Primary central nervous system lymphomas

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PRIMARY central nervous system lymphomas (PCNSLs) are aggressive tumors that occur in both immunocompetent and immunocompromised patients. Their myriad presentations and diagnostic difficulties make them challenging cases, offset in part by the gratifying response seen with adjunctive therapy. Since the advent of highly active antiretroviral therapy, the incidence of PCNSL in patients with acquired immunodeficiency syndrome (AIDS) has steadily declined, but the incidence in immunocompetent patients has continued to increase.

This issue of *Neurosurgical Focus* is divided into five sections: pathogenesis, diagnosis, clinical manifestations, treatment, and translational research. Kadoch et al. review the molecular pathogenesis of PCNSL. They point out that a variety of factors may contribute to its pathogenesis, including latent infection by Epstein-Barr virus in immunosuppressed patients, the presence of the B-cell-attracting chemokine BCA-1, and B-cell growth factors such as interleukin-4. The challenges of pathological diagnosis are emphasized by Commins, who presents the problems of intraoperative diagnosis, including the presence of common and uncommon types of PCNSL, the role of perioperative steroid agents in “melting away” lymphomas and preventing an accurate diagnosis (including interpretation of smears from stereotactic biopsy samples), and the potential role of molecular studies. Go et al. present the latest information on imaging of PCNSL, covering the use of computed tomography scanning, magnetic resonance (MR) imaging (including MR spectroscopy), and positron emission tomography in lymphoma diagnosis. Last, Hunt et al. compare PCNSL with multiple sclerosis, and provide important guidelines for neurosurgical management, including the avoidance of corticosteroid drugs and the use of diagnostic biopsy sampling rather than volumetric tumor resection.

This issue contains fascinating articles on the varied presentation of PCNSL and the different subtypes of this tumor. Fitzsimmons and Batchelor compare and contrast neuroimaging and clinical presentation between AIDS and immunocompetent patients with PCNSL. They emphasize the available laboratory, neuroimaging, and ophthalmic examinations that can be performed in these patients. Gündüz et al. present their vast experience with intraocular lymphomas, a subset of PCNSL characterized by lymphoma cell invasion of the subretinal pigment epithelial space, and vitreous. Origins, presentation, diagnosis, and treatment for intraocular lymphomas (including systemic and intraocular methotrexate and rituximab) are presented. Primary dural lymphomas are discussed by Iwamoto and

Abrey. These lymphomas arise from the dura mater and differ biologically from other PCNSLs in that they are usually low-grade marginal zone lymphomas and not high-grade diffuse B-cell lymphomas. Their neuroimaging presentation often mimics that of meningiomas; surgery and low-dose radiotherapy can often achieve excellent local control. Chamberlain presents an often underdiagnosed manifestation of PCNSL: lymphomatous meningitis, which can be present in up to 40% of patients with PCNSL. Diagnosis, surgery (placement of reservoirs for intracerebrospinal fluid chemotherapy, placement of shunts for hydrocephalus), and radiation for patients with lymphomatous meningitis are outlined. The article by Abela and Weitzman on PCNSL in children is another outstanding example of unusual variants of this tumor. Although extremely rare, pediatric PCNSL was seen in 1.5% of the patients with this lesion in the Brain Tumor Registry of Japan, and the median age at diagnosis was 9 years. Da Silva et al. summarize the remaining rare pathological subtypes of PCNSL, including low-grade, T-cell, and Burkitt lesions. Their article rounds out the unusual presentations of this tumor type. Last, Galarza et al. present a case study of a large B-cell lymphoma with invasion of the dura mater and skull.

Treatment of PCNSL can be extremely gratifying, albeit often fraught with complications from the current therapy. Omuro and Abrey present an article on the state of the art of the various chemotherapeutic regimens that are currently used for patients with PCNSL. High-dose methotrexate is the most effective agent, and can be used in combination with other drugs. Jahnke et al. present their extensive experience with treating PCNSL, and emphasize the role of blood-brain barrier disruption to enhance delivery of chemotherapy and antibody treatment for this tumor. Last, Elder and Chen discuss the role of surgery, including stereotactic biopsy procedures, in PCNSL, and they also analyze the role of craniotomies in selected patients. The use of Celebrex as a potential agent in treating PCNSL is discussed in a translational research article by Wang et al. in which the authors demonstrate the effectiveness of Celebrex in reducing tumor size and increasing survival in an in vivo model of Burkitt PCNSL.

We hope that this issue on PCNSL will garner additional interest in this tumor, the incidence of which has been increasing steadily. Further research, both basic science and clinical, is critical to increase our understanding of the pathogenesis of PCNSL and to improve current treatment approaches for this potentially curable disease.