Dural marginal zone lymphoma with massive amyloid deposition: rare low-grade primary central nervous system B-cell lymphoma

Case report

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The authors report the case of a 63-year-old woman who presented with a primary dural extranodal marginal zone lymphoma (MZL) associated with massive kappa light chain amyloidosis of the meninges. Extranodal MZL is a low-grade B-cell lymphoma that may show variable degrees of plasmacytic differentiation. Like solitary plasmacytoma of soft tissue, which can also be associated with amyloid, extranodal MZL generally responds well to local therapy and has a good prognosis. It is important to distinguish these entities from high-grade primary central nervous system (CNS) B-cell lymphomas and more aggressive and/or widespread, potentially amyloidogenic conditions such as multiple myeloma, lymphoplasmacytoid lymphoma, and chronic lymphocytic leukemia/small lymphocytic lymphoma. To the authors' knowledge this is the first reported case of dural MZL associated with massive meningeal amyloid deposition. Extranodal MZL is a rare low-grade primary CNS B-cell lymphoma that may be associated with amyloidosis. It should be considered in the differential diagnosis of CNS lymphoproliferative lesions and CNS amyloidosis.

KEY WORDS • B-cell lymphoma • amyloidosis • dural tumor

EXTRANODAL MZL is a low-grade B-cell lymphoma that occurs most often in the gastrointestinal tract, where it is referred to as a “MALT (mucosa-associated lymphoid tissue) lymphoma” or “MALToma.” It also has been found in various other sites; namely, the urinary bladder, thyroid gland, thymus, nasal mucosa, salivary glands, eye, ocular adnexa, breast, soft tissues, and meninges.

Nodal MZL arising in lymphoid organs—lymph nodes, spleen, and Peyer patches—is thought to be a primary neoplastic process. In contrast, extranodal MZL, at least in some cases, is believed to be acquired through neoplastic transformation of a reactive lymphocyte clone, for example, in response to Helicobacter pylori in the setting of chronic gastritis. It generally responds well to local therapy and is often curable.

Histologically, extranodal MZL is composed of a diffuse population of mildly atypical small- to medium-sized monoclonal B lymphocytes and reactive lymphoid follicles and may show variable degrees of plasmacytic differentiation. We report a case of extranodal MZL of the cranial dura mater associated with massive amyloid deposition involving the adjoining leptomeninges and nearby blood vessels.

Case Report

History and Examination. This 63-year-old woman presented with an acute focal sensory seizure consisting of a premonitory chilling sensation followed by confusion, slurred speech, and left arm numbness lasting for 4 minutes. She reported a 3-year history of atypical right-sided facial pain, which she described as an intermittent burning sensation involving all three trigeminal divisions. She also noted mild right-sided hearing loss and migraine headaches with visual scintillations, but denied significant systemic medical problems. Neurological examination revealed only mild right-sided facial hypesthesia and hearing loss.

Admission MR imaging demonstrated an extensive homogeneously enhancing dural-based plaquelike mass involving the adjoining leptomeninges and nearby blood vessels.

Abbreviations used in this paper: CLL/SLL = chronic lymphocytic leukemia/small lymphocytic lymphoma; CNS = central nervous system; Ig = immunoglobulin; LPL = lymphoplasmacytoid lymphoma; MALT = mucosa-associated lymphoid tissue; MR = magnetic resonance; MZL = marginal zone lymphoma.
Dural marginal zone lymphoma with massive amyloid deposition

rior tentorial leaflet, and the right anterior petrous face to compress the right occipital lobe, superior cerebellar hemisphere, and lateral pons, respectively. The plane between the mass and compressed brain was indistinct and punctuated by signal voids from intervening vessels. There was marked edema throughout the posterior half of the right cerebral hemisphere (Fig. 1E). Angiography revealed that the lesion was hypovascular and the dural sinuses were patent (Fig. 1F). Based on the neuroimaging studies, the preliminary clinical impression was meningioma en plaque.

Treatment and Outcome. The preoperative cerebral edema subsided in response to corticosteroid therapy. The largest excrescent mass was resected through a right occipital craniotomy. It was gray, firm, relatively avascular, and densely attached to the dura from which it arose. Its interface with the brain was irregular; adjacent cortex was softened and appeared infiltrated. Cultures for acid-fast bacilli, fungi, and bacteria yielded only rare examples of Propionibacterium acnes.

Subsequent investigation revealed an elevated erythrocyte sedimentation rate of 82 mm/hour, normal peripheral blood smear, normal white blood cell count, and normal results on serum and urine protein electrophoresis. Results of a radiographic skeletal survey were negative. Computerized tomography scanning of the chest, abdomen, and pelvis demonstrated only probable old pulmonary and hepatic granulomatous disease. A bone marrow aspirate was mildly hypocellular, but otherwise normal.

Fractionated whole-brain radiation therapy was delivered in 20 fractions of 180 cGy for a total dose of 36 Gy. The enhancing tumor mass was treated with an additional 14.4 Gy by using a three-field isocentric method. Eight months posttreatment, the patient remained free from seizures and pain, and had only a mild, improving, left inferior homonymous quadrantanopsia. Neuroimaging revealed that the size of the amyloid mass was unchanged from its postoperative state.

Pathological Findings. Microscopic examination of the resected mass revealed large deposits of amorphous hyaline material and concentrically laminated hyaline spherules involving the meninges (Fig. 2A and B). Both stained positively with Congo red and exhibited apple-green birefringence under polarized light (Fig. 2B). Congo red–positive, thickened, hyalinized blood vessels were noted in the subarachnoid space and nearby superficial cerebral cortex (Fig. 2A). The deposits exhibited diffuse immunoreactivity for kappa, but not lambda light chains. There was no reactivity for \( \beta \)-amyloid or transthyretin.

Juxtaposed to the large amyloid deposits was a dense cellular infiltrate mostly composed of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells diffusely infiltrating the dura (Fig. 2A, C, and D). Scattered large lymphocytes (Fig. 2C) and small secondary follicles were also present (Fig. 2E).

Immunohistochemical staining revealed that most of the infiltrate was composed of CD45+ and CD20+ B lymphocytes and plasmacytoid lymphocytes. A smaller population of CD138+ mature plasma cells was also present, as were scattered CD3+ reactive T lymphocytes. The vast majority of the lymphocytes and plasma cells displayed strong immunoreactivity for kappa, but no immunoreactivity for lambda light chains, indicating a monoclonal pop-

ulation (Fig. 2F). Some of the plasmacytoid lymphocytes and plasma cells also displayed IgM immunoreactivity.

The histological and immunohistochemical findings, along with the absence of serum monoclonal gammopathy, urinary Bence Jones protein, and bone marrow involvement, are consistent with the diagnosis of extranodal MZL with plasmacytic differentiation.

Discussion

We present the case of a 63-year-old woman with a fallopertorial and skull-based dural primary MZL with extensive meningeal Ig light chain amyloid deposition (AL amyloidosis). Primary CNS lymphomas most often occur in the deep gray nuclei or periventricular white matter of the cerebral hemispheres, but also occur in the spinal cord, eye, and, very rarely, the meninges.\(^1,17,18,22\) Most are high-grade neoplasms composed of large atypical B lymphocytes, or a mixture of large and small cells, and are usually not associated with amyloid. The prognosis is generally poor; the median survival time ranges from 30 to 60 months with combined radiation and chemotherapy.\(^1\)

Amyloid is a heterogeneous group of substances derived from different proteins in a variety of disorders. Some forms of amyloid are unique to the CNS and related structures; for example, \( \beta \)-amyloid in Alzheimer plaques and cerebral amyloid angiopathy, mutated transthyretin in familial oculeleptomeningeal amyloidosis, prolactin in certain pituitary adenomas, and prion protein in spongiform encephalopathies.\(^6,12,13,22\) Other forms of amyloid are systemic and occur in a broader group of disorders. For exam-
ple, AA amyloid is derived from the acute-phase reactant serum amyloid A. It causes systemic amyloidosis in numerous chronic inflammatory conditions (most commonly rheumatoid arthritis), and in some malignancies (for example, renal cell carcinoma, Hodgkin lymphoma, and others).

It is known that AL amyloid is mainly composed of Ig light chains and may be deposited in tissues, including the meninges, of patients with B lymphocyte–derived neoplasms, namely, multiple myeloma, solitary plasmacytoma, LPL, and, occasionally, CLL/SLL or MZL. When these conditions involve the CNS, a cerebrospinal fluid monoclonal Ig may be present.

Solitary plasmacytoma and multiple myeloma manifest as almost pure infiltrates of mature-appearing plasma cells. Multiple myeloma presents with multiple lytic bone lesions, bone marrow involvement, and monoclonal gammapathy. The median duration of survival in treated patients is approximately 36 months. Solitary plasmacytoma

Fig. 2. Photomicrographs of sections of resected tissue. A: Section showing cellular infiltrate (c) and adjacent amyloid (a) that were adherent to the leptomeningeal vessels (v) and superficial brain (b). The arrow indicates an amyloid spherule. H & E, original magnification × 40. B: Section prepared with H & E (left) and Congo red staining viewed under polarized light (right) showing Maltese cross–shaped apple-green birefringence characteristic of amyloid spherules. Original magnification × 100. C: Mixed cellular infiltrate with interspersed amyloid. H & E, original magnification × 400. D: Plasmacytoid lymphocytes. H & E, original magnification × 400. E: Secondary lymphoid follicle. H & E, original magnification × 200. F: Kappa light chain (left) and lambda light chain (right) immunoreactivity. Note the diffuse kappa reactivity of the cellular infiltrate, and rare scattered lambda-positive plasma cells. Original magnification × 200.
of bone often predicts the development of multiple myeloma and thus also has a poor prognosis. In contrast, solitary plasmacytoma of soft tissue tends to respond well to local therapy and has a good prognosis.6,14,27

Although LPL and CLL/SLL may appear similar to MZL histologically, LPL produces IgM monoclonal gammapathy (Waldenström macroglobulinemia) and involves the bone marrow and other sites. It has been found that CLL/SLL may also produce monoclonal IgM, but can usually be differentiated from LPL and MZL by CD23 reactivity. Both LPL and CLL/SLL are indolent low-grade systemic diseases that, although treatable, are currently not curable, and most patients eventually succumb to these disorders.

The plasma cell variant of Castleman disease may also closely resemble MZL. Castleman disease, however, displays more frequent follicles and hyalinized vessels and is associated with AA, not AL amyloid. Furthermore, cases of Castleman disease that show monotypic plasmacytoid cell proliferations display lambda, not kappa light chain restriction.24

Castleman disease, solitary plasmacytoma, CLL/SLL, and MZL have all been reported to mimic meningioma en plaque radiographically.17,22,23 As a group these lesions have a propensity to involve the Meckel cave, body of the sphenoid, cavernous sinus, petrous apex, tentorium, and falx, and appear to occur more frequently in women.17,27 Trigeminal hypoesthesia, facial paralysis, and hearing loss are common symptoms. Some authors have suggested that, because of their histological similarity, some cases originally diagnosed as Castleman disease, solitary plasmacytoma, LPL, or CLL/SLL might have actually been MZL.14,17 Furthermore, the similarity of certain rare low-grade primary intracerebral B-cell lymphomas associated with amyloid to MALT lymphomas has also been noted, based on their indolent clinical behavior.19

The deposition of AL amyloid has previously been reported in MZL involving the gastrointestinal tract, lung, minor salivary gland, and breast.5,8,9,23,24 To our knowledge this is the first reported confirmed case of extranodal MZL associated with significant AL amyloid deposition within the meninges of the brain.

Extranodal MZL, unlike most primary CNS lymphomas, usually responds well to local therapy such as excision and/or radiation treatment and most often has a good prognosis.2,3,7,10,23 Its accurate diagnosis is therefore of considerable therapeutic and prognostic significance. A low-grade B-cell primary CNS lymphoma, MZL may be associated with amyloid deposition. Although it is rare, MZL should be considered in the differential diagnosis of primary CNS lymphoproliferative lesions and CNS amyloidosis.

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References


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