



MULTI-CENTRIC GLIOMA MIMICKING MULTIPLE SCLEROSIS

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<p>Article Info <i>Received 15/01/2015</i> <i>Revised 27/02/2015</i> <i>Accepted 25/03/2015</i></p> <p>Key words: multifocal glioma, multiple sclerosis, stereotactic biopsy, high grade gliomas</p>	<p>ABSTRACT High-grade gliomas (HGG) and multiple sclerosis (MS) can be multi-focal and have similar radiographic appearance making neurosurgical intervention imperative to establish correct diagnosis and appropriate treatment. The authors describe a 44 years old male who presented with a left facial weakness. Magnetic resonance imaging (MRI) demonstrated several T2-weighted image and FLAIR hyperintensity lesions, as well as a large cystic lesion within the right basal ganglia with mild peripheral bright T2-weighted image and FLAIR signal. CSF was negative for viral antibodies and oligoclonal bands; IgG were normal. A clinical diagnosis of MS was made and the patient prescribed prednisone. Six months after symptoms’ onset, the patient’s weakness progressed to a left hemiparesis. A repeated brain MRI demonstrated an increase in size of the cystic lesion and faintly ring enhancement. Additional hyperintense lesions in the left centrum semiovale and throughout the corpus callosum were seen. MR perfusion images showed increased blood flow and blood volume within the superior aspect of the right basal ganglia. A brain biopsy revealed an anaplastic astrocytoma WHO III. This report highlights the importance of tissue diagnosis when radiographic appearance is not definitive and treatment strategies for MS are not successful.</p>
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INTRODUCTION

High-grade gliomas (HGG) represent the most common primary brain tumor in adults, with an incidence of 5–10 per 100,000 people annually [1]. Although most gliomas are solitary lesions, multiple gliomas have an incidence ranging from 0.5% to 20% [2-5] among all patients with gliomas. HGG with multiple lesions are generally categorized in two groups: multicentric, if they arise independently in multiple sites presenting as widely separated lesions, or multifocal, if they spread from the primary focus to other parenchymal area(s), growing through dissemination along an established route, spreading through commissural pathways, CSF channels, blood, or through local extension with satellite formations[6].

MS is one of the most common diseases of the central nervous system, and has a variety of clinical and radiological presentations. The diagnosis of MS is mainly

based on the clinical symptoms and supported by CSF protein electrophoresis, IgG banding, and MRI findings. However, lack of oligoclonal bands in the CSF is reported in up to 10 % of cases [7,8].

Several cases of demyelinating processes mimicking a mass lesion have been reported, where the MS lesion was indistinguishable from a brain tumor [9-18], however the reverse, a multi-centric glioma mimicking MS, is not reported.

The MRI features of multi-centric gliomas and MS have been reported, [2,19,20]. However, at times, the radiographic diagnosis combined with the neurological presentation and other laboratory findings might not be sufficient to establish a definitive diagnosis. This report addresses one such case where ultimately tissue diagnosis was necessary to establish the correct diagnosis and start the appropriate treatment.



Case report:

A 44 years old male with a past medical history of hypertension, presented with a one month history of progressive left facial weakness. Brain MRI revealed bright bilateral lesions on T2-weighted image and FLAIR within the subcortical, periventricular and callosal white matter, as well as a cystic lesion within the right basal ganglia with mild amount of peripheral signal hyperintensity on T2 weighted image and on FLAIR (Figure 1). CSF was negative for viral antibodies and oligoclonal bands with normal IgG. A clinical diagnosis of demyelinating disease was made. The patient was started on prednisone (60mg/day).

Six months later, the patient also began to experience difficulty with balance, had several falls, and developed a left hemiparesis. A new MRI with advanced imaging demonstrated additional new lesions and an increase in size of the cystic lesion. Perfusion brain assessment showed increased blood flow and blood

volume within the superior aspect of the right basal ganglia (Figure 2a, 2b).

An exploratory craniotomy for cortical wedge resection of the right frontal lesion and stereotactic aspiration of the right basal ganglia cyst with biopsy was performed. Approximately 10 cc of yellow clear fluid were aspirated from the cyst. Histopathological examination of the right basal ganglia was consistent with WHOIII HGG and the right frontal tissue with astrocytoma WHO II (Figure 3). The immunohistochemical phenotype revealed widespread numerous glial cells reactive for WT1, scattered parenchymal cell nuclei reactive for p53, and an elevated Ki67 with scattered reactive atypical nuclei. Post-operatively, the patient's left sided weakness and spasticity demonstrated marked improvement, which was sustained during the outpatient post-operative visits. The patient was treated with radiation therapy and concomitant temozolomide (TMZ), followed by TMZ cycles.

Figure 1. MR images T2WI (A,B), T1WI after contrast (C,D) and FLAIR (E,F,G,H) at presentation demonstrate bilateral hemispheric lesions within the subcortical white matter and corpus callosum and a cystic lesion within the right basal ganglia. Axial T1 contrast images (C,D) demonstrates a lack of enhancement.

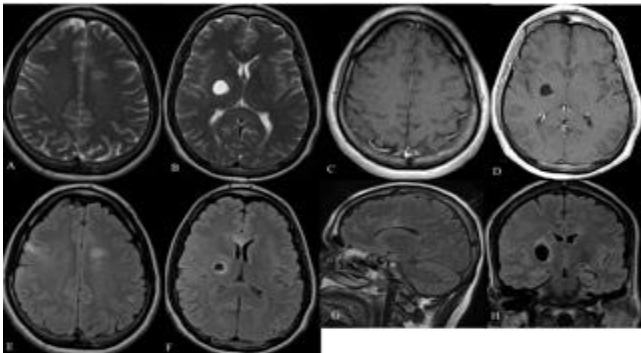


Figure 2b. MR perfusion imaging. Note the increased blood flow (A, B) and blood volume (D, E) within the superior aspect of the cystic lesion (arrow) and the decreased flow and volume centrally (*). The left frontal white matter lesion demonstrates elevated blood flow (C) and blood volume (F) (arrow). Increased blood flow and volume are not typical of demyelination and supportive of glioma.

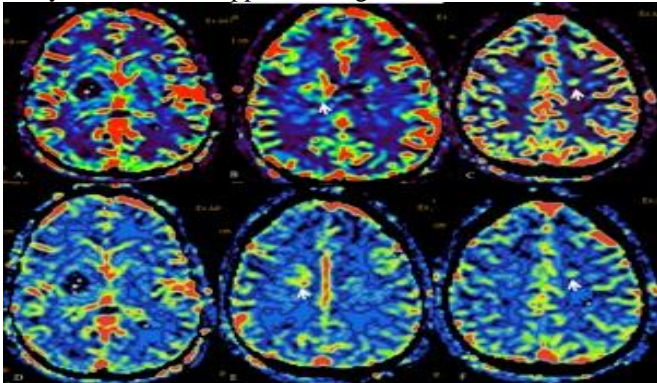


Figure 2a. MR images T2WI (A, B), T1WI after contrast (C, D) and FLAIR (E,F,G,H) six month after prednisone therapy demonstrate lesion progression. Additionally, the cystic lesion appears slightly bigger and with a faintly ring enhancement (D).

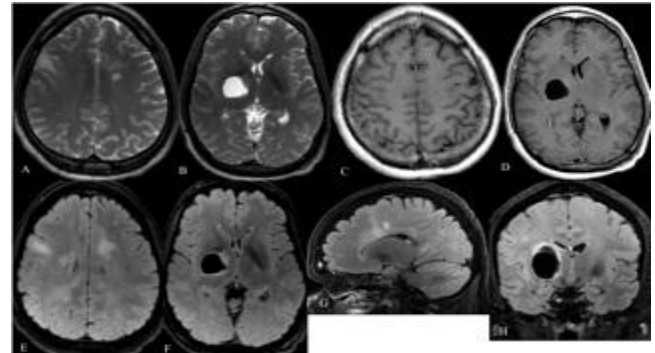
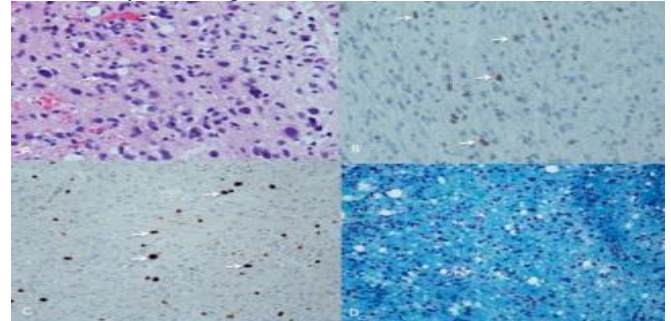


Figure 3. Microphotographs of right basal ganglia lesion stereotactic biopsy demonstrate (A) moderately cellular infiltrate with pleomorphic astrocytic cells with irregular nuclei and nucleic membranes (arrows), (B) p53- positive cells (arrows), (C) MIB1/Ki67-positive cells (arrows), and (D) preserved myelin sheath. A: Hematoxylin-eosin stain; B: Immunohistochemistry for p53; C: Immunohistochemistry for MIB1/Ki67(C); D: Luxol Fast Blue for myelin. Mag: 40X.



DISCUSSION

The resemblance of MS lesions to brain tumors is encountered in about 1% of cases and differentiation of these remains difficult [21]. In our case, the patient treated for presumptive MS did not improve and brain biopsy was obtained showing a multi-focal HGG. Since the treatment options for these two conditions are drastically different, this case highlights the importance of tissue diagnosis.

The radiological features of multi-focal gliomas have been reported on MR as hypo- or isointense lesions on T1 and hyperintense on T2 and FLAIR. These lesions enhance strongly after contrast administration in a heterogeneous or ring-enhancing fashion, at times associated with moderate edema and mass effect [19]. Meningeal or ventricular enhancement, suggestive of a possible way of dissemination, is rare [19]. The classical appearance of MS plaques is ovoid lesion, bright on T2-weighted image and on FLAIR, predominantly in the periventricular white matter but also frequently located in the corpus callosum, subcortical region, optic nerve, and at times infra-tentorial. MS lesions do not produce focal space-occupying lesions and although acutely, these lesions may enhance, they do not usually present ring enhancement [22]. They can also present with a minimal surrounding edema and mass effect relative to the size of the lesions [23].

Several publications reported on MS lesions mistaken for tumor [9-18,24,25], however the reverse, a case of multi-focal glioma mimicking MS, is not documented in the literature. In this reported case, given the patient's relatively mild symptoms and the radiological

findings on the initial MR, a clinical diagnosis of MS was reasonable at presentation. The diagnosis of tumefactive demyelinating lesion, an uncommon manifestation of demyelinating disease, was considered in the differential. Its incidence is reported to be 1-2/1000 MS cases. It is defined in radiological terms as pseudotumoural demyelinating lesions greater than 2 cm and they are normally well circumscribed lesions with a predilection for the frontal and parietal lobes [26]. In this subtype of MS, CSF findings are less likely to be positive for oligoclonal bands [27], which was the result in our patient. However, as treatment strategies proved unsuccessful and the symptoms evolved the need for MR with advanced imaging was obvious. This suggested the presence of highly metabolic lesion corroborating the need for tissue diagnosis.

This case highlights the importance of ruling out the diagnosis of multi-focal glioma in patients with clinical and radiographic findings suggestive of MS with persistent symptoms after steroids administration trial.

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DISCLOSURES

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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