Lymphomatosis cerebri

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A case study in 1999 coined the term 'lymphomatosis cerebri' (LC) to describe an exceedingly rare variant of Primary central nervous system lymphoma PCNSL characterised by diffuse parenchymal infiltration of lymphomatous cells [1].

Clinical Features

The patient with lymphomatosis cerebri may have variable clinical symptoms such as gait abnormality, focal weakness, cognitive decline, memory disturbance, personality changes, dementia, anorexia, orthostatic hypotension, paraparesis and weight loss [2] [3].

The tumors infiltrating to the diencephalon have been reported to cause the diencephalic syndrome [4].

Diagnosis

MRI

MRI study of LC typically reveals diffuse leukoencephalopathy.

Typical MR findings of the lymphomatosis cerebri are extensive, diffuse T2 and FLAIR-weighted hyperintense lesions without contrast enhancement in both cerebral hemispheres and brainstem [5].

Diagnosis of LC requires additional examinations generally not performed in the other white matter disorders. In suspected cases, biopsy should be performed to avoid deferring adequate cytostatic treatment

Diffuse infiltrations of both cerebral hemispheres by lymphoma cells without discernible lesions [6] [7].

Differential diagnosis

It is not well recognized and may be misdiagnosed with infiltrating tumors, degenerative disorders, ischemic diseases, and infectious diseases developed in the brain [8].

Awareness of the possibility of this rare disease and early biopsy are required for differential diagnosis and preventing poor clinical outcomes.

Subtle or patchy enhancements may be seen in some cases in MRI. These radiological findings may be similar with those of the gliomatosis cerebri which has to be differentiated in this case. In the

gliomatosis cerebri, T1-weighted hypo-intense lesions on MRIs, low-density lesions on CT, and focal enhancements are typical radiological findings [9].

Anaplastic large cell lymphoma

Treatment

Where LC was diagnosed premortem, many cases responded to steroids alone, at least initially.

To achieve complete remission, steroid use has been followed by radiotherapy, cisplatin or methotrexate [10].

Optimal treatment for lymphomatosis cerebri remains unclear. However, better outcomes may be expected than previously reported ones because lymphomatosis cerebri is identical to PCNSL pathologically [11].

Case series

2005

3 immunocompetent individuals who developed rapidly progressive dementia. Magnetic resonance imaging features mimicked other disorders of white matter and prompted preoperative diagnoses of Binswanger's disease (subcortical ischemic vascular dementia), unknown leukoencephalopathy, viral infection, or infiltrating glioma. Neuropathologic examination at biopsy and autopsy demonstrated nonnecrotic, diffusely infiltrating, large-cell B-cell lymphoma of white matter, with relative sparing of gray matter, and without significant leptomeningeal involvement or bulky periventricular disease at autopsy. Microglial and astrocytic reactions, but only subtle myelin pallor, were evident as individual tumor cells permeated the entire brain and spinal cord, albeit with considerable variation in cell density. Individual tumor cells could be identified from the optic nerve to spinal cord, documenting the “whole-brain” nature of the disease. CD20 immunostaining was necessary to fully appreciate the extent of individual lymphoma cell percolation through the white matter. The neurobehavioral deficits manifested by these patients demonstrate that lymphomatosis cerebri is an additional neoplastic cause of white matter dementia and can be added to the growing list of disorders responsible for this syndrome [12].

1999

2 cases from the UCLA Medical Center who developed a rapidly progressive dementia due to extensive gray and white matter cerebral lesions involving much of the brain. In the patient who came to autopsy, widely infiltrating, focally necrotic B-cell plasmacytoid lymphoma was noted throughout the cerebral neuraxis. MRI findings in case 2 were consistent with diffuse lymphomatous brain infiltration without mass lesions, which was biopsy proven. We conclude that PCNSL may occur in a diffusely infiltrating form which may occur without MRI evidence of mass lesions or blood-brain barrier compromise. We refer to this entity as 'lymphomatosis cerebri' and add it to the differential diagnosis of a rapidly progressive dementia [13].

Case reports

It has been reported less than 20 cases till 2012 [14].

2015

A 71-year-old immunocompetent man developed cognitive decline and gait abnormality. Brain magnetic resonance imaging (MRI) revealed bilateral diffuse leukoencephalopathy without a mass lesion. An analysis of the cerebrospinal fluid (CSF) showed elevated levels of interleukin 10 (IL-10). The condition of the patient progressively deteriorated, and intravenous high-dose steroids proved ineffective. Detection of non-destructive, diffusely infiltrating, large B cell lymphoma in biopsy and autopsy specimens led to a diagnosis of lymphomatosis cerebri (LC). On serial MRI, the basal ganglia and white matter lesions increased in parallel with the levels of IL-10. These findings suggest that the IL-10 level in the CSF may represent a potentially useful biomarker for the early diagnosis and monitoring of the disease progression in LC [15].

2013

A case with lymphomatosis cerebri who presented with rapid neurological deterioration [16].

2012

A 55-year-old man presenting with subacute progressive dementia and ataxic gait. Brain MRI showed diffuse hyperintense lesions in the cerebral white matter of both hemispheres, left amygdala, brainstem and cerebellar peduncles on FLAIR image. No contrast-enhanced lesion was observed. Cerebrospinal fluid analysis showed elevated levels of soluble interleukin-2 receptor and β2-microglobulin. Based on MRI findings and 123I-IMP SPECT, stereotactic biopsy targeting white matter of the left medial temporal lobe was performed (day 0). On the day after the brain biopsy, corticosteroid therapy was initiated and improved the patient's cognitive function and gait disturbance. Pathological diagnosis of large B-cell lymphoma was obtained on day 9. High-dose intravenous methotrexate chemotherapy was started on day 14 and led to complete remission by day 52. This case highlighted the importance of brain biopsy for diagnosis of LC. This report raises a possibility that timely and proper treatment leads to a favorable outcome of LC that has been regarded as an intractable disease with poor prognosis [17].

A 56-year-old immunocompetent woman who complained of rapid deterioration of her higher brain function over a 4-month period. Magnetic resonance imaging showed extensive white-matter lesions. During brain biopsy, a diffusely infiltrating lymphoma with distinctive immunohistochemical features was detected. Awareness of this unique presentation and early tissue diagnosis provide the best hope for instituting appropriate treatments [18].

2009

A patient with subacute dementia and diffuse bilateral white matter changes in the cerebral hemispheres and additional involvement of the brainstem, basal ganglia and thalamus on MRI. Initially, she was considered to suffer from an autoimmune encephalitis, transiently responded to immunosuppression but then developed multiple solid appearing cerebral lymphomas [19].

2008

A 53-year-old, immunocompetent man who had an insidiously progressive dementia and right weakness. On serial MRI in 4 months duration, diffuse white matter lesions without contrast enhancement gradually progressed, which was clinically consistent with his worsening condition. Biopsy specimen demonstrated nondestructive, diffusely infiltrating, large B-cell lymphoma, diagnosing LC. After the biopsy, corticosteroids were initiated, which dramatically alleviated his symptoms. Afterwards, he was treated by whole brain irradiation (total 36Gy) and discharged without noticeable deficits [20].

A 56-year-old female who had clinical signs and symptoms of sub-acute dementia. Computerised axial tomography and MRI of the head revealed extensive, diffuse and bilateral involvement of the white matter, basal nuclei, mesencephalon and pons, with no mass effect or contrast enhancement. A stereotactic biopsy of the white matter (which was not conclusive) showed a perivascular mixed mononuclear-cell inflammatory infiltrate of B and T cells. No cytologic atypia was observed. Treatment was established with corticoids, which produced a clinical and radiological improvement in the first two months. During the next month the patient underwent rapid clinical deterioration with sleepiness and a worsening of the ability to walk. In an MRI scan the lesion had a more heterogeneous appearance with mass effect on adjacent structures and patchy contrast enhancement. A wedge biopsy of brain tissue led to a diagnosis of high-grade B-cell lymphoma.

The imaging and histological appearance of LC may not be the one typically found in primary lymphomas of the central nervous system, and its clinical presentation may be similar to that of other diffuse processes involving compromise of the white matter (cerebral gliomatosis, inflammatory diseases of the white matter, such as Behçet's disease, Sjögren's disease or systemic lupus erythematosus) [21].

2007

A 64-year-old woman presenting with rapidly progressive dementia, brain magnetic resonance imaging revealed a diffuse leukoencephalopathy without gadolinium enhancement, and the 14.3.3 protein was found to be positive in the cerebrospinal fluid. An electroencephalogram showed diffused slow waves and epileptic seizures without periodic paroxysmal activity. The patient died 3 months after onset of symptoms, and an autopsy restricted to the brain was performed. Gross examination was not informative, and only microscopic examination permitted identification of scattered lymphomatous cells on all sections from the brain hemispheres, brain stems and cerebellum. Immunopositivity of these tumor cells for CD20 attested their B phenotype [22]

A case of an elderly patient referred to a tertiary-care center for further evaluation of a rapidly progressive dementia, whose definitive diagnosis was delayed by nonspecific MRI findings, presence of 14-3-3 protein in the CSF, and nonspecific cutaneous lesions. At brain biopsy, he was thought to have a diffusely infiltrating lymphoma, with distinctive immunohistochemical features.

This case is notable in that it presents a patient with progressive dementia whose diagnosis of primary central nervous system lymphoma (PCNSL) was delayed because of the lymphoma's atypical diffusely infiltrating nature. Awareness of this unique presentation may hasten the time between clinical presentation, diagnosis, and subsequent treatment [23].

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