Available online at www.sciencedirect.com

SCIENCE DIRECT

Surgical Neurology 65 (2006) 590–594

SURGICAL NEUROLOGY

www.surgicalneurology-online.com

Neoplasm

Secondary central nervous system involvement by follicular lymphoma: case report and review of the literature

N.L. Grupka, MD[a], J. Seinfeld, MD[b], J. Ryder, MD[a], K.O. Lillehei, MD[b], B.K. Kleinschmidt-DeMasters, MD[a,b,c,*]

Departments of [a]*Pathology,* [b]*Neurosurgery, and* [c]*Neurology, University of Colorado, Denver, CO 80262, USA*

Received 25 May 2005; accepted 26 August 2005

Abstract

Background: We report a patient with indolent stage IV follicular lymphoma, grade 1, initially successfully treated with chemotherapy, who later developed aggressive diffuse large B-cell lymphoma in the parieto-occipital lobe 8 years after initial presentation. The differing patterns of lymphomatous involvement of the central nervous system (CNS) are briefly reviewed, with a focus on the patterns seen in secondary CNS spread by low-grade lymphomas.

Case Description: A 53-year-old man was diagnosed with stage IV follicular lymphoma, grade 1, in 1996. Although initial chemotherapy was successful, he developed several recurrences of lymphoma over the following years. In May 2004, he presented with a discrete, single, massive parieto-occipital lobe brain lesion. The mass failed to regress with empiric cranial external beam radiotherapy. Because of suspicion of an unusual infection, the lesion was surgically excised in its entirety. The mass proved to be an aggressive diffuse large B-cell lymphoma, transformed from his previous follicular cell lymphoma, with retention of strong Bcl-2 and Bcl-6 immunoreactivity.

Conclusions: Parenchymal brain involvement, as opposed to dural or leptomeningeal, is a relatively uncommon pattern of spread to the CNS for systemic lymphomas. More significantly, follicular lymphomas are one of the least frequent types of indolent lymphomas to develop clinically apparent, secondary CNS spread. The presentation of an indolent follicular lymphoma with transformation to an aggressive diffuse large B-cell lymphoma within the brain parenchyma is rare. Its manifestation as a massive, singular lesion is unique and prompted diagnostic confusion.

Keywords: Indolent lymphoma; Follicular lymphoma; Diffuse large B-cell lymphoma; Secondary CNS involvement; Parenchymal CNS involvement

1. Introduction

The CNS is often involved with both primary and secondary lymphomas, but different types of lymphoma manifest considerably different patterns of disease that may variably mimic infections, metastatic carcinomas, leukoencephalopathies, or gliomas. Oncologists, internists, neuroradiologists, and pathologists need to be aware of these different patterns of CNS involvement to formulate appropriate differential diagnoses and treatment approaches. Systemic indolent lymphomas are the least frequent type of systemic lymphoma to involve the CNS. However, as indolent lymphomas are more successfully treated with evolving chemotherapeutic regimens and survival is prolonged, it is anticipated that increasing numbers of cases with secondary CNS spread will be seen, as this report illustrates.

2. Case report

A 53-year-old man was diagnosed with stage IV follicular lymphoma, grade 1, in 1996 (Fig. 1A-D) and initially treated with an unknown number of cycles of CVP

Abbreviations: CNS, central nervous system; CVP, cyclophosphamide, vincristine, prednisone; EBER, Epstein barr virus encoded RNA; EBV, Epstein barr virus; MRI, magnetic resonance imaging; PCNSL, primary central nervous system lymphoma; PCNSLs, primary central nervous system lymphomas; WHO, World Health Organization.

* Corresponding author. Denver, CO 80262, USA. Tel.: +1 303 315 7298; fax: +1 303 315 4792.

E-mail address: bk.demasters@uchsc.edu (B.K. Kleinschmidt-DeMasters).

0090-3019/$ – see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.surneu.2005.08.027

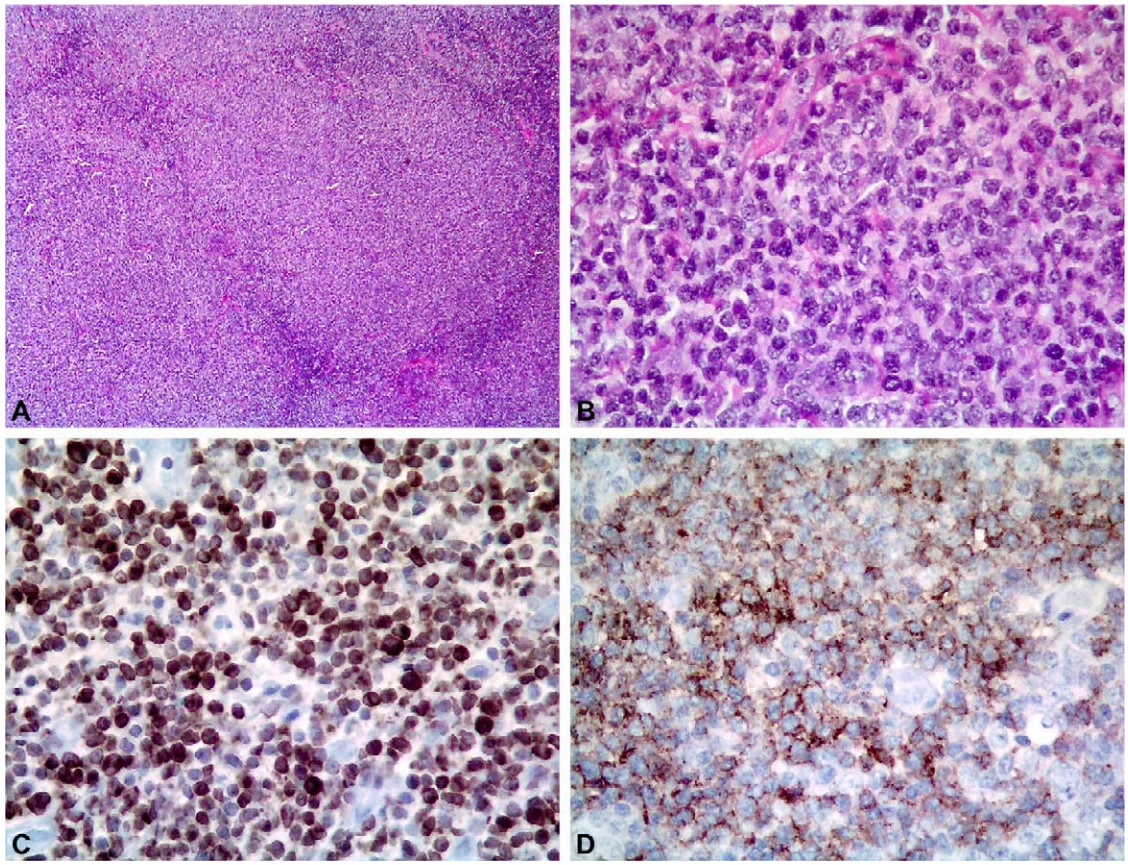

Fig. 1. Follicular lymphoma, grade 1, in a cervical lymph node removed in 1999. A: Histologically, there is complete nodal architectural effacement by numerous closely packed follicles (hematoxylin-eosin, magnification ×100). B: The neoplastic cleaved cells have clefted to angulated nuclei with clumped chromatin and inconspicuous nucleoli (hematoxylin-eosin, magnification ×400). C: Neoplastic lymphocytes show strong nuclear staining with Bcl-2 antibody (magnification ×400). D: In addition, there is strong staining of the neoplastic lymphocytes with CD10 antibody (magnification ×400).

chemotherapy. In October 1999, he presented to the University Hospital, Denver, Colo, with cervical lymphadenopathy. A cervical lymph node biopsy was performed that showed follicular lymphoma, grade 1. In September 2000, he developed symptomatic inguinal lymphadenopathy that caused lower extremity edema and paresthesias. He was treated with 4 cycles of CVP for each occurrence of lymphadenopathy, both in 1999 and 2000, with good response. In June 2003, he presented with spinal cord compression with disease at T2-T5 vertebra for which he was treated with emergent radiation therapy, one cycle of CVP and 6 cycles of rituximab, and cyclophosphamide, vincristine, adriamycin, and prednisone. In May 2004, a parieto-occipital lobe lesion was identified on MRI, which was treated with whole brain external beam radiation. The lesion regressed but did not disappear. In September 2004, a repeat MRI showed enlargement of the tumor within the parieto-occipital lobe, which now measured up to 4.0 cm in diameter (Fig. 2A). The lesion was surgically excised. Postoperative MRI scans additionally revealed a paraspinal mass at the T1 level, with epidural extension and extensive cervical and focal thoracic (T1) spine bony involvement. An MRI performed in December 2004 showed significant worsening of the patient's brain lesions. The patient's clinical condition has declined steadily since that time, with loss of the ability to read or complete sentences. He has also become increasingly somnolent and is currently receiving only palliative therapy and supportive care.

3. Pathological findings

Grossly, the specimen obtained from the occipital lobe consisted of a red-tan piece of tissue measuring 4.5 × 3.5 × 3.0 cm. Microscopy revealed a diffuse large B-cell lymphoma (Fig. 2B-D). The tumor was highly necrotic with sharp demarcation from the adjacent brain. Brisk mitotic activity was evident. The tumor was strongly and diffusely immunoreactive for CD10, CD20, Bcl-2, and Bcl-6, as is frequent in high-grade lymphomas of B-cell type. Immunostaining for CD3 was negative in tumor cells and in situ hybridization for EBV was negative. Flow cytometry showed the tumor to be positive for CD19, CD20, CD22, CD23, and CD10 and was λ light chain restricted. The immunohistochemistry and flow cytometry results supported the interpretation that the diffuse large B-cell lymphoma was not secondary to immunosuppression