# Glioblastoma Multiforme in Multiple Sclerosis: A Diagnostic Challenge

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## OBJECTIVE

To present a diagnostically-challenging case of glioblastoma multiforme (GBM) in a patient with longstanding relapsing remitting multiple sclerosis (RRMS).

## BACKGROUND

The concurrence of long-standing multiple sclerosis (MS) and GBM is a rare, but well-documented phenomenon that has been presented in a number of case reports. Due to the clinical and radiographic resemblance between GBM and an acute MS exacerbation, GBM in this setting remains a diagnostic challenge that is often missed in its early stages. No clear consensus has been made regarding predisposing risk factors or identifiable associations between GBM and MS. Prior hypotheses suggest a possible role for immunosuppression, tumor growth in areas of MS plaques, and/or de novo tumor occurrence, although science is still lacking in these areas due to rarity of this concurrence.

## CASE REPORT

Forty-five-year-old, right-handed woman with history of RRMS diagnosed in 2006 with initial manifestations including numbness and tingling in both legs and gait imbalance. She was started on glatiramer acetate at that time although the details of her piror work-up are unknown.

Over the following few years, she failed multiple disease modifying therapies including glatiramer acetate, interferone beta 1a, and interferone beta 1b and was therefore started on natalizumab in 2009. Due to JC virus antibodies being positive, this was discontinued in 2011. Fingolimod caused bradycardia so was never initiated and she was eventually started on mycophenolate mofetil in 2012.

She presented to the hospital in September 2013 with worsening left hemiparesis with MRI brain showing a contrast-enhancing lesion in the left frontal subcortical area suspected to be a new MS exacerbation or progressive multifocal leukoencephalopathy. Lumbar puncture was performed and cerebrospinal fluid (CSF) analysis revealed normal leukocytes, RBCs, and glucose and was negative for JC virus DNA. CSF protein was mildly elevated at 63mg/dl. She was started on intravenous steroids with significant improvement of her symptoms and was discharged home on an oral steroid taper.

Within two weeks of discharge, the patient developed complex partial seizures with repeat imaging revealing rapid growth of the contrast-enhancing lesion. Biopsy of the lesion confirmed the diagnosis of GBM.

## NEURORADIOGRAPHIC FINDINGS

08/26/13 09/07/13

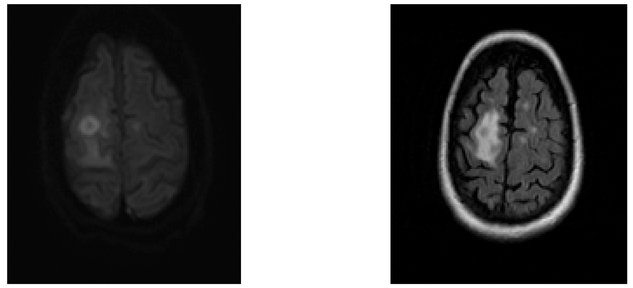

**Fig. 1: MRI diffusion-weighted images**

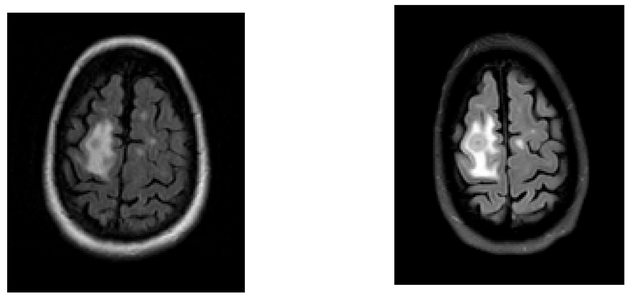

**Fig. 2: MRI T2/FLAIR images**

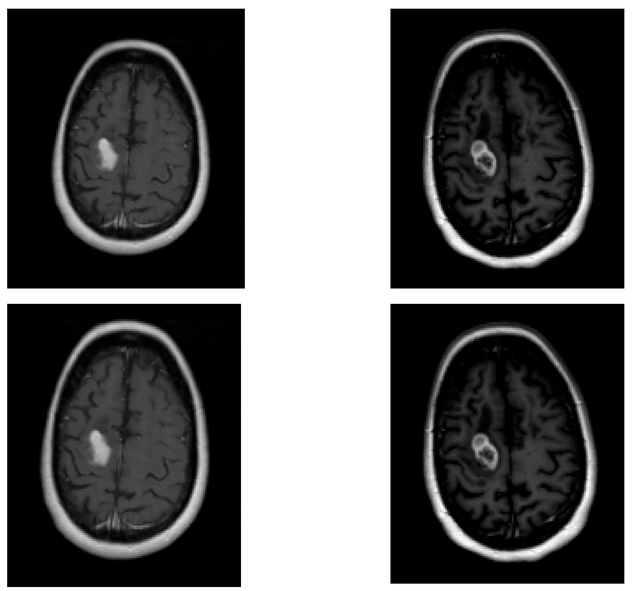

**Fig. 3, row 1: MRI T1 without contrast images**
**Fig 3, row 2: MRI T1 with contrast images**

## DISCUSSION

Our case represents a unique and diagnostically-challenging case of concurrent GBM and MS. The first suggestion brain tumors in patients with MS was described by Bosh in 1912. Since that time, extraordinary advances in neuromimaging have made possible earlier and more accurate diagnosis of neurologic diseases like MS. Such advances have also presented physicians with an often difficult task of recognizing and diagnosing disease when neuroimaging studies are unclear.

One case series reviewed MS patients who underwent autopsy and found that six percent of lesions were incorrect diagnoses, of those 0.57% were primary central nervous system neoplasms.

The debate about concomitant glioma and MS began in 1983 when Sherer described a case of MS with acute findings of periventricular gliomatosis which he called *glioblastomatose en plaque* suggesting an increased propensity for development of glioma within long-standing MS plaques. In each of the case reports we reviewed, glioma was discovered in patient's with long-standing, often severe forms of MS, highlighting the question of a causal relatonship beween the two. Opinions regarding this cause-and-effect hypothesis still differ and more research is necessary to more clearly understand the relationship between glioma and MS.

## CONCLUSION

Recognition of the possibility of central nervous system (CNS) tumors in patients with previously-diagnosed MS is important because it presents a diagnostic dilemma. In addition, early recognition may alter the course of management in such patients and potentially patient outcome. Our case presents insight into these diagnostically-challenging cases as well as raises further question regarding the association between disease-modifying therapy (DMT) and CNS tumors.

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