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Lymphomatoid granulomatosis of the brain: A case report

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Abstract

Background: Lymphomatoid granulomatosis is a rare disorder of the central nervous system (CNS) with few cases being reported in literature. We present the case of an adult with an unusual lesion of the CNS who presented with motor seizures and was diagnosed with lymphomatoid granulomatosis, followed by a discussion of the process of evaluation and management.

Case Description: A 42-year-old male presented with motor seizures and loss of consciousness for 10 minutes along with dysarthria and left hemiplegia. Neurological examination and imaging with magnetic resonance imaging (MRI) of the brain revealed a mass in the right striatum. The patient was hospitalized and underwent an image-guided right frontal craniotomy using the Leksell Stereotactic G-Frame. Pathology reported a lymphomatoid granulomatosis. Being immunocompetent, the patient received medical treatment with prednisone and rituximab. Two years after his diagnosis, the patient had no active disease and his brain MRI did not show contrast enhancement. After almost 3 years of follow-up, the patient has a mild weakness in the left-side of his body (4/5), is seizure-free, and can walk and perform daily activities.

Conclusions: This rare lesion in an adult, immunocompetent patient, debuting with motor seizures represents a challenge in terms of diagnosis and treatment. After surgical and medical treatment, the patient had a satisfactory recovery. Clinical features, imaging, differential diagnosis, and pathology are discussed.

Key Words: Brain tumor, lymphomatoid granulomatosis, stereotactic neurosurgery, symptomatic epilepsy

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INTRODUCTION

Lymphomatoid granulomatosis (LG) is a disease that was first described in 1972 by Liebow *et al.*,[13] however, little is known about the disease. It is a lymphoproliferative angiodestructive systemic disease associated with the Epstein-Barr virus. It mainly affects the lungs (80%) but it has also been described to involve other organs such as the skin (40%) and the central nervous system (CNS) (20%).[8,10]

Because there is still much to be learned about this disease, we present the following case along with a detailed description of its radiological, pathological, and clinical findings.

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CASE REPORT

A 42-year-old man, previously healthy, was living with his step father and other members of an extended family in a small farm. He presented with a first episode of a motor seizure that started on the left side of his body before becoming generalized. Shortly afterwards, he noticed left hemiparesis and dysarthria; he was admitted to our institution through the emergency department.

After a physical examination, magnetic resonance imaging (MRI) of the patient revealed a well-defined, spherical lesion, located in the superior aspect of the anterior limb of the internal capsule and right striatum, with surrounding edema [Figure 1]. Laboratory studies found no systemic compromise and no underlying immunocompromise. We decided to excise and analyze the aforementioned lesion. Performing an image-guided frontal craniotomy, using the Leksell Stereotactic G-Frame (Elekta Instruments AB, Stockholm, Sweden), we planned the trajectory to avoid the head of the caudate nucleus, the genu of the internal capsule, the putamen, and other critical structures. The mass was completely excised and the thalamostriate vein, which was adhered to the mass, was preserved. Craniotomy was performed, instead of a stereotactic biopsy, because we suspected the lesion to be a high-grade glioma that was accessible to surgical resection.

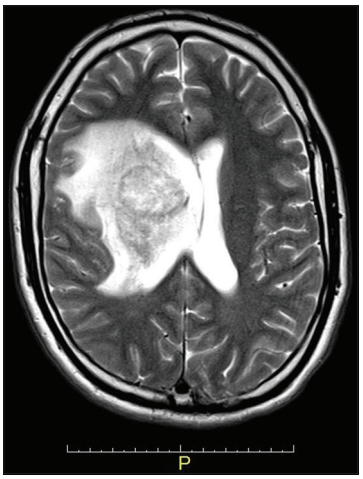

Figure 1: Magnetic resonance T1 image. A round-shaped, well-limited lesion, with contrast enhancement, located in the right striatum besides the the lateral ventricle with compressive effect on the brain parenchyma and adjacent structures deviation midline approximately 8.0 mm. Surrounding edema is observed

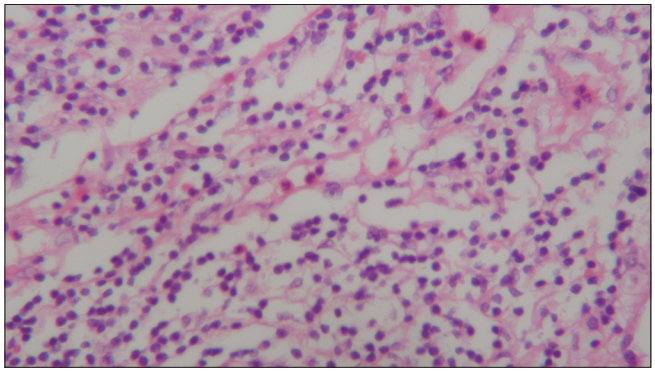

Figure 3: Cerebral parenchyma, architectural distortion by lymphoplasmacytic inflammatory infiltrate with histiocytes, and some atypical cells. Atypical cells were CD20 + with a mature T lymphocyte background

In the pathological analysis, there was an evident atypical T and B infiltrate; morphological and phenotypical characteristics of Grade 1 lymphomatoid granulomatosis. The patient was subjected to thoracic and abdominal screening, which revealed paratracheal, jugular, and inguinal adenopathies, but no other masses.

After consulting with the hematology group, the patient received a four-cycle medical treatment with rituximab and prednisone. Clinically, he recovered almost completely with strength of 4/5 and complete reintegration to his daily activities, which involved bimanual work. Six months after his diagnosis, a new MRI showed the absence of new or residual lesions.

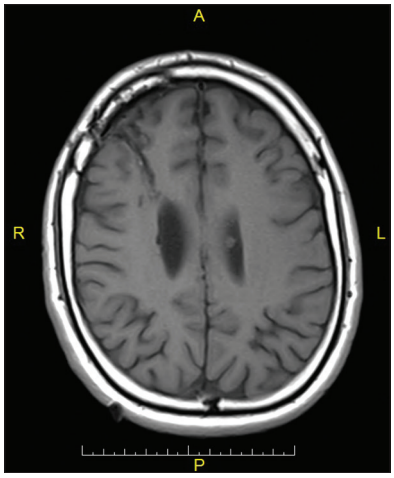

Figure 2: Magnetic resonance imaging performed 2 years after the surgery. No residual or recurrent masses are identified; there are no signs of intracranial hypertension, no extra-axial collections, or deviations from the midline

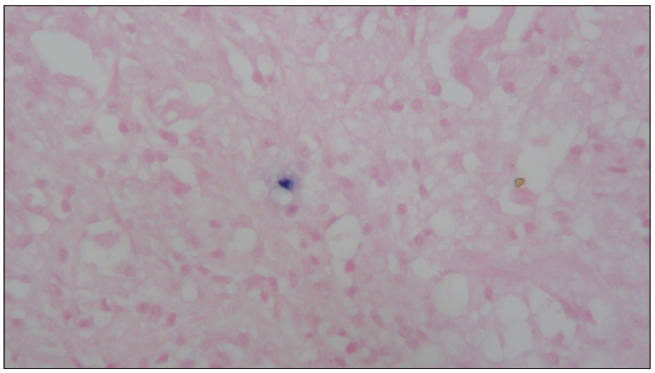

Figure 4: *In situ* hybridization for Epstein-Barr virus, with some expression in lymphoid cells

Table 1: Radiological Comparison: lymphomatoid granulomatosis and central nervous system lymphoma

Lymphomatous granulomatosis	CNS lymphoma
Intraparenchymal lesions, which may be unifocal or multifocal, supra or infratentorial[3,22]	Solitary lesions located in the cerebral parenchyma, most cases are supratentorial (75-81%), with a small percentage affecting the leptomeninges[1,7,21]
Lesions with solid or ring-like enhancement, with variable degree of edema associated with leptomeningeal enhancement[3,22]	In immunocompetent patients, 90% have a homogeneous enhancement and 10% have a ring-like enhancement. In immunocompromised, patients there is irregular enhancement, and, in up to 75% of cases, ring-like enhancement[7,11,21]
On T1-weigthed imaging, lesions have a low signal intensity, and varying intensities on T2[7,11,21]	MRI reveals lesions that appear as clearly delineated masses, iso to hypointense on T1, and mostly hypointense on T2 for immunocompetent patients[7,11,21]
No favorable response to treatment with corticosteroids or chemotherapy	Favorable to response to treatment with chemotherapyr[13,18]

CNS: Central nervous system,MRI: Magnetic resonance imaging

Table 2: Summary of image findings in various reports

Reference	Number of cases	Location	Treatment	Outcome	Follow-up
Ishiura *et al*., 2008[9]	1	Pons, cerebellum, and cortex	Rituximab (375 mg/m^2, once weekly) for 4 weeks	Resolution of lesions Improvement of neurological manifestations No recurrence	18 months
Patsalides *et al*., 2005[17]	25	Varied	Interferon alpha and chemotherapy	Lacunar infarctions in 3 patients Complete resolution of neurologic manifestations in 4 patients Partial improvement in 5 3 died from systemic manifestations of disease	2 to 19 months
González-Darder *et al*., 2011[5]	4	Left cerebellar hemisphere	Whole brain and spine radiotherapy, and chemotherapy	No local recurrence, died of systemic disease	3 years
		Left temporal lobe, cavernous sinus, orbital apex	Combined chemotherapy and whole brain and spine radiotherapy	Improvement of neurological deficits No recurrence	4 years
		Right temporal lobe	Total surgical resection	No recurrence	5 years
		Left cavernous sinus and orbital apex	High dose steroid pulses before surgery Continued low-dose steroid treatment after surgery	Improvement of neurological symptoms No recurrence	2 years
Yang *et al*., 2011[23]	1	Cerebellum	Not reported	Not reported	Not reported
Gupta *et al*., 2010[6]	1	Left frontoparietal	Systemic combination chemotherapy, whole brain radiotherapy	Resolution of symptoms No recurrence	6 months
Tateishi *et al*., 2001[22]	4	Right parietal lobe, corpus callosum, brain stem	Pulsed and maintenance corticosteroid treatment and radiation therapy	Recurrence 15 months after radiation therapy Died	Not reported
		Occipital lobe, cerebellum, brain stem	Pulsed and maintenance corticosteroid treatment Followed by cyclophosphamide	Partial remission	Not reported
		Cerebral cortex, bilaterally	Pulsed and maintenance corticosteroid treatment and radiation therapy	Relapsing-remitting clinical course	Not reported
		Cerebellum, brainstem, right cingulate gyrus	Pulsed and maintenance corticosteroid treatment and radiation therapy	Partial remission	Not reported
Okuda *et al*., 2008[15]	1	Right cerebellar hemisphere, Left occipital lobe	Steroid pulse therapy	No malignant transformation, no signs of recurrence	3.5 years

Contd...

Table 2: Contd...

Reference	Number of cases	Location	Treatment	Outcome	Follow-up
Seifried *et al*., 2007[20]	1	Subcortical	High dose steroid treatment before diagnosis Three cycles of Rituximab and prednisolone Later added cyclophosphamide	Died of cardiovascular failure	3 months

Two years after the surgery the patient continued to be free of seizures, and his MRI showed no evidence of new lesions, areas of restriction of diffusion, or anomalous enhancements that could indicate residual or recurrent tumor [Figure 2].

DISCUSSION

LG is a lymphoproliferative disorder, in which tumorous B cells transform after infection with the Epstein-Barr virus.[4] This disease has a mortality rate of 60–90% and cerebral involvement occurs in 30% of cases. Primary CNS involvement is rare, being higher in men (2:1) with or without immunosuppression.[16,19]

The pathogenesis of LG is unknown. Studies based on clinicopathological, immunophenotypic, and clonal evidence have shown that this is a unique type of extranodal, malignant lymphoma.[12] Tumor cells are often found to be accompanied by plasmatic cells, immunoblastic lymphoid cells, small CD4+ T cells, and histiocytes. Occasionally, neutrophils and eosinophils are also found [Figures 3 and 4].[4]

LG can be graded based on the relative amount of tumor reactive cells and accompanying tumor cells.[4,14] When there is a predominance of small lymphocytes without cytological atypia, less than five Epstein-Barr virus (EBV) infected cells, and no necrosis, the condition may be said to be Grade 1. Grade 2 is characterized by a variable number of lymphoid cells transformed by EBV (5–20) and some necrosis. In Grade 3, there are more EBV-transformed cells (more than 20), some small lymphocytes, and larger areas of necrosis.[13,19]

Radiological, lymphomatoid granulomatosis (LG) appearance in a brain computed tomography (CT) varies. It is common to find intraparenchymal lesions, which may be unilateral or multifocal, supra or infratentorial. These lesions may appear as low-density areas within the cerebral white matter; they may be solid or ring-like, sometimes with accompanying edema.[22]

Because of its angiocentric and angiodestructive character, LG can debut with intraparenchymal hemorrhage, stroke, or aneurysms.[4,22] Cerebral angiography may reveal changes consistent with vasculitis.[22]

LG and CNS lymphoma share similar radiological features that may be difficult to distinguish on an MRI or CT image [Table 1].

Our patient, unlike what literature reports [Table 2], responded well to chemotherapy with rituximab and prednisolone (4 cycles every 2 months). Whether tumor resection prior to chemotherapy is the cause of success or not in tumor control is a subject of discussion. Blood–brain barrier penetrance of rituximab is poor, which means a potential deficit in its CNS tumor control ability.[2] Several reports have mentioned rituximab to be a good option, however, it would be advisable to procure a total resection as in high-grade gliomas prior to chemotherapy. Is necessary to do further research to answer this question.

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Conflicts of interest
There are no conflicts of interest.

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