

Primary central nervous system T-cell lymphoma in AIDS patients: case report and literature review

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ABSTRACT

According to the published data, most primary central nervous system lymphomas (PCNSLS) are B-cell lymphomas; primary T-cell lymphomas are rare. In a search of the MEDLINE database, we found only 6 cases of primary T-cell PCNSL. Here, we present the case of a 43-year-old man with AIDS, not on highly active antiretroviral therapy, who presented with focal neurologic symptoms and was found on magnetic resonance imaging to have multiple brain lesions. A biopsy showed T-cell lymphoma, and the patient was subsequently treated with whole-brain radiation, to marked clinical response. Reported cases from the literature of primary T-cell PCNSL in AIDS patients are summarized in this review.

KEY WORDS

Primary CNS lymphoma, T cells, non-Hodgkin lymphoma, AIDS

1. INTRODUCTION

Primary central nervous system lymphomas (PCNSLS) are an uncommon form of extranodal non-Hodgkin lymphoma, but they are becoming increasingly more frequent [1]. Currently, the incidence has increased to 4%–7% of newly diagnosed primary central nervous system (CNS) tumours, and in the general population, the incidence rate is approximately 30 cases per million person–years [2]. More than 95% of PCNSLS are B-cell lymphomas. T-Cell PCNSL is less well defined; its biologic behaviour and response to treatment have been difficult to evaluate because of its rarity.

In AIDS patients, the reported incidence of PCNSL is 1000 times that seen in the general population [3,4]. Most of the reported cases are B-cell PCNSL. A search of the MEDLINE database for PCNSL in AIDS patients found only 6 cases [5–9]. Here, we present another case of an AIDS patient with T-cell PCNSL, treated successfully with whole-brain radiation and highly active antiretroviral therapy (HAART).

2. CASE DESCRIPTION

A 43-year-old man presented to our hospital with headaches and right facial twitching for few days, associated with nausea and dizziness. His past medical history was significant for infection with HIV diagnosed 10 years earlier. Because of financial circumstances, the patient had stopped his HAART 10 months earlier.

On physical examination, the patient was alert and oriented. His vital signs were normal. He had a mild word-finding deficit, right facial droop, right pronator drift, and mild right arm hyperreflexia. The rest of the physical examination was normal.

Laboratory work up showed a white blood cell count of 3400/mL, a CD4 count of 78/mL (normal: 493–1666/mL), an HIV viral load above 500,000/mL, positive *Toxoplasma* immunoglobulin G antibodies, negative serum cryptococcal antigen, and a nonreactive rapid plasma reagin test.

Magnetic resonance imaging (MRI) of the brain showed a large mass in the left frontoparietal region, with small non-enhancing lesions in the brain (Figure 1). A presumptive diagnosis of cerebral toxoplasmosis was made, for which the patient was treated with pyrimethamine, sulfadiazine, and leucovorin, with phenytoin for seizure prophylaxis. To avoid possible complications of anemia and immune reconstitution syndrome, HAART was planned to be restarted 2 weeks later.

The patient improved symptomatically and was discharged home. A follow-up brain MRI 10 days later demonstrated no significant changes.

One month later, the man came to our emergency department with a history of progressively increasing partial focal seizures that had started after he had stopped his medications 2 weeks earlier because of financial concerns. Brain MRI showed a slight increase of the old left frontoparietal lesion

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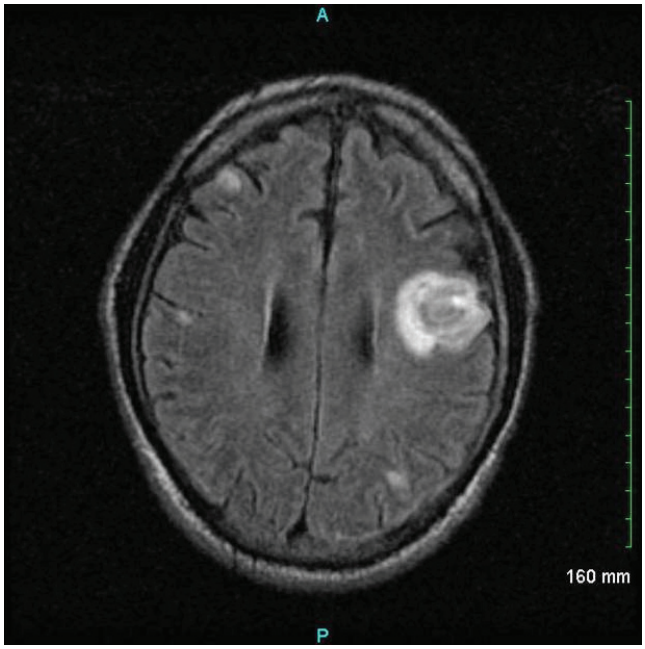


FIGURE 1 *Magnetic resonance imaging of the brain demonstrates an enhancing 2×3-cm mass involving the left frontoparietal region, and some small non-enhancing lesions in the brain bilaterally.*

and small new enhancing lesions bilaterally. A computed tomography–guided brain biopsy showed atypical lymphocytes (Figure 2), positive staining for lymphocyte common antigen and the T-cell marker CD3 (Figure 3), and no staining for the B-cell marker CD20 (Figure 4). Immunoperoxidase staining for cytomegalovirus, *Herpes simplex* virus, and *Toxoplasma* was also negative. Giemsa, Gram, and acid-fast stains were also negative.

The patient refused chemotherapy, but underwent whole-brain external-beam radiation therapy and was started on HAART. At the time of writing, he has been closely followed for 31 months; serial brain MRI has shown stable disease, and the patient has been symptom-free.

3. DISCUSSION

A search of the MEDLINE database found only 6 other cases of T-cell PCNSL in AIDS patients [5–9]. Table I summarizes the clinical features of those cases and the present case. Median age of the patients is 38 years. The patients are predominantly male.

Primary central nervous system lymphoma can present with focal or non-focal signs and symptoms that have usually been present for fewer than 3 months. Patients with AIDS are more likely than other patients to present with altered mental status and seizures (50% vs. 35%) and less likely to show increased intracranial pressure (14% vs. 32%) [10]. Most of the patients in this review presented with focal neurologic symptoms.

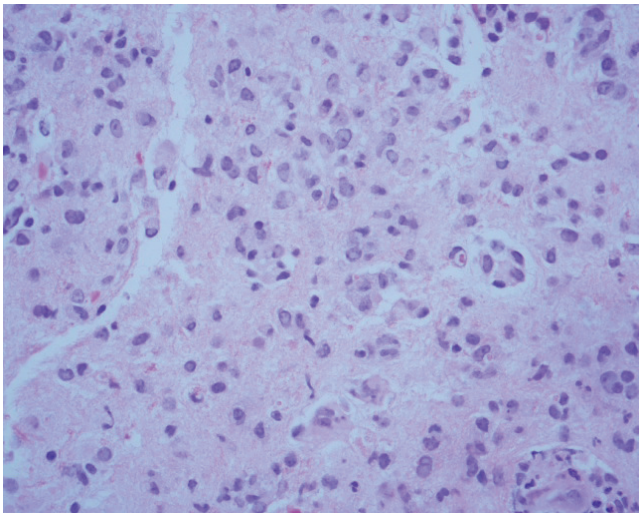


FIGURE 2 *Brain mass biopsy shows atypical lymphocytes (40× magnification).*

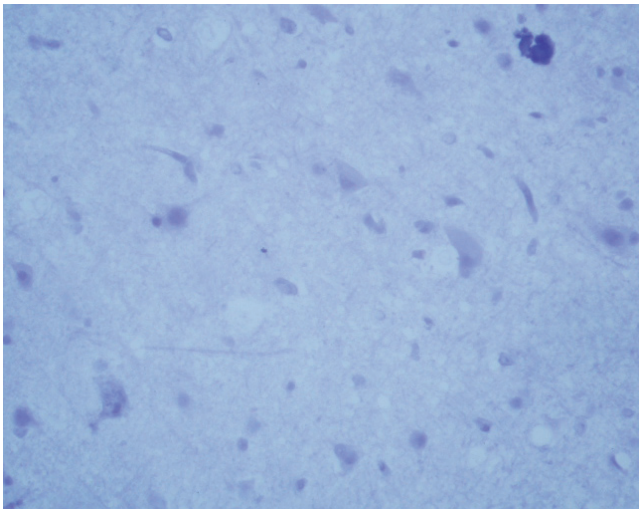


FIGURE 3 *Immunoperoxidase staining of the brain mass biopsy with the T-cell marker CD3 is extensive.*

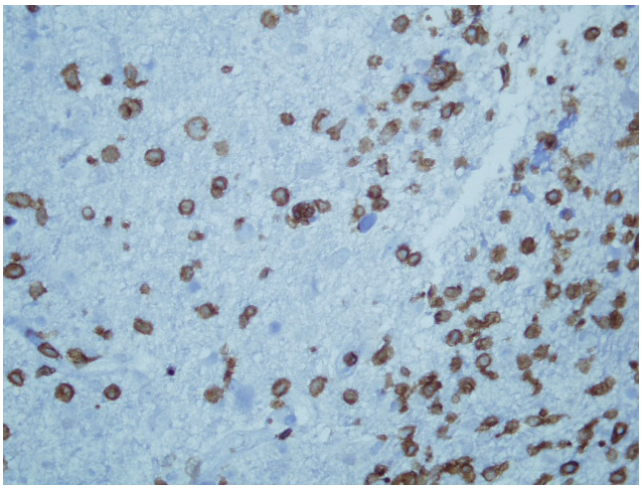


FIGURE 4 *Immunoperoxidase staining of the brain mass biopsy with the B-cell marker CD20 is absent.*

TABLE I Cases of primary central nervous system T-cell lymphoma in the literature

Characteristic	*Case and reference*						
	1	*2*	*3*	*4*	*5*	*6*	*7*
	Aydin et al., *1998* [7]	*Smith* et al., *1996* [8]	*Rao* et al., *1989* [9]	*Bataille* et al., *2000* [10]	*Chappell* et al., *1992* [11]	*Bashir* et al., *2000* [12]	*(present case)*
Age (years)	43	36	38	53	30	36	43
Sex	Male	Male	Male	Male	Female	Male	Male
Presenting symptoms	Fever, seizures, altered mental status	Dysarthria, headache, arm weakness	Headache, hearing loss, amblyopia	Progressive ataxia	Ataxia	Seizures	Nausea, dizziness facial palsy, hyperreflexia
CD4 count (cells/mL)	NA	<50	28–90	110	NA	NA	78
HAART at time of diagnosis?	Yes	Yes	NA	Yes	NA	NA	NA
History of opportunistic infections	NA	PCP	Disseminated MAC, *Candida* esophagitis, salmonellosis, HSV	Oral candidiasis	NA	NA	NA
Presenting lesions	Single	Single	Multiple	Multiple	Single	Multiple	Multiple
Site of disease	Left parietal	Right cerebellum	Right frontoparietal	Right frontoparietal and left cerebellum	Cerebellar vermis	NA	Bilateral frontoparietal
Method of diagnosis	Stereotactic biopsy	NA	Stereotactic biopsy	Brain biopsy	Brain biopsy	Brain biopsy	CT-guided brain biopsy
Pathology	Extranodal NK cell and T-cell lymphoma	NA	NA	Atypical pleomorphic lymphocytes	Pleomorphic immunoblastic T-cell lymphoma	Pleomorphic large T-cell lymphoma	NA
Immunophenotype	Positive for CD45, CD3 (cytoplasmic), CD2, CD56, perforin; negative for CD20, CD4, CD8	NA	Positive for CB3	Positive for CD45 (LCA), CD45RO; negative for CD20	Positive for pan T-cell marker, negative for pan B-cell marker	Positive for pan T-cell marker, negative for pan B-cell marker	Positive for CD45 (LCA), CD3
PCR for EBV	Positive	NA	Positive	NA	NA	NA	NA
Other serology	Negative for *Toxoplasma* IgM antibody, *Cryptococcus* antigen	Serum *Toxoplasma* titres < 1:16	Negative for *Toxoplasma* antibody	NA	NA	NA	Positive for *Toxoplasma* IgG antibody; negative for serum *Cryptococcus* antigen
Treatment	NA	NA	NA	Whole-brain radiation and CNS chemotherapy	NA	NA	Whole-brain radiation
Outcome	Death a few days after diagnosis	NA	Death months later	Clinically improved	Death	NA	Clinically improved

NA = not available; HAART = highly active antiretroviral therapy; PCP = *Pneumocystis carinii* pneumonia; MAC = *Mycobacterium avium* complex; HSV = *Herpes simplex* virus; CT = computed tomography; NK = natural killer; LCA = leukocyte common antigen; PCR = polymerase chain reaction; EBV = Epstein–Barr virus; IgM = immunoglobulin M; IgG = immunoglobulin G; CNS = central nervous system.

Patients with AIDS presenting with signs and symptoms suggestive of CNS disease should be evaluated radiologically. On computed tomography imaging, PCNSL usually appears as a well-defined focal lesion that can be isodense or hyperdense. The diagnostic yield is higher with MRI.

In immunocompetent patients, T-cell lymphomas present more frequently as infratentorial lesions. In the present review, most patients had lesions in the supratentorial region (Table I).

Measurement of Epstein–Barr viral DNA in a sample of cerebrospinal fluid can aid in making the diagnosis, but stereotactic brain biopsy remains the definitive method [11]. Diagnosis of T-cell tumours can be difficult, and their incidence, despite being low, is possibly overestimated. Furthermore, B-cell neoplasms are frequently infiltrated by reactive T cells, complicating the interpretation of immunophenotyping. Staging is generally not indicated because PCNSL almost always remains confined to the CNS.

Optimal treatment for PCNSL in AIDS patients is not yet defined. Standard first-line treatment of radiation therapy and corticosteroids can achieve a complete response in 20%–50% of patients; median survival is 13.5 months, however [12]. The short survival reflects deaths from the opportunistic infections that are a result of the profound immunodeficiency that most patients with PCNSL already have [13]. Chemotherapy combined with radiation therapy may provide some benefit to patients with relatively high CD4 counts [13,14]. Among the patients in our review, treatment was reported for only 2, both of whom were treated with whole-brain radiation.

Some studies have suggested that survival is longer for patients with T-cell PCNSL [15]. Of the 7 patients in this review, 3 died soon after diagnosis, and the 2 that received treatment improved clinically; the fates of the other 2 were not reported (Table I).

4. CONCLUSIONS

In general, T-cell PCNSL is rare; it appears to be even more rare in immunocompromised patients. More reports of cases are needed to help improve diagnosis, treatment, and prognosis in this kind of lymphoma.

5. CONFLICT OF INTEREST DISCLOSURES

All authors declare that no financial conflicts of interest exist.

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