Primary dural lymphoblastic B-cell lymphoma: a rare subtype of aggressive dural lymphoma

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Abstract Lymphomas arising in the dura mater represent a rare subset of primary central nervous system lymphoma (PCNSL). The majority of primary dural lymphoma (PDL) are low-grade marginal zone lymphomas (MZL) characterized by an indolent course and favorable long-term outcomes. Primary aggressive dural lymphomas are exceedingly rare with a paucity of cases reported in the literature. Herein, we describe a case of primary lymphoblastic dural lymphoma. To our knowledge, this is the second report of an isolated dural B-lymphoblastic lymphoma (B-LBL) in an immunocompetent patient.

Keywords B-lymphoblastic lymphoma · Primary CNS lymphoma · Dural lymphoma · Acute lymphoblastic lymphoma · B-ALL

Introduction

Primary dural lymphoma is a rare form of PCNSL, mostly described by case reports. The incidence of PDL is reported as 0.6–3 % of all primary central nervous system lymphomas (incidence variable in studies) [1, 2]. Aggressive NHL

dural subtypes are unique as most aggressive lymphomas of the meninges are associated with brain parenchymal or systemic involvement. The majority of PDL are low-grade, B-cell marginal zone lymphoma (MZL) with rare cases of low-grade follicular subtypes reported [1]. Aggressive dural lymphomas including diffuse large B-cell lymphoma (DLBCL) and lymphoblastic subtypes are limited to case reports and small case series [1, 3–6] (Table 1). PDL have favorable outcomes and the indolent forms are biologically distinct from parenchymal PCNSL or systemic lymphoma metastatic to the CNS [1]. Whether B-lymphoblastic subtypes will follow this favorable trajectory remains unclear. The paucity of dural lymphoblastic lymphoma cases in the literature make standardized treatment and prognostication difficult.

Case history

A 42-year-old immunocompetent male presented with several weeks of a left frontal headache, lack of coordination, and tendency to drift to the left while driving. Magnetic resonance imaging (MRI) revealed a large enhancing extra-axial mass along the right posterior superior parietal convexity invading the calvarium (Fig. 1a). A second 18-mm focus of enhancement was also noted within the left parietal calvarium distinct from the tumor bulk (Fig. 1b). The tumor was protruding from the outer table of the calvarium and in areas, invaded the meninges and infiltrated into the subdural space. Excision of the tumor was performed and submitted for pathology. A diagnosis of B-LBL was rendered. Complete blood count was only notable for a mild thrombocytosis: platelet count 454,000/ μ L which was present since

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Table 1 Previous reports of primary CNS aggressive dural-based lymphomas

Reference	Age (years)/gender	Histology	Treatment	Survival (months)
Amaker [4]	49/F	T-cell rich B-cell lymphoma	S, CHOP, WBRT, IT MTX	14 (+)
Abdullah [5]	33/M	Lymphoblastic B-cell lymphoma	S, Hyper-CVAD × 8 cycles, IT MTX + Ara-C, RT to tumor bed	30 (+)
Brito [6]	52/F	DLBCL	DHAP × 2 cycles, (s) Ara-C and MTX	22 (+)
Lee [14]	47/F	DLBCL	S, R-CHOP × 6 cycles	72 (+)
Gao [15]	65/M	DLBCL	S, CHOP × 4 cycles, IT Ara-C, dex × 4	4
Rezaei-Kalantari [16]	42/M	DLBCL	S, CHOP × 2 cycles at last follow-up	UNK
Berget [17]	75/F	DLBCL with follicular component	S, R-CHOP × 3 cycles, IT Ara-C, MTX, methylprednisolone, RT	48 (+)
Said [18]	42/F	DLBCL	S, (s)MTX, vincristine, procarbazine × 4 cycles R-CHOP × 4 cycles	34 (+)
Ochiari [19]	72/M	DLBCL	S, WBRT, CHOP	12 (+)
Sachio [20]	46/M	DLBCL	S, (s) MTX × 3 cycles	Died during tx
Galarza [7]	61/M	DLBCL	S, CHOP × 6 cycles, WBRT	23 (+)
Yamada [21]	59/M	DLBCL	S, MTX, Ara-C, ifosfamide, vincristine, cyclophosphamide × 4 cycles	30 (+)
Freudenstein [22]	50/F	B-cell centroblastic/centrocytic	S, (s) MTX, RT	36 (+)
Present case	42/M	Lymphoblastic B-cell lymphoma	S, Hyper-CVAD IT MTX + Ara-C	Undergoing tx 6(+) after diagnosis

F female, M male, DLBCL diffuse large B-cell lymphoma, S surgical resection, (R) CHOP (rituximab) cyclophosphamide, doxorubicin, vincristine, prednisone, WBRT whole brain radiation therapy, IT intrathecal, MTX methotrexate, (s) systemic, Ara-C cytarabine, Dex dexamethasone, DHAP dexamethasone, cisplatin, cytarabine, UNK unknown, (+) still alive, tx treatment

Fig. 1 MRI (T1 axial flare, post-contrast). **a** Large extra-axial enhancing mass along the right parietal convexity measuring 8.7×5.9×6.6 cm. **b** Separate abnormal foci of enhancement within the left calvarium distinct from the larger mass

2007. His thrombocytosis fluctuated in the range of 450,000–650,000/ μ L. Computed tomography (CT) of the chest, abdomen, and pelvis and positron emission tomography (PET) revealed no abnormalities. Cerebrospinal fluid examination was unremarkable.

The patient was treated with hyper-CVAD (fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose cytarabine and methotrexate in conjunction with prophylactic intrathecal methotrexate and cytarabine. Six months since diagnosis, he has tolerated 7 cycles of treatment without complication and will receive consolidative radiation therapy at systemic therapy completion. MRI of the brain after 5 months showed no evidence of recurrence.

Results

Tumor resection pathology Touch imprint from the brain tumor biopsy revealed numerous small to medium-sized lymphoid cells with scant cytoplasm, irregular nuclei with open vesicular chromatin, and occasional prominent nucleoli resembling blasts (Fig. 2a). Hematoxylin and eosin (H&E) stain showed sheets of numerous small/medium lymphoid cells with frequent apoptotic bodies and occasional mitosis (Fig. 2b). Immunohistochemistry (IHC) was performed on deparaffinized, formalin-fixed brain tissue and showed the lymphoma cells to be diffusely positive for CD45, BCL-2, CD79a, PAX5, CD 10, and TDT and negative for CD20, CD3, CD5, BCL-6, BCL-1, and EBER (EBV by in situ hybridization) (Fig. 2c). Ki-67 showed high proliferation index. Fluorescence in situ hybridization (FISH) analysis on paraffin-embedded sections of brain tissue showed copy gain of *BCL-2* (81 % cells) and *MALT1* (77 % cells) with loss of *CEP9* (65 % cells) and *ETV6* (68 % cells). No *BCL-6*, *CCND1/IGH*, or *MYC/IGH* rearrangements were found.

Bone marrow biopsy Bone marrow biopsy revealed trilineage hematopoiesis and slight megakaryocytic hyperplasia without morphologic or immunophenotypic evidence of a hematolymphoid neoplasm. Bone marrow molecular studies performed by polymerase chain reaction (PCR) were negative for *JAK2* V617F, *calreticulin* and *MPL* codon 505 and 515 gene mutations, cytogenetics showed 46, XY [7], myeloproliferative disorder FISH panel showed normal signal patterns for *CHIC2*, *PDGFRB*, *FGFR1*, and *BCR/ABL*.

Peripheral blood Molecular studies by PCR were negative for *JAK 2* exon 12 mutation.

Discussion

Primary dural-based lymphoblastic lymphoma are sparsely reported in the literature. The pathogenesis of PDL is poorly understood as the dura is devoid of lymphoid tissue. Postulated mechanisms, although this has not been definitively proven, include the action of an antigen-independent environmental stimulus or an autoimmune mechanism that could initiate an inflammatory response with subsequent selection of a clonal lymphoid population [1, 8].

The optimal induction therapy for adult B-LBL has not been fully delineated. The most commonly used induction regimes are derived from pediatric protocols and include intensive chemotherapy with CNS prophylaxis followed by prolonged maintenance therapy. ALL (acute lymphoblastic leukemia)-specific chemotherapy regimens have been favored over lymphoma-specific regimens for high risk patients with LBL [9–11].

Fig. 2 **a** Touch imprint showing multiple lymphoblasts with small- to medium-sized cells, scant cytoplasm and open vesicular chromatin (original magnification $\times 1000$). **b** Hematoxylin and eosin stains showing sheets of small lymphoid cells with frequent apoptotic bodies and occasional mitosis (original magnification $\times 500$). **c** The tumor cells are diffusely reactive for CD79a, PAX5, and TdT and negative for CD20 (original magnification $\times 200$)

In our case, complete resection of the tumor was performed followed by treatment with an ALL protocol using hyper-CVAD chemotherapy and intrathecal CNS prophylaxis with each course. He also underwent surveillance with bone marrow biopsy after four courses of treatment which remained negative. The role of consolidative radiation therapy in our particular case is less well defined. Prior reports of patients with B-LBL of various sites reveal high rates of complete remission and overall survival [12]. The prognosis of dural DLBCL based on limited case reports, appears favorable [6]. An interesting aspect of our case was the patient's history of thrombocytosis and findings of slight megakaryocytic hyperplasia on bone marrow biopsy. This raised initial concern for an underlying myeloproliferative disorder (MPD). Concurrency of B-lymphoblastic leukemia and myeloproliferative neoplasm harboring a *MPL* W515S mutation has been previously reported [13]. However, the *MPL* mutation was not detected in our patient.

To our knowledge, this is the second reported case of B-LBL with isolated dural involvement in the absence of other systemic sites of disease. The majority of B-LBL present

systemically with concomitant bone marrow involvement and/or leukemic component. As we gain further insight into the natural history and pathogenesis of primary (aggressive) dural lymphoma, our understanding of its behavior will broaden and improve our therapeutic approach.

Compliance with ethical standards

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional guidelines and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the patient included in this case report.

Conflict of interest Christine Saraceni declares no conflicts of interest. Nicole Agostino declares no conflicts of interest, and Shereen Gheith declares no conflicts of interest.

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