Association of Brain Lymphoma and WHO Grade II Oligodendroglioma in a Same Immunocompetent Patient

A 59-year-old man with no previous medical history presented with generalized seizures in December 2006. Brain magnetic resonance imaging (MRI) revealed a unique nonenhancing T1 hypointense and fluid-attenuated inversion-recovery (FLAIR) hyperintense lesion, involving the left frontal lobe (Fig 1). Awake surgery with intraoperative language mapping was performed, with a complete resection verified on postoperative MRI. The neuropathologic examination demonstrated a WHO grade 2 oligodendroglioma (Fig 2).

There was a codeletion 1p19q.

The patient had no postoperative deficit and returned to a normal life. Neither radiotherapy nor chemotherapy was administrated. Corticosteroid therapy with prednisolone was stopped 6 weeks after surgery. Follow-up cerebral MRIs conducted at 3 months and 9 months revealed no signs of tumor recurrence. The patient had no seizures under levetiracetam treatment at 2 g/d during 15 months. The patient was rehospitalized in March 2008 for complex partial status epilepticus with slowness of initiation and a persistent motor aphasia. He was afebrile with normal laboratory results. Brain MRI showed multiple lesions, involving the right temporal, frontal, and central regions, with a hypersignal on T2 FLAIR and contrast uptake on injected T1 (Fig 3A). Sudden occurrence of multifocal enhanced contralhemispheric lesions after more than 1 year of complete stabilization was very atypical for a WHO grade 2 glioma. Immunologic evaluation as well as lumbar puncture were normal, with normal cytchemistry, lactate dehydrogenase, and Beta 2 microglobulin assays. HIV, Epstein-Barr virus, Herpes virus, and cytomegalovirus serologies were negative. The ophthalmologic examination was also normal, especially with no uveitis. Epilepsy was controlled under fosphenytoin. Corticosteroid therapy with prednisolone at 1 mg/kg was administrated, with neurologic improvement. A new MRI performed 1 month later revealed a total disappearance of the right hemispheric lesion (Fig 3B).

Such history was not compatible with anaplastic transformation of a WHO grade 2 glioma.

Corticosteroid therapy was progressively decreased in 5 months. At this moment, the patient again presented with repeated partial epileptic seizures, with reoccurrence of language disorders combined to a right hemihyparesis. A new cerebral MRI revealed the appearance of several nodular contrast uptakes involving both hemispheres as well as the corpus callosum, and associated with a left frontoinsular hyperintensity on FLAIR-weighted MRI (Fig 4). A cerebral biopsy was thus performed, with no corticosteroid therapy. The neuropathologic study described lesions demonstrating a diffuse large B-cell lymphoma, polymorphic centroblastic type (revised European-American lymphoma [REAL] classification). On immunocytochemistry, the CD20 and the MUM1 were strongly positive (Fig 5).

The pelvic-abdominal-thoracic scanner as well as the positron emission tomography scan did not reveal any abnormalities. It was, therefore, a primitive non-Hodgkin’s cerebral lymphoma. It is worth noting that the samples from the first surgery 18 months before were re-examined, with confirmation of the diagnosis of WHO grade 2 oligodendroglioma. Chemotherapy was instituted with an RMVB
protocol (methotrexate, lomustine, etoposide, and prednisolone). Clinical and biologic tolerance was good. His neurologic status improved. A control MRI 2 months after the treatment revealed a dramatic shrink of the size of the lesions. Additional cycles of chemotherapy were administered during 6 months, adding rituximab to the previous protocol, and after an autologous narrow graft. Brain irradiation was also performed at the end of the chemotherapy. Presently, with 9 months of follow-up since the interruption of the oncologic treatment, the patient has a normal life with no neurologic deficit and no seizures (Karnofsky performance status, 90). All the lesions disappeared on brain MRI (Fig 6).

To our knowledge, this is the first report of an association between a WHO grade 2 glioma and a primitive non-Hodgkin’s cerebral lymphoma, in the same immunocompetent patient with negative HIV, Epstein-Barr virus, and cytomegalovirus serologies—leading to difficulties in diagnosis and therapeutic management. Three cases of association of oligodendrogliomas and lymphomas have been reported in a recent article. However, these did not involve cerebral lymphomas. The three cases involved large B-cell lymphomas, occurring several months after the diagnosis of oligodendroglioma with anaplastic transformation. A lymphoma of the neck was involved in the first case, stomach in the second case, and a disseminated lymphoma in the third case. One fatal case, despite chemotherapy, of a
The shrink of the lesions on repeated MRIs can be considered favorable. Associated with a less favorable prognosis. The tumor-suppressor chromosome 6q seems more frequent than in systemic lymphomas and is associated with any virus. At the molecular level, the deletion of chromosome 6q seems more frequent than in systemic lymphomas and is associated with a less favorable prognosis. The tumor-suppressor gene PTPRK, located in this region, could be involved in the oncogenesis of these tumors. Furthermore, relatively recent work suggests that the tumor cells involved in PCL originate from germinal centers of activated B-cell-like phenotypes, which could explain their poor prognosis compared to systemic B-cell lymphoma.

Mechanisms of gliomagenesis are also poorly understood. The oligodendrogliomas are distinguished from astrocytic tumors by the rarity of mutations of the TP53 gene and by the frequent codeletion of chromosomes 1p and 19q. Moreover, it was recently demonstrated that IDH1 mutation was frequently encountered in WHO grade 2 glioma, was tightly associated with a 1p19q codeleted genotype, and was associated with a better outcome. Therefore, the different molecular mechanisms underlying origin of PCL versus WHO grade 2 glioma may explain why their association was never described before our case.

In practice, our report shows that when the clinical and MRI history is not in agreement with the natural course of a WHO grade 2 glioma (ie, a slow and continuous growth of the mean diameter), notably in case of acute occurrence of multifocal and bilateral enhancing lesions, and especially if they are able to dramatically shrink spontaneously or after corticosteroid therapy, a search for a cerebral lymphoma should be performed. Moreover, because the patient currently enjoys a normal life (> 3 years after the first symptom) without oncologic therapy, we suggest that active and parallel treatments (adapted both for glioma and PCL) should be systematically considered in presence of these two tumors, with the goal to optimize survival and quality of life.

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AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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