strategies for how this disease progresses and how it should be managed. We all recognize that there have to be better endpoints than time to progression or malignant transformation. We also have to consider clinical issues, such as the time it takes to return to a normal quality of life and functional status as equally important to the more standard endpoints used previously.

This is exactly why this book represents a more personalized approach to patients with diffuse low-grade gliomas. New strategies must be considered that take into consideration the concept of plasticity, which allows function to leave given areas and provides the surgeon the opportunity to remove what was once thought to be inoperable. The theme of this book, in terms of an individualized approach to a patient with a diffuse low-grade glioma, lets us think about different concepts such as allowing plasticity to help us shape the course of this disease and its treatment. We also need to think about the use of neoadjuvant therapy to shrink the tumor with chemotherapy and to first understand the growth kinetics of the lesion prior to just operating at the initial diagnosis. All of these factors contribute to the personalized approach, as explained throughout this textbook, to this lesion. I also like the concept of a supratotal resection, in which the goal with all of these functional considerations is to operate, not on the anatomy but to remove the lesion and a significant margin, as function permits, around the lesion. This will enable us to once again change the approach in an individualized way to the patient who has this maximal extent of resection. So far, the data seems quite convincing that patients who have these more aggressive supratotal resections might have a lower risk of malignant transformation, thus enabling surgery to change the natural history of the disease.

All in all, this is a major contribution that will be significant in the history of neurosurgery and neuro-oncology as it pertains to patients with diffuse low-grade gliomas. We cannot think in traditional terms any more about how to manage this disease. We have to employ the new strategies and concepts as described throughout this textbook to better individualize the approach to a given patient, therefore making more of an impact in the long run. I thoroughly enjoyed reading this book, and without a doubt, if you only have one reference source on diffuse low-grade gliomas, this must be it!

San Francisco, CA Mitchel S. Berger, MD

Contents

Contributors

Mitchel S. Berger, MD Department of Neurosurgery, University of California at San Francisco, San Francisco, CA, USA

Luc Bauchet, MD, PhD Institute for Neurosciences of Montpellier, Team "Brain Plasticity, Stem Cells and Glial Tumors", National Institute for Health and Medical Research (INSERM), Montpellier University Medical Center, Montpellier, France

Department of Neurosurgery, Gui de Chauliac Hospital, Montpellier University Medical Center, Montpellier, France

French Brain Tumor DataBase, Groupe de Neuro-Oncologie du Languedoc-Roussillon, Registre des Tumeurs de l'Hérault, Centre de Lutte Contre le Cancer Val d'Aurelle, Montpellier, France

Kevin P. Becker, MD, PhD Department of Neurology, School of Medicine, Yale University, New Haven, CT, USA

Antonio Paolo Beltrami, MD, PhD Interdepartmental Center for Regenerative Medicine, University of Udine, Udine, Italy

Department of Medical and Biological Sciences, University of Udine, Udine, Italy

Department of Pathology, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Carlo Alberto Beltrami Interdepartmental Center for Regenerative Medicine, University of Udine, Udine, Italy

Department of Medical and Biological Sciences, University of Udine, Udine, Italy

Department of Pathology, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Luca Bertero, MD Division of Neuro-Oncology, Departments of Neuroscience and Oncology, University and San Giovanni Battista Hospital, Turin, Italy

Alberto Bizzi, MD Department of Neuroradiology, Instituto Clinico Humanitas IRCCS, Rozzano, Milan, Italy

Rolf Bjerkvig, PhD NorLux Neuro-Oncology Laboratory, Department of Oncology, Centre de Recherche Public de la Santé (CRP-Santé), Luxembourg City, Luxembourg

NorLux Neuro-Oncology Laboratory, Department of Biomedicine, University of Bergen, Bergen, Norway

Sébastien Bourgnaud NorLux Neuro-Oncology Laboratory, Department of Oncology, Centre de Recherche Public de la Santé (CRP-Santé), Luxembourg City, Luxembourg

Evgenia Bourkoula Interdepartmental Center for Regenerative Medicine, University of Udine, Udine, Italy

Department of Medical and Biological Sciences, University of Udine, Udine, Italy

Department of Pathology, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Daniela Cesselli, MD, PhD Interdepartmental Center for Regenerative Medicine, University of Udine, Udine, Italy

Department of Medical and Biological Sciences, University of Udine, Udine, Italy

Department of Pathology, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Stephanie E. Combs, MD Department of Radiation Oncology, University Hospital of Heidelberg, Heidelberg, Germany

R.F. Deighton Centre for Cognitive and Neural Systems, University of Edinburgh, Edinburgh, UK

Division of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh, UK

Hugues Duffau, MD, PhD Doctor Honoris Causa, Department of Neurosurgery, Gui de Chauliac Hospital, Montpellier University Medical Center, Montpellier, France

Institute for Neurosciences of Montpellier, Team “Brain Plasticity, Stem Cells and Glial Tumors”, National Institute for Health and Medical Research (INSERM), Montpellier, France

Frank Willi Floeth Department of Spine and Pain, St.-Vinzenz-Hospital, Düsseldorf, Germany

Norbert Galldiks, MD INM-3: Cognitive Neuroscience, Institute of Neuroscience and Medicine, Forschungszentrum Jülich, Jülich, Germany

Department of Neurology, University Hospital Cologne, Cologne, Germany

A.M.J. Gerth Centre for Clinical Brain Science, Western General Hospital, University of Edinburgh, Edinburgh, UK

Centre for Cognitive and Neural Systems, University of Edinburgh, Edinburgh, UK

Catherine Godfraind, MD, PhD Department of Pathology, Cliniques Universitaires Si-Luc, Brussels, Belgium

Catherine Gozé, PharmD, PhD Department of Cellular Biology, Montpellier University Medical Center, Montpellier, France

Institute for Neurosciences of Montpellier, Team "Brain Plasticity, Stem Cells and Glial Tumors", Montpellier University Medical Center, Montpellier, France

Pierre-Olivier Guichet INSERM U1051, Institute for Neuroscience of Montpellier, Hopital Saint Eloi, Montpellier, France

Rémy Guillevin, MD, PhD Department of Radiology and MPIM Laboratory, Teaching Hospital, University of Poitiers, Poitiers, France

Functional Laboratory Imaging, Neuroradiology Department, Teaching Hospital, University of Poitiers, Poitiers, France

Zahra Hassani, PhD INSERM U1051, Université Montpellier 2, Institute for Neurosciences of Montpellier, Hôpital Saint Eloi, Montpellier, France

Team "Brain Plasticity, Stem Cells and Glial Tumor", UM2-UM1-INSERM U1051, Institute of Neurosciences of Montpellier, Montpellier, France

Jan J. Heimans, MD, PhD Department of Neurology, VU University Medical Center, Amsterdam, The Netherlands

Guillaume Herbet National Institute for Health and Medical Research (INSERM), U1051, Team "Plasticity of the Central Nervous System, Human Stem Cells and Glial Tumors", Institute for Neurosciences of Montpellier, Montpellier University Medical Center, Montpellier, France

Department of Neurosurgery, Gui de Chauliac Hospital, Montpellier University Medical Center, Montpellier, France

Jean-Philippe Hugnot, PhD INSERM U1051, Université Montpellier 2, Institute for Neuroscience of Montpellier, Hopital Saint Eloi, Montpellier, France

Team "Brain Plasticity, Stem Cells and Glial Tumor", UM2-UM1-INSERM U1051, Institute of Neurosciences of Montpellier, Montpellier, France

Tamara Ius, MD Department of Neurosurgery, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Karl-Josef Langen, MD INM-4: Medical Imaging Physics, Institute of Neuroscience and Medicine, Forschungszentrum Jülich, Jülich, Germany

Emmanuel Mandonnet, MD, PhD Department of Neurosurgery, Lariboisière Hospital, Paris, France

Nicholas F. Marko, MD Department of Neurosurgery, University of Texas MD Anderson Cancer Center, Houston, USA

J. McCulloch Centre for Cognitive and Neural Systems, University of Edinburgh, Edinburgh, UK

Sylvie Moritz-Gasser National Institute for Health and Medical Research (INSERM), U1051, Team "Plasticity of the Central Nervous System, Human Stem Cells and Glial Tumors", Institute for Neurosciences of Montpellier, Montpellier University Medical Center, Montpellier, France

Department of Neurology, CHRU Montpellier, Gui de Chauliac Hospital, Montpellier University Medical Center, Montpellier, France

Simone P. Niclou, PhD NorLux Neuro-Oncology Laboratory, Department of Oncology, Centre de Recherche Public de la Santé (CRP-Santé), Luxembourg City, Luxembourg

Hiroko Ohgaki, PhD Section of Molecular Pathology, International Agency for Research on Cancer (IARC), Lyon, France

Joseph M. Piepmeier, MD Department of Neurosurgery, School of Medicine, Yale University, New Haven CT, USA

Anja Pucer, PhD Interdepartmental Center for Regenerative Medicine, University of Udine, Udine, Italy

Department of Medical and Biological Sciences, University of Udine, Udine, Italy

Department of Pathology, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Jaap C. Reijneveld, MD, PhD Department of Neurology, VU University Medical Center, Amsterdam, The Netherlands

Valérie Rigau, MD, PhD Cytology and Anatomical Pathology Laboratory, Montpellier University Medical Center, Montpellier, France

Team "Neuronal Death and Epilepsia", CNRS UMR 5203 INSERM U661 UM1-UM2, Montpellier, France

Roberto Rudà, MD Division of Neuro-Oncology, Departments of Neuroscience and Oncology, University and San Giovanni Battista Hospital, Turin, Italy

Michael Sabel, MD Department of Neurosurgery, Heinrich-Heine-University, Düsseldorf, Germany

Miran Skrap, MD Department of Neurosurgery, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Anja Smits, MD, PhD Department of Neuroscience, Neurology Uppsala University, Uppsala, Sweden

Riccardo Soffietti, MD Division of Neuro-Oncology, Departments of Neuroscience and Oncology, University and San Giovanni Battista Hospital, Turin, Italy

Cornelius J. Stam, MD, PhD Department of Clinical Neurophysiology, VU University Medical Center, Amsterdam, The Netherlands

Luc Taillandier, MD, PhD Neurooncology Unit, Department of Neurology, Nancy University Medical Center, Nancy, France

Martin J.B. Taphoorn, MD, PhD Department of Neurology, VU University Medical Center, Amsterdam, The Netherlands

Department of Neurology, Medical Center Haaglanden, The Hague, The Netherlands

Juan Torres-Reveron, MD, PhD Department of Neurosurgery, School of Medicine, Yale University, New Haven, CT, USA

Marco Vindigni, MD Department of Neurosurgery, Azienda Ospedaliero Universitaria di Udine, Udine, Italy

Robert J. Weil, MD Department of Neurosurgery, Brain Tumor and Neuro-Oncology Center, Cleveland Clinic, Cleveland, OH, USA

Ian R. Whittle, MD, PhD Division of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh, UK

Department of Clinical Neurosciences, Western General Hospital, Edinburgh, Scotland, UK