

# Primary MALT Lymphoma of the Dura in a Patient With Active Scleroderma

Michael Miller, DO  
Vladimir Ioffe, MD  
W. Kirkland Ruffin, MD  
P. G. Shankar Giri, MD

Eastern Virginia Medical School  
Norfolk, Virginia

## Case Report

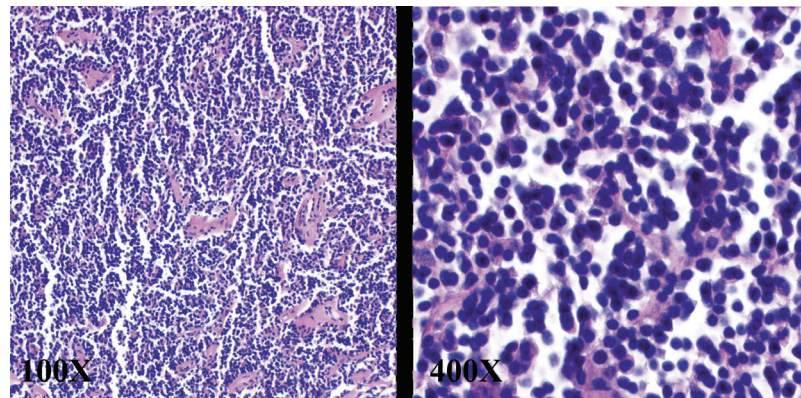
A 49-year-old woman presented to her family practitioner with a complaint of severe headaches for 3 months. She had a past medical history significant for active scleroderma. Initial workup consisted of a magnetic resonance imaging (MRI) scan of the brain that revealed a plaque like extra-axial mass lying against the left anterolateral frontal lobe. The mass also passed onto the floor of the anterior cranial fossa and measured 4 cm × 1 cm with a “dural tail.” With a preoperative diagnosis of meningioma, a partial resection was performed in which gross tumor remained on the floor of the anterior cranial fossa.

Histological examination revealed a dural-based mass with infiltration of the bone. Sheets of cells showed monocytoid, plasmacytic, and lymphoplasmacytic B-cell differentiation (Figure 1). Immunohistochemical analysis revealed the infiltrate was positive for CD20, CD10 (weakly positive), CD38, and *bcl-2*. The cells had a surface lambda light chain restriction. Computed tomography (CT) scans of the neck, chest, abdomen, and pelvis were negative for evidence of systemic lymphoma. Cerebrospinal fluid, obtained via a lumbar tap, was negative for malignancy. A positron emission tomography (PET) scan showed no abnormal uptake. The patient was treated postoperatively with 3,600 cGy (180 cGy/fraction) of whole-brain radiation therapy (WBRT) followed by a boost dose to the tumor bed of 900 cGy using 3-D conformal radiation therapy. The patient then received one cycle of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy but elected to discontinue this treatment due to toxicity. At last follow-up, 6 months after completion of radiation therapy, she was asymptomatic and reported no adverse effects from her treatment. An MRI scan of the head showed no evidence of disease.

## Discussion

Two comprehensive reviews showed that non-Hodgkin lymphoma (NHL) most commonly involves the central nervous system (CNS) secondary to dissemination from a non-CNS

**Address correspondence to:** Michael Miller, DO, Department of Radiation Oncology and Biophysics, 600 Gresham Drive, Norfolk, VA 23507-1999; E-mail: millerml@evms.edu.



**Figure 1.** Sheets of effaced small round darkly blue staining centrocyte-like cells (H&E stains).

primary. Secondary involvement of the CNS occurs in 5–9% of NHL and presents as either a leptomeningeal infiltrate or a parenchymal mass.<sup>1,2</sup> Such meningeal spread usually involves an aggressive histology lymphoma and is associated with a poor prognosis.

Primary CNS lymphoma (PCNSL) is a group of aggressive histology cell types that arise from and are confined to the CNS and account for 1.5% of all extranodal lymphomas. Isolated leptomeningeal involvement occurs in 7% of PCNSL and generally carries an unfavorable prognosis.<sup>3</sup> Although the treatment for PCNSL has improved in the last decade, according to a recent Radiation Therapy Oncology Group (RTOG) trial, the median overall survival is 36.9 months with aggressive chemotherapy and radiation.<sup>4</sup>

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) lymphoma was first described by Isaacson and Wright in 1983.<sup>5</sup> It is now recognized as a unique lymphoma with unique clinicopathologic features.<sup>6</sup> Gastric MALT lymphoma is the most common and the most studied, although it can arise in a wide variety of anatomical sites (gastrointestinal tract, lung, salivary glands, thyroid gland, thymus, breast, kidney, prostate, bladder, skin, conjunctiva, and other mucosal sites)<sup>7</sup>; however, it has rarely been reported to involve the dura mater.

The histological features of MALT lymphoma are similar regardless of the site of origin. The tumor cells are small to medium sized with moderately abundant cytoplasm and irregularly shaped nuclei, and they have been designated

**Table 1.** Dural-Based MALT Lymphoma Reported in the English Literature Since 1983

	Reference	Age	Sex	Presentation	Location	Pathology	Immunostain	Treatment and Follow-Up
1	Kumar S <sup>8</sup>	40	F	Numbness left lip & cheek with visual field defects	Right cavernous sinus	Small lymphocytes with plasmacytoid difference	CD20+, lambda light chain restriction	Partial excision/Bx, radiation, NED at 63 mo
2	Kumar S <sup>8</sup>	62	F	Seizures	Biparietal dura	Small lymphocytes with plasmacytoid difference	CD20+, lambda light chain restriction, VJ PCR+	Partial excision/Bx, systemic fludarabine, NED at 22 mo
3	Kumar S <sup>8</sup>	52	F	Seizures, numbness right hand	Left frontal dura	Infiltrate of marginal zone type cells, reactive follicles	CD20+, kappa light chain restriction, VJ PCR+	Partial excision/Bx, radiation, systemic AraC and methotrexate, intrathecal methotrexate; NED 7 mo
4	Kumar S <sup>8</sup>	43	F	Dizziness, headaches, blurring vision, facial numbness	Left tentorium	Infiltrate of marginal zone type cells, small lymphocytes, plasma cells	CD20+, lambda light chain restriction	Partial excision/Bx, radiation, NED at 9 mo
5	Kumar S <sup>8</sup>	57	F	Seizures	Left anterior falx cerebri	Small lymphocytes with plasmacytoid differentiation	CD20+, No light chain restriction, VJ PCR+	Partial excision/Bx, radiation, NED at 14 mo
6	Kambham N <sup>31</sup>	39	F	Hearing loss, pain, weakness	Left cerebellar pontine angle	Small centrocyte-like cells with focal prominent plasma cell differentiation, atrophic germinal centers	CD20+, CD79+, kappa light chain restriction	Partial excision, NED after 4 years
7	Kambham N <sup>31</sup>	62	F	Recent onset headaches	Left parieto-occipital area	Small monocytoid B cells, prominent reactive germinal centers	CD20+, CD79+, No light chain restriction	Biopsy, radiation, NED after 6 mo
8	Goetz P <sup>32</sup>	64	F	Left hemiparesis	Right frontoparietal dura	Lymphoid cells with plasmacytoid features	CD20+, kappa chain restriction	Partial excision, radiotherapy, NED at 3 mo
9	Itoh T <sup>14</sup>	28	F	Tinnitus, nausea, headache, bilateral papilledema	Left cerebellar pontine angle	Reactive lymphocytic infiltration with follicle formation with slightly atypical lymphocytes and plasmacytes with B-cell markers	CD20+, CD10+, no light chain restriction and <i>bcl-2</i> +	Gross total excision, NED at 2 years (Sjogren syndrome)
10	Lima VS <sup>33</sup>	36	F	Seizure, headache	Parietal convexity, posterior falx cerebri, right cerebellar tentorium	Lymphoid tissue with follicular and mantle zone hyperplasia	CD20+, kappa chain restriction	Partial excision/Bx, high-dose methotrexate & WBRT (outcome not stated)
11	Bodi I <sup>14</sup>	56	F	Dizziness, focal seizures, paresis	Right frontal lobe	Lymphoid infiltrates, centrocyte-like cells admixed with plasma cells and lymphoid follicles	CD20+, kappa chain restriction	Gross total excision, NED 18 mo
12	Lehman NL <sup>35</sup>	63	F	Focal sensory seizure, right-sided hearing loss, headaches	Supra- and infra-tentorial compartments involving the right occipital and superior cerebellar areas	Large amyloid deposits juxtaposed to dense cellular infiltrate mostly composed of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells infiltrating the dura	CD45+, CD20+, kappa chain restriction. Note: elevated ESR	Partial excision, WBRT, 36 Gy in 180 cGy fractions followed by 14.4 Gy boost using a 3-field arrangement; no progression 8 mo posttreatment
13	Sanjeevi A <sup>15</sup>	46	F	Left-sided headache, ophthalmalgia	Left cavernous sinus with mass extending into left orbital apex	Dense atypical lymphoplasmacytic infiltrate	L26+, kappa chain restriction, VJ PCR+	Partial excision and RT 45 Gy in 25 fractions (type of radiation not specified), NED 15 mo (Graves disease)
14	Altundag MK <sup>36</sup>	66	F	Syncope and seizures	Right parietal lobe	Diffuse dural infiltration with mononuclear cells composed of small lymphocytes, histiocytes, plasma cells, and immunoblasts	CD20+, L26+, light chain restriction not reported	Partial excision and WBRT 30 Gy then 20 Gy boost to primary site, NED 12 mo postsurgery
15	Freudenstein D <sup>37</sup>	50	F	Headache and seizures	Parafalcine and bilateral convexity lesion	Centrocytes and centroblasts with follicular growth pattern	CD20+, LCA+, no light chain restriction	Partial excision, MTX IV and IT, WBRT 45 Gy, cytosinaraiboside IV 2 cycles; NED 36 mo
16	(current)	49	F	Headache	Left frontal lobe	Sheets of neoplastic lymphoid cells with monocytoid, plasmacytic and lymphoplasmacytic B-cell differentiation	CD20+, CD10+, <i>bcl-2</i> +, lambda light chain restriction	Partial excision, WBRT (36 Gy), 3-D conformal boost (9 Gy), 1 cycle CHOP; NED 6 mo

RT=radiation therapy; WBRT=whole-brain RT; IT=intrathecal; IV=intravenous; MTX=methotrexate; Bx=biopsy; NED=no evidence of disease; VJ PCR=light chain polymerase chain reaction; ESR=erythrocyte sedimentation rate.

centrocyte-like cells. In gastric MALT lymphomas the key feature is the presence of lymphoepithelial lesions that can be described as an invasion and destruction of the gastric glands by aggregates of centrocyte-like cells.<sup>7</sup> It has been hypothesized that for dural-based MALT lymphomas the meningeothelial cells are analogous to epithelia. Meningeothelial cells are present throughout the arachnoid membrane and are concentrated in the arachnoid villi within the dural venous sinuses. In fact, nests of meningeothelial cells entrapped in a lymphoid infiltrate have been described for dural-based MALT lymphoma purporting an analogy to the lymphoepithelial lesions at other sites.<sup>8</sup> The histological features can range from small lymphocytic to plasmacytoid to marginal zone type cells.<sup>8</sup>

Immunohistochemical staining is used to help differentiate MALT lymphoma from other low-grade lymphomatous processes with similar histology. These entities include small lymphocytic lymphoma (SLL), chronic lymphocytic leukemia (CLL), and lymphoplasmacytoid lymphoma (LPL). SLL and CLL are CD23-positive and usually Leu 22-positive.<sup>9</sup> Although LPL can be CD23-negative and display variable Leu 22 expression, clinical correlation generally allows differentiation. SLL, CLL, and LPL are systemic processes and generally display bone marrow, peripheral blood, and lymph node involvement. Additionally, a monoclonal immunoglobulin spike is usually present in the serum of LPL patients.<sup>8</sup> MALT lymphomas present with localized extranodal disease and lack of systemic involvement, and are more common in women. In fact, for dural-based MALT lymphoma, no male patient has ever been reported in the English literature since 1983. MALT lymphomas are immunohistochemically characterized by the expression of the B-cell antigens CD19, CD20, CD22, and CD79a.

Since the description of MALT lymphoma as a unique clinicopathologic entity in 1983, there have been isolated reports in the medical literature describing MALT lymphoma originating in and confined to the dura. Table 1 summarizes the reports that were identified by searching PubMed using the words, "primary lymphoma of dura." Kumar et al<sup>8</sup> state that other cases in the literature may represent dural-based MALT lymphoma but were classified as solitary meningeal plasmacytomas, SLL, or leptomeningeal Castleman's disease prior to 1983.

On neuroimaging, all cases demonstrated well defined, localized, intracranial dural-based masses that were deemed either meningioma or subdural hematoma preoperatively. All patients were female and presented with focal neurological symptoms such as seizures, visual field defects, headaches, or hemiparesis.

The current case represents the only published report of a dural-based MALT lymphoma in a patient with active scleroderma. Scleroderma is a diffuse connective tissue disease causing fibrosis of the skin, lungs, gastrointestinal tract, and other visceral organs. Evidence exists in the medical literature indicating that scleroderma increases the risk for developing NHL.<sup>10-13</sup> An epidemiological study from Sweden of 233 patients with scleroderma found a standardized incidence ratio of 9.6 (analogous to relative risk) for the development of NHL.<sup>12</sup>

There are 2 other cases in the medical literature of dural-based MALT lymphoma (Table 1) associated with autoimmune disease. Itoh et al<sup>14</sup> reported a patient with Sjögren syndrome, in which the risk of developing a B-cell lymphoma is increased by a factor of 44. Sanjeevi et al<sup>15</sup> reported a patient with dural-based MALT lymphoma in the region of the cavernous sinus in the setting of Graves disease. Another example of the immunologic role in the development of lymphoma is Hashimoto thyroiditis, which is associated with a relative risk of 67 for developing thyroid lymphoma.<sup>16</sup>

Gastric lymphoma is the most well studied model demonstrating an autoimmune role in the development of low-grade lymphoma. Hessel et al<sup>17</sup> have demonstrated that *Helicobacter pylori* antigens induce the growth of gastric MALT lymphoma. Eradication of *H pylori* was shown to result in tumor regression.<sup>18</sup> Harttunen has suggested that *H pylori* stimulates T cells, which in turn release cytokines that aid in B-cell growth.<sup>19</sup> It is currently believed that MALT lymphoma is acquired through the neoplastic transformation of such reactive lymphocytic clones.<sup>7</sup> We propose that autoimmune disease is a significant risk factor in the development of MALT lymphoma and, as suggested by others, may play a role in the etiology of malignant lymphoma.<sup>20,21</sup>

Table 2 summarizes the treatment modalities used in the 16 cases reported since 1983. Fifty percent of patients were treated with a partial excision or biopsy followed by radiation therapy. Most reports did not specify how the radia-

**Table 2.** Summary of Treatment Modalities and Results

	Complete Excision	Partial Excision/Bx	Partial Excision/Bx + RT	Partial Excision/Bx + Chemotherapy	Partial Excision/Bx + Chemo-RT
Number of cases	2 (12%)	1 (6%)	8 (50%)	1 (6%)	4 (25%)
Crude survival, mo*	18, 24	48	3, 6, 8, 9, 12, 14, 15, 63	22	6, 7, 36, 1 unknown

\*Crude survival reported as of publication of report. No treatment failures reported as of the time of publication for any report.

Bx=biopsy; RT=radiotherapy.

tion was delivered, but from the information available it appears that WBRT was given to a range of 30–36 Gy followed by a cone down to the area of gross disease via 3-D conformal techniques to a final dose in the range of 45–50 Gy. Such regimens appear to successfully control the disease with follow-up extending 63 months. Four patients (25%) were treated with partial excision or biopsy followed by a combination of radiation and chemotherapy. These treatments were based on the DeAngelis protocol for PCNSL or some variation thereof.<sup>4</sup> The current patient received 1 cycle of CHOP chemotherapy after radiation therapy because of the high volume of residual postsurgical disease. As described in Table 2, disease control has been reported up to 36 months with such regimens. Interestingly, none of the 16 patients failed their respective treatment at the time of reporting. This includes those who received complete or partial excision without adjuvant therapy. This is consistent with the notion that MALT lymphoma is a slow growing, indolent malignancy that responds well to a single local treatment modality.

Primary radiotherapy (RT) is considered by most to be the standard treatment for localized stage IE MALT lymphoma.<sup>22,23</sup> Excellent local control of MALT lymphoma has been reported with involved field radiation therapy alone. Tsang et al reported a crude local control rate of 95.3% with a median follow-up time of 5.1 years for 85 patients with MALT lymphoma of various extranodal sites. The overall 5-year survival rate was 98%, and the disease-free survival rate was 77%, with a median dose of 30 Gy.<sup>24</sup> In the treatment of localized orbital MALT lymphoma, 100% local control rates have been achieved in several series with doses in the range of 30 Gy.<sup>25-27</sup> Additionally, a small randomized study of 39 patients with MALT lymphoma of the salivary glands showed no advantage to combined modality over RT alone with OS and freedom from progression of 90% in both groups.<sup>22</sup> How these doses and control rates translate to dural-based MALT lymphoma is not clear.

Our recommendation for the treatment of dural-based MALT lymphoma is complete excision if it involves a neurosurgical procedure with acceptable morbidity. Otherwise, partial excision and/or biopsy with adjuvant radiation therapy to the whole brain (30–36 Gy) followed by a local boost field (total dose 45–50 Gy) is a reasonable alternative.

WBRT in the dose range of 30–36 Gy delivered in fractions of at least 300 cGy has been associated with significant long-term neurological toxicity, such as progressive dementia, ataxia, and urinary incontinence.<sup>28</sup> Avoiding this toxicity in patients with MALT lymphoma, many of whom are expected to survive for many years, by delivering treatment at a dose per fraction of greater than 300 cGy would clearly benefit their quality of life.<sup>28</sup>

The ideal way to minimize toxicity would be to omit WBRT and deliver therapeutic doses of radiation via partial brain irradiation. Unfortunately, although intellectually appeal-

ing as excellent disease control has been achieved with surgical resection alone, such an experimental approach has never been tested.

A paucity of information is available for the treatment of localized MALT lymphoma with chemotherapy alone. Hammel et al<sup>29</sup> reported treating 24 consecutive patients with localized gastric MALT lymphoma with 12–24 months of an oral alkylating agent (cyclophosphamide or chlorambucil [Leukeran, GlaxoSmithKline]). Eighteen patients (75%) had a complete response, although 5 of those relapsed with a median follow-up of 45 months. A recent phase II study was completed examining the clinical activity of rituximab in extranodal MALT lymphoma.<sup>30</sup> The overall response rate was 73% with 15 complete responses (CR) and 10 partial responses (PR) out of 35 patients. The response rate was 87% in chemotherapy-naïve patients. The median response duration was 10.5 months, and most adverse events were of mild to moderate severity with no grade 4 toxicity. Future studies of the role of rituximab and other chemotherapeutic agents in the treatment of CNS lymphoma are needed.

It must be cautioned that the preceding recommendations are based on a very small number of patients and should not supercede individualized patient management decisions based on the clinical and anatomical features of each case. We need further reports and longer follow-up information on this rare entity so that we may further elucidate the optimal treatment for extralymphatic MALT lymphoma of the dura.

## Conclusion

It is critical to differentiate primary dural-based MALT lymphoma from PCNSL or other extralymphatic low-grade lymphomas in order to avoid exposing patients to unnecessary therapy. Although additional cases and further follow-up are necessary, we contend that single-modality treatment of dural-based MALT lymphoma may be appropriate.

## References

1. Law IP, Dick FR, Blom J, Bergevin PR. Involvement of the central nervous system in non-Hodgkin's lymphoma. *Cancer*. 1975;36:225-231.
2. Herman TS, Hammond N, Jones SE, Butler JJ, Byrne GE, McKelvey EM. Involvement of the central nervous system by non-Hodgkin's lymphoma: the Southwest Oncology Group Experience. *Cancer*. 1979;43:390-397.
3. Lachance DH, O'Neill BP, Macdonald DR, et al. Primary leptomeningeal lymphoma: report of 9 cases, diagnosis with immunocytochemical analysis, and review of the literature. *Neurology*. 1991;41:95-100.
4. DeAngelis LM, Seiferheld W, Schold SC, Fisher B, Schultz CJ. Combination chemotherapy and radiotherapy for primary central nervous system lymphoma: Radiation Therapy Oncology Group Study 93-10. *J Clin Oncol*. 2002;20:4643-4648.
5. Isaacson P, Wright DH. Malignant lymphoma of mucosa-associated lymphoid tissue: a distinctive type of B-cell lymphoma. *Cancer*. 1983;52:1410-1416.
6. Harris NL, Jaffe ES, Diebold J, et al. World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee Meeting-Airlie House, Virginia, November 1997. *J Clin Oncol*. 1999;17:3835-3849.
7. Zucca E, Roggero E. Biology and treatment of MALT lymphoma: the

- state-of-the-art in 1996. A workshop at the 6th International Conference on Malignant Lymphoma. *Ann Oncol.* 1996;7:787-792.
8. Kumar S, Kumar D, Kaldjian EP, Bauserman S, Raffeld M, Jaffe ES. Primary low-grade B-cell lymphoma of the dura: a mucosa associated lymphoid tissue-type lymphoma. *Am J Surg Pathol.* 1997;21:81-87.
  9. Zuckerberg LR, Medeiros LJ, Ferry JA, Harris NL. Diffuse low-grade B-cell lymphomas. Four clinically distinct subtypes defined by a combination of morphologic and immunophenotypic features. *Am J Surg Pathol.* 1993;100:373-385.
  10. Varoczy L, Gergely L, Zeher M, Szegedi G, Illes A. Malignant lymphoma-associated autoimmune diseases—a descriptive epidemiological study. *Rheumatol Int.* 2002;22:233-237.
  11. Duncan SC, Winkelmann RK. Cancer and scleroderma. *Arch Dermatol.* 1979;115:950-955.
  12. Rosenthal AK, McLaughlin JK, Linet MS, Persson I. Scleroderma and malignancy: an epidemiological study. *Ann Rheum Dis.* 1993;52:531-533.
  13. Roumm AD, Medsger TA Jr. Cancer and systemic sclerosis. An epidemiologic study. *Arthritis Rheum.* 1985;28:1336-1340.
  14. Itoh T, Shimizu M, Kitami K, et al. Primary extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue type in the CNS. *Neuropathology.* 2001;21:174-180.
  15. Sanjeevi A, Krishnan J, Bailey PR, Catlett J. Extranodal marginal zone B-cell lymphoma of malt type involving the cavernous sinus. *Leuk Lymphoma.* 2001;42:1133-1137.
  16. Holm L-E, Blomgren H, Lowhagen T. Cancer risks in patients with chronic lymphocytic thyroiditis. *N Engl J Med.* 1985;312:601-604.
  17. Hussell T, Isaacson PG, Crabtree JE, Spencer J. The response of cells from low-grade B-cell gastric lymphomas of mucosa-associated lymphoid tissue to *Helicobacter pylori*. *Lancet.* 1993;342:571-574.
  18. Wotherspoon AC, Dogliani C, Diss TC, et al. Regression of primary low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of *Helicobacter pylori*. *Lancet.* 1993;342:575-577.
  19. Harttunen R. Blood lymphocyte proliferation, cytokine secretion, and appearance of T-cells with activation surface markers in cultures with *Helicobacter pylori*. *Clin Exp Immunol.* 1991;83:396-400.
  20. Isaacson PG, Spencer J. Malignant lymphoma and autoimmune disease. *Histopathology.* 1993;22:509-510.
  21. Amft N, Bowman SJ. Chemokines and cell trafficking in Sjogren's syndrome. *Scand J Immunol.* 2001;54:62-69.
  22. Yahalom J. MALT lymphomas: a radiation oncology viewpoint. *Ann Hematol.* 2001;80(suppl 3):B100-B105.
  23. Malek SN, Hatfield AJ, Flinn IW. MALT lymphomas. *Curr Treat Options Oncol.* 2003;4:269-279.
  24. Tsang RW, Gospodarowicz MK, Pintilie M, et al. Localized mucosa-associated lymphoid tissue lymphoma treated with radiation therapy has excellent clinical outcome. *J Clin Oncol.* 2003;21:4157-4164.
  25. Jakobiec FA, Iwamoto T, Patell M, Knowles DM 2nd. Ocular adnexal monoclonal lymphoid tumors with a favorable prognosis. *Ophthalmology.* 1986;93:1547-1557.
  26. Hardman-Lea S, Kerr-Muir M, Wotherspoon AC, Green WT, Morell A, Isaacson PG. Mucosal-associated lymphoid tissue lymphoma of the conjunctiva. *Arch Ophthalmol.* 1994;112:1207-1212.
  27. Le QT, Eulau SM, George TI, et al. Primary radiotherapy for localized orbital MALT lymphoma. *Int J Radiat Oncol Biol Phys.* 2002;52:657-663.
  28. DeAngelis LM, Delattre JY, Posner JB. Radiation-induced dementia in patients cured of brain metastases. *Neurology.* 1989;39:789-796.
  29. Hammel P, Haioun C, Chaumette MT, et al. Efficacy of single-agent chemotherapy in low-grade B-cell mucosa-associated lymphoid tissue lymphoma with prominent gastric expression. *J Clin Oncol.* 1995;13:2524-2529.
  30. Conconi A, Martinelli G, Thieblemont C, et al. Clinical activity of rituximab in extranodal marginal zone B-cell lymphoma of MALT type. *Blood.* 2003;102:2741-2745.
  31. Kambham N, Chang Y, Matsushima AY. Primary low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) arising in dura. *Clin Neuropathol.* 1998;17:311-317.
  32. Goetz P, Lafuente J, Revesz T, Galloway M, Dogan A, Kitchen N. Primary low-grade B-cell lymphoma of mucosa-associated lymphoid tissue of the dura mimicking the presentation of an acute subdural hematoma. *J Neurosurg.* 2002;96:611-614.
  33. Lima VS, Leite EB, Fonseca RP, Fernandes ASJ. Diagnosis in oncology: patients presenting with CNS lesions. Case 1. Primary low-grade mucosa-associated B-cell lymphoma of the dura. *J Clin Oncol.* 2003;21:4058-4060.
  34. Bodi I, Hussain A, Gullan RW, Safa AS. January 2003: 56-year-old female with right frontal tumor of the dura. *Brain Pathol.* 2003;13:417-418.
  35. Lehman NL, Horoupian DS, Warnke RA, Sundram UN, Peterson K, Harsh GRI. Dural marginal zone lymphoma with massive amyloid deposition: rare low-grade primary central nervous system B-cell lymphoma. *J Neurosurg.* 2002;96:368-372.
  36. Altundag MK, Ozisik Y, Yalcin S, Akyol F, Uner A. Primary low grade B-cell lymphoma of the dura in an immunocompetent patient. *J Exp Clin Cancer Res.* 2000;19:249-251.
  37. Freudenstein D, Bornemann A, Ernemann U, Boldt R, Duffner F. Intracranial malignant B-cell lymphoma of the dura. *Clin Neuropathol.* 2000;19:34-37.

# Review

**Carol S. Portlock, MD**

*Memorial Sloan-Kettering Cancer Center*

In considering the literature of primary dural marginal zone lymphoma (MZL), we must address the clinical case, staging evaluation, and recommended treatment. These raise several questions:

**Does the patient have an isolated extranodal MZL?** Without a bone marrow evaluation and serum protein electrophoresis, one cannot be certain. The pathologic description may be consistent with MZL, but the finding of a weakly positive CD10 immunostain suggests a possible follicular center cell lymphoma. Dural extension of bone marrow lymphoma is not uncommon in indolent lymphoma, whereas primary dural involvement is rare, and meningeal disease is very rare in these histologies.

**Does stage matter?** Yes—if it is stage IV in this location, one would be more likely to recommend systemic therapy alone (such as rituximab [Rituxan, Genentech] plus chemotherapy—CVP [cyclophosphamide, vincristine, prednisone] or fludarabine) rather than radiotherapy to this potentially morbid site.

**What is the required dose of radiation?** As the authors discuss, primary radiotherapy for gastric MZL is now well accepted. Its therapeutic intent is local control and, possibly, “cure.” But in indolent lymphoma, late relapse in other sites many years later is not uncommon. The dose required for local control is not certain, but generally no more than 3,000–3,600 cGy to the mass is needed. The whole brain field may not be needed at all, and 1,800–2,400 cGy would be considered adequate (used for extensive dural deposits).

**Is any systemic or intrathecal chemotherapy warranted as an adjunct to primary radiotherapy (if primary dural lymphoma is suspected)?** Neither is probably required, although the data are scanty, as emphasized by the authors. Systemic therapy is not needed for local control, and meningeal involvement would not be expected as a site of relapse.

**How does the history of autoimmune disease influence treatment?** There is growing data that rituximab is an effective therapy for rheumatoid arthritis. If this patient required systemic treatment for her B-cell lymphoma, rituximab would be recommended as a component (see above). This pan-B-cell antibody therapy might have a salutary effect on her autoimmune disorder, although this has not been reported.

Of greater concern is the possible late effect of radiotherapy in the setting of scleroderma.<sup>1</sup> In a 49-year-old patient with anticipated long survival, late fibrosis within the radiation portal might produce significant morbidity in this site.

On the other hand, is it possible that the scleroderma is a paraneoplastic phenomenon and that with successful lymphoma treatment it will remit (as may happen with some other autoimmune disorders)?<sup>2,3</sup>

**Finally, what role does surgery play in this case?** The authors rightly emphasize the diagnostic nature of the neurosurgical procedure. With such a radiosensitive tumor, debulking surgery is not indicated. In the more common presentation of gastric MALT, surgery has been entirely abandoned in favor of endoscopic biopsy and primary irradiation (if *H pylori* antibiotic therapy is unsuccessful).

This report provides very brief follow-up (6 months) in an indolent disease presentation. Many years of follow-up will be required to determine the efficacy of the treatment employed and its potential late effects.

## References

1. Phan C, Mindrum M, Silverman C, Paris K, Spanos W. Matched-control retrospective study of the acute and late complications in patients with collagen vascular diseases treated with radiation therapy. *Cancer J*. 2003;9:461-466.
2. Prochorec-Sobieszek M, Mielnik P, Wagner T, Chwalinska-Sadowska H. Mucosa-associated lymphoid tissue lymphoma (MALT) of salivary glands and scleroderma: a case report. *Clin Rheumatol*. 2004;23:348-350.
3. Varoczy L, Gergely L, Zeher M, Szegedi G, Illes A. Malignant lymphoma-associated autoimmune diseases—a descriptive epidemiological study. *Rheumatol Int*. 2002;22:233-237.

**Address correspondence to:** Carol S. Portlock, MD, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021; E-mail: portlocc@mskcc.org.