Primary Central Nervous System Lymphoma*

L. M. DeAngelis

Department of Neurology and Neuroscience, Cornell University Medical College, New York, and Department of Neurology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021, USA

Introduction

Primary central nervous system lymphoma (PCNSL) is a non-Hodgkin’s lymphoma which arises within and is confined to the central nervous system. For many years this tumor was called microglioma, reticulum cell sarcoma, or perivascular sarcoma, but the lymphocytic origin of the malignant cell which comprises this neoplasm is now well established [1–3]. While it is clear that PCNSL is a malignant lymphocytic tumor, how and why a lymphoma develops within the CNS which lacks lymph nodes and lymphatics remains an unanswered question.

Until recently, PCNSL has been a rare tumor, accounting for only 0.5%–1.2% of all intracranial neoplasms; it is associated with a variety of congenital, acquired, and iatrogenic immunodeficiency states [2, 4, 5]. The highest incidence has been reported in patients with the acquired immunodeficiency syndrome (AIDS) where it is seen in 1.9%–6% of patients [6, 7]. However, a recent epidemiological study revealed a threefold increase in the incidence of this tumor in otherwise apparently normal individuals which could not be attributed to new diagnostic techniques or the adoption of a uniform nosology [8]. The reason for this marked rise in PCNSL is unknown, but physicians are seeing these patients with increased frequency. At Memorial Sloan-Kettering Cancer Center, we have seen a 17-fold increase in PCNSL in the 5 years between 1985–1990 compared to the previous 20 years.

*Portions of the text are reprinted from Principles and Practice of Oncology. Update Series, DeVita VT, Hellman S, Rosenberg SA (eds), Lippincott, Philadelphia, PA. with permission from the publisher.

O. D. Wiestler et al. (eds.), Molecular Neuro-oncology and Its Impact on the Clinical Management of Brain Tumors © Springer-Verlag Berlin Heidelberg 1994
Clinical Features

General

PCNSL affects all ages, from the very young to the elderly. Its peak incidence occurs in the 6th and 7th decades in immunocompetent patients and younger in immunosuppressed patients [9]. Among apparently immunocompetent individuals, there is a 3:2 male to female ratio. By definition, PCNSL excludes the presence of systemic lymphoma. Extensive testing of newly diagnosed patients with PCNSL, using abdominal, pelvic, and chest computed tomography (CT) and bone marrow biopsy, has never revealed systemic lymphoma [10]. The absence of systemic tumor in virtually all patients confirms the primary nature of this brain tumor even though the cell of origin is not neuroectodermal.

Brain

Most PCNSLs present with symptoms of an intracranial mass lesion. The specific presenting symptoms and signs reflect the location of the tumor, with focal cerebral deficits occurring in about half of patients [9]; however, there are some differences in the presentation of PCNSL from other brain tumors. Because PCNSL involves the frontal lobes frequently and multiple lesions are often seen, changes in personality and level of alertness are common presenting symptoms. Headaches and symptoms of increased intracranial pressure are also seen frequently. Seizures are less common than in patients with other types of brain tumors, occurring in only 10% of patients as a presenting sign, because most PCNSLs are more likely to involve deep structures. Symptoms are usually present only for a short duration, weeks to a few months, before a diagnosis is made.

PCNSL is usually disseminated within the nervous system at diagnosis. Brain lesions are multifocal in roughly half of immunocompetent patients. Multiple lesions often cause diagnostic confusion with brain metastases, particularly since 13% of PCNSL patients have a history of a prior systemic malignancy [11]. Multiple lesions may be connected to each other by tumor which has infiltrated the brain microscopically but is not apparent on CT or magnetic resonance imaging (MRI) scan; however, the majority of patients with multiple masses appear to have multifocal disease with no continuity among the lesions. Many lesions are periventricular, and thus tumor cells can easily gain access to the CSF. The reported incidence of meningeal seeding by PCNSL varies from 0% to 25% [12–15], but if a vigorous search is conducted, a positive cytology is seen in one-third of patients and a suspicious cytology is obtained in another one-third [10]. Therefore, at least 67% of patients have definitive or probable leptomeningeal lymphoma, and this is probably still an underestimate. At autopsy 100% of patients have leptomeningeal tumor either from direct invasion into the ventricular system by periventricular tumor or by local involvement of the leptomeninges overlying a cortical lesion.