

# Primary low-grade B-cell lymphoma of mucosa-associated lymphoid tissue of the dura mimicking the presentation of an acute subdural hematoma

## Case report and review of the literature

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✓ The authors present the case of a 64-year-old woman who experienced a left hemiparesis. An initial diagnosis of subdural hematoma was made based on results of computerized tomography scanning. Subsequent magnetic resonance imaging indicated an extraaxial meningioma. Histological findings confirmed an extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT). The authors outline the natural history of central nervous system lymphomas and of MALT lymphomas in other tissues. They review seven previously reported cases and emphasize the importance of recognizing these tumors as a distinct clinicopathological entity.

**KEY WORDS** • mucosa-associated lymphoid tissue lymphoma • acute subdural hematoma • meningioma

ISAACSON and Wright<sup>14</sup> first identified MALT-type lymphomas, which are B-cell neoplasms, in the gastrointestinal tract. These tumors have subsequently been described in a variety of other sites, including mucosal extranodal and nonmucosal locations. These other sites include breast,<sup>25</sup> conjunctiva,<sup>34</sup> genitourinary tract,<sup>29</sup> liver,<sup>15</sup> lung,<sup>1</sup> salivary glands,<sup>13</sup> and thyroid.<sup>2</sup> We present the case of a woman in whom SDH was initially diagnosed, in whom a MALT-type lymphoma was later identified. We also discuss the seven other cases that have been reported to date.<sup>19,20</sup>

**History and Examination.** This 64-year-old Nigerian woman presented to the emergency department with a history of headache and sudden onset of left-sided weakness. She had a history of systemic hypertension and had recently completed a course of warfarin for postoperative pulmonary embolism following a total hip replacement. Neurological examination revealed a Grade 3/5 left hemiparesis. An up-going left plantar reflex was identified, but the remainder of the results of the examination were normal. Results of routine laboratory tests were normal, including prothrombin time. A CT study demonstrated a right frontoparietal mass identified as an SDH (Fig. 1 *left*). A small incidental meningioma was noted in the left frontal region.

*Abbreviations used in this paper:* CNS = central nervous system; CT = computerized tomography; MALT = mucosa-associated lymphoid tissue; MR = magnetic resonance; SDH = subdural hematoma.

**Initial Treatment and Response.** Initial treatment included low-dose oral dexamethasone. Over the next 48 hours the patient made a complete neurological recovery and a follow-up CT scan demonstrated resolution of the hematoma. She was discharged home with no dexamethasone, but was readmitted 4 days later with similar, recurrent neurological symptoms. On MR imaging a large enhancing extraaxial meningeal based lesion appearing in the right frontoparietal region was identified as a meningioma (Fig. 2).

**Operation and Immunohistological Studies.** The patient underwent a right frontoparietal craniotomy and excision of a meningeal based tumor. The mass was firmly attached to the dura of the convexity as well as to the cortical surface. An intraoperative frozen tissue section demonstrated an infiltration of the dura by plasma cells and by numerous small lymphoid cells, many of which had plasmacytoid features. The infiltrate exhibited focal nodularity. The differential diagnosis based on the frozen section included a plasma cell-rich meningioma, plasma cell granuloma, or lymphoma. Analysis of paraffin sections confirmed these findings (Fig. 3). Immunophenotyping of the lymphoid cells showed a mixture of immunoglobulin D–positive, CD20-positive small lymphocytes; immunoglobulin D–negative, CD20-positive lymphoplasmacytoid cells; and CD20-negative, CD138-positive plasma cells. Lymphoplasmacytoid cells and plasma cells demonstrated kappa light chain restriction, whereas small lymphocytes were polytypic, indicating that they were residual mantle cells. Staining for lymphocytic markers CD5, CD23, cyclin D1, MNF116 (an epithelial

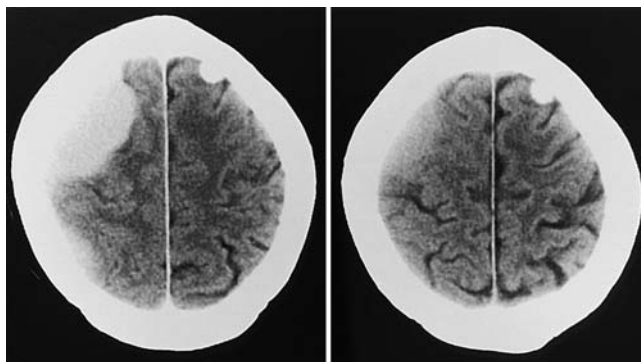


FIG. 1. Admission CT scan (*left*) demonstrating a right frontoparietal SDH. Follow-up CT scan (*right*) obtained 6 days later demonstrating resolution of the SDH after dexamethasone treatment.

marker), epithelial membrane antigen (a meningotheelial marker), and synaptophysin (a neuroendocrine marker) was negative. The proliferation fraction, which was assessed using Ki-67 immunocytochemistry, was 6.9%.

The appearance of this tumor is that of a lymphoid neoplasm. The majority of intracranial lymphoid neoplasms are diffuse large B-cell lymphomas, which are high-grade lesions. In our case there is immunocytochemical evidence of B-cell and plasma cell differentiation; however, the low proliferation fraction and the cellular morphological features indicate a low-grade neoplasm. In the context of an extranodal presentation, the histological features and immunophenotype are those of an extranodal marginal zone lymphoma of the MALT type, according to the new World Health Organization classification.<sup>9</sup>

**Postoperative Course.** There was no clinical, laboratory, or radiological evidence of systemic lymphoma. The patient was discharged after having made a full recovery, underwent whole-brain radiation therapy as an outpatient, and is free of symptoms.

### Discussion

In 5 to 9% of non-Hodgkin lymphomas, CNS involvement occurs in the form of leptomeningeal infiltrates or parenchymal masses. Such involvement is typically the result of secondary spread from disseminated Grade IV disease and has a poor prognosis.<sup>7,10,22</sup>

Primary CNS non-Hodgkin lymphoma is even less common, representing 0.1 to 1%.<sup>26,28</sup> It usually presents as large single or multiple masses in the hemispheric white or deep gray matter. Although infiltration into adjacent meninges is occasionally seen, exclusively meningeal involvement is exceedingly rare.

One variant is primary leptomeningeal lymphomas. Lachance, et al.,<sup>21</sup> estimated that such lesions represent 7.6% of all primary CNS lymphomas. The majority are high grade and of the B-cell type, although T-cell lymphomas have been described.<sup>8</sup> The clinical presentation is variable and includes headache, meningismus, ataxia, cranial nerve palsy, and progressive paraparesis.<sup>11</sup> The clinical course is usually rapid, with systemic symptoms occurring very shortly after the initial clinical presentation.

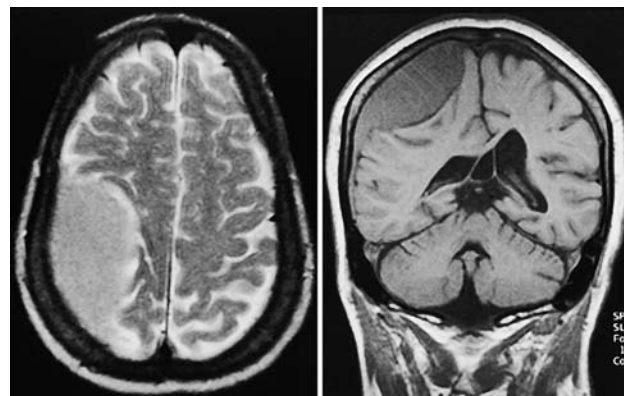


FIG. 2. Axial T<sub>2</sub>-weighted (*left*) and coronal T<sub>1</sub>-weighted (*right*) MR images demonstrating a right frontoparietal convexity MALT lymphoma.

The MALT-type lymphomas are B-cell neoplasms that were first identified in the gastrointestinal tract by Isaacson and Wright<sup>14</sup> in 1983. Since then, these tumors have been described in a variety of nongastrointestinal mucosal extranodal as well as nonmucosal sites. These include breast,<sup>25</sup> conjunctiva,<sup>34</sup> genitourinary tract,<sup>29</sup> liver,<sup>15</sup> lung,<sup>1</sup> salivary glands,<sup>13</sup> skin,<sup>3</sup> and thyroid.<sup>2</sup> As shown in Table 1, seven cases of localized intracranial dura-based low-grade B-cell MALT lymphomas have been reported in the literature to date.<sup>19,20</sup>

All seven patients were middle-aged women (range 40–62 years, average age 51 years) who presented with focal neurological symptoms requiring further investigation. Seizures were the presenting symptoms in three cases; one patient had visual field defects; two had worsening headaches; one had hearing loss; our patient had hemiparesis. Only one patient (Case 2) had a preexisting neurological disorder; this woman had a 40-year history of seizures, which were therefore deemed unrelated to the lymphoma. Neuroimaging (CT and MR studies) demonstrated well-defined, localized, intracranial dura-based masses mimicking meningiomas or SDH in each case, with lesions confined to the right cavernous sinus, biparietal, left frontal, left tentorial, left falx, left cerebellopontine angle, and left parietooccipital regions. Our patient had a right frontoparietal lesion. The preoperative diagnosis was meningioma in all cases. There was no long-term evidence of recurrence or dissemination.

The diagnosis was confirmed by histological and immunophenotyping results. Kumar, et al.,<sup>20</sup> suggest that several other previously reported cases of meningeal plasmacytomas and lymphomas may in fact have been MALT tumor subtypes.<sup>5,18,23,24,27,30,31,33</sup> They propose that meningotheelial cells are analogous to epithelia at other sites where MALT lymphomas arise. These cells are present throughout the arachnoid membrane, but are concentrated in the arachnoid villi within the dural venous sinuses.<sup>6</sup> Interestingly, the cases reported are all localized to regions where these cells tend to be relatively numerous, sites which for the same reason are common locations for meningiomas.<sup>4</sup> Isaacson and Spencer<sup>17</sup> propose that individuals with chronic autoimmune disorders such as Hashimoto thyroiditis may be at higher risk of developing MALT lymphomas. Hussel, et al.,<sup>12</sup> and Isaacson and Spencer<sup>16</sup> assert that there is a rela-

## Primary low-grade B-cell lymphoma of MALT

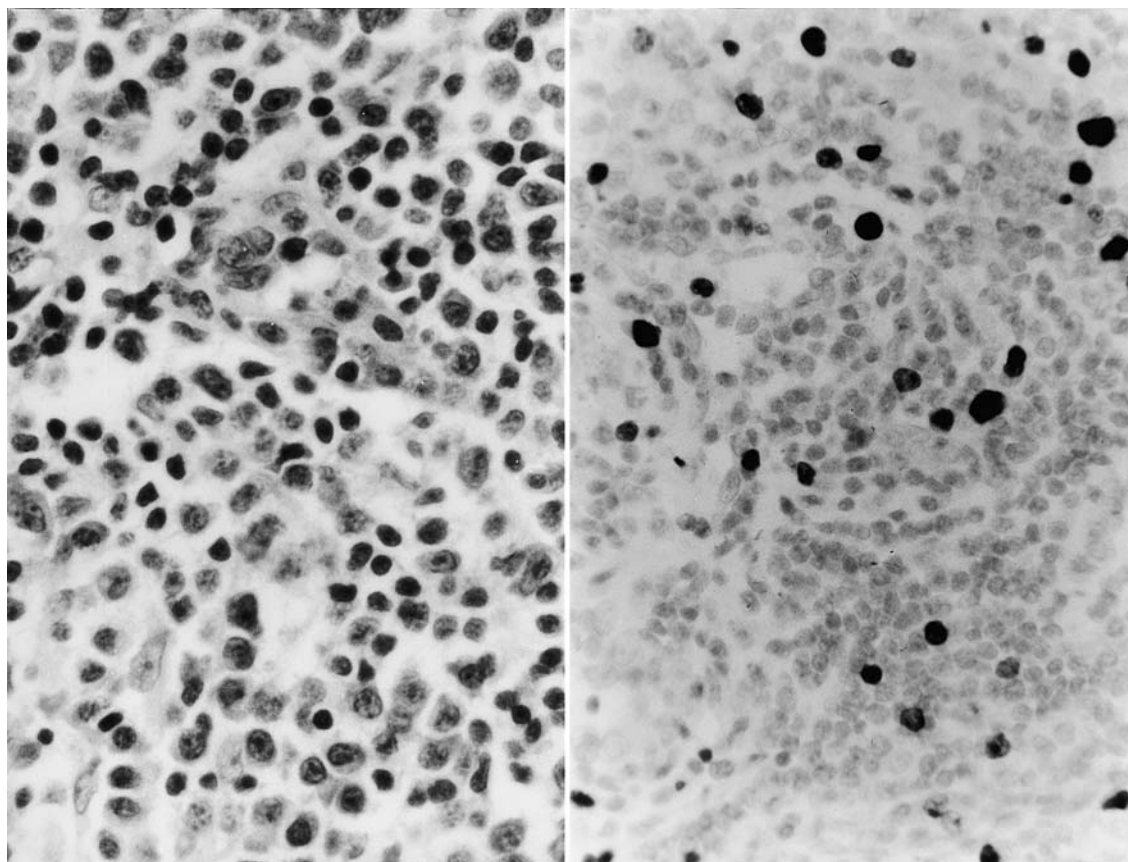


FIG. 3. *Left:* High-power photomicrograph of the tumor showing infiltration by neoplastic lymphoid cells, many of which exhibit plasmacytoid features. H & E, original magnification  $\times 63$ . *Right:* Immunohistochemical preparation demonstrating the relatively low Ki-67 index. Nuclei of cells in the cell cycle are stained brown. Original magnification  $\times 40$ .

tionship between MALT lymphomas and localized chronic inflammatory conditions such as *Helicobacter pylori*-associated chronic active gastritis. No patient with dural MALT lymphomas had any recognizable predisposing condition, and local contributory factors remain unknown.

Limited studies of the treatment of extranodal MALT

lymphoma have shown favorable response to minimally aggressive therapy.<sup>32,35</sup> The MALT lymphomas in the dura are biologically indolent and have been treated with partial excision, radiation, and systemic chemotherapy.<sup>19,20</sup> They typically present with localized disease and can therefore be cured with local therapy.

TABLE 1  
*Literature review of primary low-grade B-cell dura-based lymphomas\**

Authors & Year	Patient Age (yrs), Sex	Presenting Symptoms	Tumor Location	Therapy	Outcome
Kumar, et al., 1987 <sup>†</sup>	40, F	focal numbness, visual field defect	rt cavernous sinus	radiation	NED at 63 mos
	62, F	seizures	biparietal dura	systemic chemo (fludarabine)	NED at 22 mos
	52, F	seizures, focal numbness	lt frontal dura	radiation & chemo	NED at 7 mos
	43, F	dizziness, headache, blurred vision	lt tentorium	radiation	NED at 9 mos
Kambham, et al., 1998	57, F	seizures	lt anterior falx cerebri	radiation	NED at 14 mos
	39, F	hearing loss, pain, weakness	lt cerebellopontine angle	subtotal excision	A & W after 4 yrs
	62, F	recent-onset headache	lt parietooccipital dura	radiation	A & W after 6 mos
present study	64, F	lt hemiparesis	rt frontoparietal dura	subtotal excision & radiotherapy	NED at 3 mos

\* A & W = alive and well; chemo = chemotherapy; NED = no evidence of disease.

<sup>†</sup> As documented by Kumar, et al., there are numerous previously reported cases not included in this table that most likely represent dural MALT lymphomas.

## Conclusions

Despite the small number of patients diagnosed and in whom follow up was available, the clinicopathological findings in these cases of intracranial dura-based low-grade B-cell MALT-type lymphomas support the notion that these tumors are the same neoplasms as those in other commonly occurring mucosa-associated sites. They display indolent behavior and bear a good prognosis. This contrasts with the aggressive behavior of primary CNS lymphomas and those where meningeal involvement occurs as part of secondary dissemination, and underlines the importance of recognizing these as a distinct clinicopathological entity.

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