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Case Report

Primary cerebellar T-cell lymphoma with acquired immunodeficiency syndrome

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We report a 33-year-old man with the acquired immunodeficiency syndrome (AIDS) and a solitary T-cell lymphoma. Systemic sites of lymphomatous involvement could not be identified. Subtotal resection of the lesion with cranial irradiation resulted in a marked neurologic improvement. Our case suggests that T-cell lymphomas should be considered in the differential diagnosis of a solitary mass of the cerebellum in patients with AIDS and that aggressive therapy may be warranted.

Keywords: cerebellum; T-cell lymphoma; acquired immunodeficiency syndrome; human immunodeficiency virus; brain

Introduction

Primary central nervous system lymphomas (PCNSL) can occur in both, immuno-competent and immuno-compromised patients, such as transplant recipients and those with the acquired immunodeficiency syndrome (AIDS) (Jellinger and Paulus, 1992; Lowenthal *et al*, 1988). In patients with AIDS, PCNSL are almost exclusively of B-cell origin (Lowenthal *et al*, 1988). Of the 29 reported cases of PCNSL of T-cell origin (Grant and Isaacson, 1992; Rao *et al*, 1989; Inoue *et al*, 1990; Hayakawa *et al*, 1994; Novak and Katzin, 1995), 23 were immuno-competent (Grant and Isaacson, 1992; Hayakawa *et al*, 1994; Novak and Katzin, 1995), two patients had AIDS (Rao *et al*, 1989) and one was infected with the human T-cell lymphotropic virus type 1 (Inoue *et al*, 1990). In this communication, we report a patient with AIDS and a T-cell PCNSL and review the literature.

Case report

This 33-year-old homosexual man was human immunodeficiency virus (HIV) seropositive since 1986. Serology for human T-cell leukemia virus (HTLV)-I and HTLV-II were negative. He had a past history of syphillis, disseminated mycobacterium avium-intracellulare infection and varicella zoster. His circulating CD4 (T helper) cell count had been 0 cells/mm^3, 18 months prior to his neurological presentation. Medications included zidovudine, fluconazole, trimethoprim/sulfamethoxazole, clarithromycin and ethambutol.

In January 1993, he developed a daily headache which was diffuse, constant, throbbing and associated with episodic nausea and vomiting. Concurrently, he had a weight loss of 12 kg, daily fever and chills. He was unsteady on ambulation and had fallen several times.

On presentation in February 1993, he had an oral temperature of 39°C, a slurred speech, finger to nose ataxia worse on the right side and truncal ataxia. A computerized tomography (CT) scan of the brain revealed a solitary, well circumscribed, cystic, ring enhancing mass in the inferior vermis and right cerebellar hemisphere with surrounding edema (Figure 1). The patient was treated empirically with sulphadiazine, pyrimethamine and folinic acid for a presumed toxoplasma abscess. Serology for *Toxoplasma gondii* was requested and reported to be negative 2 weeks later. Over the ensuing 12 days, however, his ataxia increased and his level of consciousness decreased. A repeat CT scan of the brain showed an increase in the size of the lesion. Intravenous dexamethasone was initiated and a biopsy and subtotal resection of the cerebellar lesion was performed. Hematoxylin and eosin preparation revealed a malignant lymphoma (Non-Hodgkin's, diffuse large cell, immunoblastic, T cell origin, high grade in accordance with the Interna-

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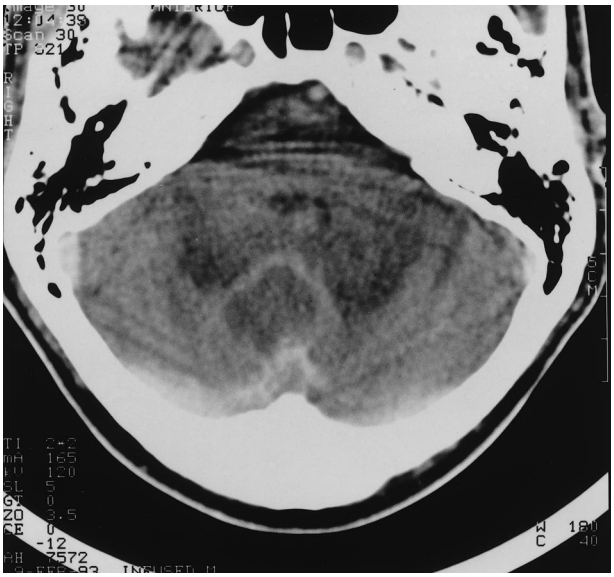

Figure 1 Contrast enhanced computed tomographic scan of the posterior fossa demonstrating a 2 cm (diameter) cystic ring enhancing mass centered in the inferior vermis.

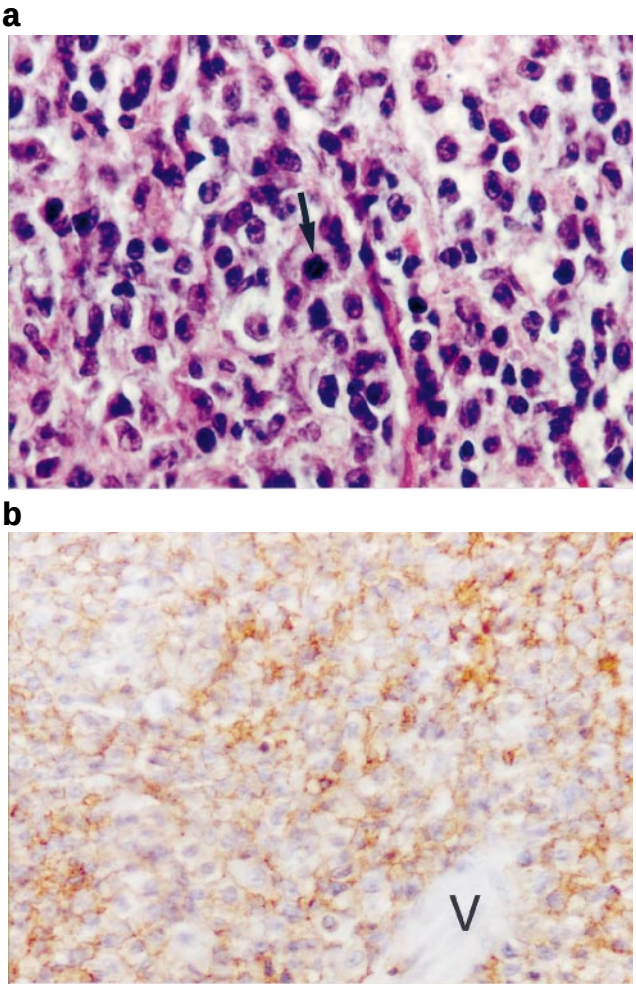

Figure 2 (a) A mitotic figure is demonstrated (arrow) in this cerebellar neoplasm, (haematoxylin and eosin stain, magnification 960×). (b) Neoplastic cells expressing T-cell antigens as determined by immunohistochemical reaction with MT-1 antibody (brown reaction product). A blood vessel (V) shows lack of staining (magnification 960×).

tional Working Formulation). Immunohistochemical studies with the pan T-cell marker MT-1 showed strong reactivity (Figure 2A and B). The tissues did not react with the T-suppressor cell immunohistochemical marker CD45R nor did it react with the anti-B-cell antibody, MB-2 (CD22). Rare neoplastic cells reacted with the T-helper cell markers, CD4. Stains and cultures of the tissue did not reveal any micro-organisms.

No evidence for systemic lymphoma was found by bilateral iliac crest bone marrow biopsies and CT scans of the chest, abdomen and pelvis. Further treatment with corticosteroids and whole brain irradiation resulted in a marked neurological improvement. He returned to live independently but died 6 months later of pneumonia due to *Aspergillus fumigatus*. An autopsy was not performed.

Discussion

Central nervous system lymphomas occur either as a consequence of metastatic seeding or may arise spontaneously within the central nervous system. The latter is thus known as a PCNSL (Fine and Mayer, 1993). Over the past two decades there has been an increase in the diagnosis of PCNSL which has been attributed to better diagnostic regimens, an increase in the number of individuals who are immune-suppressed either as a result of acquired or congenital immune-deficiencies and organ transplantation (Grant and Isaacson, 1992) and an overall increased incidence in the general population (Grant and Isaacson, 1992; Fine and Mayer, 1993). The overwhelming majority of PCNSL in the afore mentioned patient population are of B-cell origin. Genetic material from Epstein-Barr virus (EBV) has been detected within these neoplasms from patients with AIDS suggesting that this virus may play an etiopathogenic role in the induction of these tumors both in the central nervous system and in systemic locations (DeAngelis *et al*, 1992; Wang *et al*, 1995).

PCNSL of T-cell origin are rare (Table 1). Most reported patients were male (21/27; 78%) and immuno-competent (26/30; 87%). The neoplasms were predominantly monocentric (Table 1) and had a predisposition for the cerebellum (10/25; 40%).

The brain may also be secondarily involved from a systemic T-cell lymphoma. These patients usually have advanced metastatic disease and it usually involves the leptomeninges (Morgello *et al*, 1989)

Table 1 Summary of all reported cases of primary central nervous system lymphoma of T-cell origin

Location	n	*ICS/ICT*	*Median age years (range)*	*Median survival months (range)*	*Gender* n (%) *Male*	*Female*	*References*
Cerebellum	10	2/8	33 (2–64)	14 (2–76)	6 (60)	4 (40)	4*, 5–8, present case
Leptomeninges	5	0/5	33 (17–64)	1.8 (1.5–2)	5 (100)	0	4
Cerebrum	9	1/8	36 (16–66)	14 (7–20)	7 (78)	2 (22)	4,5
Intraventricular	1	0/1	51	16	1 (100)	0	4
Site not specified	5	0/5	41 (17–64)	unknown	2 (100)	0	4
Total	30	3/27	37 (2–64)	11 (1.5–76)	21 (78)	6 (22)	

ICS – immunocompromised patients
ICT – immuno-competent patients
*Reference #4 is a review of 22 cases

however leptomeningeal lymphoma may also occur as an initial presentation of PCNSL. In either case, the prognosis was poor with survival less than 2 months despite therapeutic intervention (Grant and Isaacson, 1992). In contrast 57% and 63% of all patients with cerebellar and hemispheric T-cell PCNSL respectively survived greater than 1 year after intervention (Table 1). Our patient survived 6 months after diagnosis and treatment which included surgical debulking of the neoplasm, systemic corticosteroids and whole brain irradiation. The patient did not die from the neoplasm but rather from an opportunistic infection related to profound immune suppression. These results are similar to those of patients who are immunocompromised with PCNSL of B-cell origin the median survival being between 2 to 5 months irrespective of location and death also occurs secondary to immune-suppression (Baumgartner *et al*, 1990; Forsyth *et al*, 1994). A recent report documented that there may be T-cell infiltration of PCNSL of B-cell origin in both immune-competent and AIDS patients (Bashir *et al*, 1996). In our patient, immunohistochemical evaluation revealed that the PCNSL was exclusively of T-cell origin, with no detectable B-cells. Although T-cell PCNSL in patients with AIDS have not been published previously except in abstract form (Rao *et al*, 1989), peripheral lymphomas of CD4 cell origin have been reported in patients with HIV/AIDS (Nasr *et al*, 1988; Lust *et al*, 1989). The exact mechanism by which these tumors arise remains unknown. Possible etiological agents include the HIV itself, an unrecognised oncogenic virus, prolonged antigenic stimulation, altered cellular proliferation, genetic mutation and deregulation of tumor-suppressor genes (DeAngelis *et al*, 1992; Wang *et al*, 1995). It is also possible that the altered immune surveillance in these patients may contribute to the pathogenesis/proliferation of these T-cell tumors. However, it is interesting to note that our patient with PCNSL had some CD4 tumor cells despite no detectable CD4 cells in the peripheral circulation.

As patients with posterior fossa lesions can deteriorate and decompensate quickly, we conclude that early biopsy of posterior fossa mass lesions may be warranted and the cell type of all PCNSL should be determined by immunostaining at the time of biopsy. Tumors of T-cell origin appear to have a predilection for the cerebellum. However, in patients with AIDS despite aggressive treatment for the tumor, long term survival may be a few months and is determined by the underlying immune status of the patient rather than the cell type of the tumor.

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