American Journal of Brain Disorders & Tumors
ISSN 2641-2454

Case Report Open Access

Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report.

Aseem Mehra[1*] Sandeep Grover[2*] Rahul Chakravarty[3*]

Dr. Alberto Negro, M.D., Neuroradiology Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail:Alberto.Negro@hotmail.it;
Dr.ssa Mariaevelina Prudente, M.D., Neuroradiology Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail: evelinaprudente@hotmail.it
Dr.ssa Ottavia Vargas, M.D., Neuroradiology Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail:ottaviavargas@gmail.com
Dr.ssa Rossana Scala, M.D., Neurology Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail:rosscala@libero.it
Dr.ssa Antonella Capasso, M.D., Pathological Anatomy Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail:antonella.capasso24@libero.it
Dr. Alessandro Villa, M.D., Neurosurgery Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail:alessandrovilla@gmail.com
Dr.ssa Pasqualina Giordano, M.D., Oncology Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA, e-mail:giopas@email.it

***Corresponding Author: Dr. Alberto Negro, M.D.,** Neuroradiology Department Ospedale del Mare Via Enrico Russo, 80147 Napoli NA; E-mail: Alberto.Negro@hotmail.it

Citation: Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report. Am J Bra Dis and Tum. 2019; 3(1): 01-05.

Submitted: 12 September 2020; **Approved:** 16 September 2020; **Published:** 18 September 2020

Abstract

Autoimmune encephalitis (AE) also known as autoimmune limbic encephalitis (ALE) is diagnosed based on clinical presentation, magnetic resonance imaging (MRI) findings and identification of specific associated autoantibodies. The autoantibody test is not always available in many centers and its negativity does not exclude AE. For these reasons, the status of Ab was not included in the recent consensus document as part of the required diagnostic criteria , especially in order to prevent delays in starting immunotherapy. Therefore it is possible that other (AE-like) conditions may be diagnosed and treated as AE. We present an atypical case of high-grade, isocitrate dehydrogenase (IDH) wildtype glioma with limbic system infiltration, mimicking the clinical and radiographic features of an AE/ALE, in order to emphasize this unusual and confusing clinical presentation.

Keywords: Autoimmune encephalitis; Brain Glioma; MRI

INTRODUCTION

Autoimmune encephalitis (AE) also known as autoimmune limbic encephalitis (ALE) is diagnosed based on clinical presentation, magnetic resonance imaging (MRI) findings and identification of specific associated autoantibodies. Patients often have seizures, subacute memory deficits, psychiatric and behavioral symptoms, variously combined with each other. Typical MRI anomalies include hyperintense signal on T2-weighted fluid-reversed reversal recovery sequences (FLAIR),which selectively involve limbic structures, unilaterally or bilaterally. The autoantibody test is not always available in many centers and its negativity does not exclude AE. For these reasons, the status of Ab was not included in the recent consensus document as part of the required diagnostic criteria , especially in order to prevent delays in starting immunotherapy. Therefore it is possible that other (AE-like) conditions may be diagnosed and treated as AE.

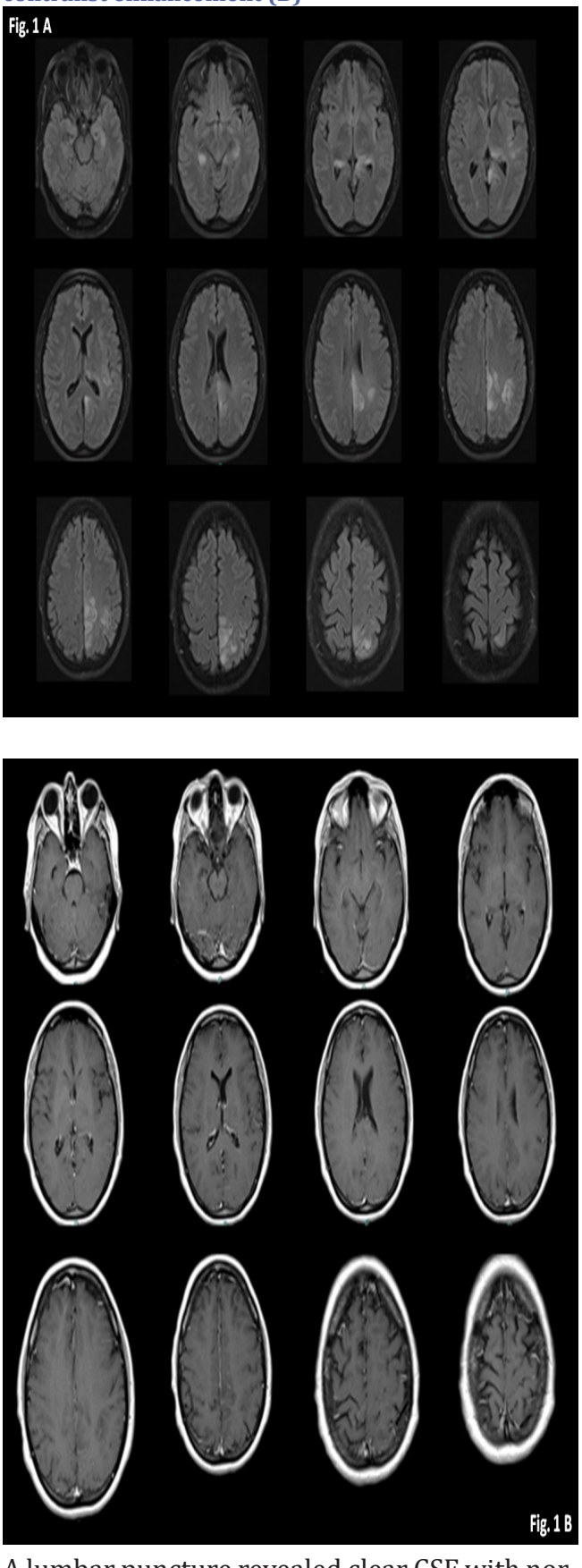
Cite this article: Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report. Am J Bra Dis and Tum. 2019; 3(1): 01-05.

Primary brain tumor presenting as AE is rare. Symptoms at presentation usually are represented by those of an increased intracranial pressure related condition (e.g. nonspecific headache, nausea / vomiting) and focal deficits, which reflect the location of the tumor (e.g. hemiparesis, aphasia or field defect visual). Rarely, all these symptoms may be absent and the patients may develop a syndrome characterized by cognitive, behavioral and epileptic characteristics can be prominent. The radiological characteristics of GBM are quite typical in the advanced stages of the disease. They are represented by central necrosis, contrast enhancement and edema of the surrounding white matter. In many cases, however, it takes time for these changes to occur, especially when GBM results from the evolution of a lower grade glioma. To date, it is particularly difficult to differentiate AE from neoplastic disorders limited to the mesial temporal lobes. Our knowledge is largely unsatisfactory and based mainly on case reports. Moreover, diagnostic delay could result in unnecessary and potentially dangerous initiation of stepwise immunotherapy escalation, as expected for refractory cases of AE (1). We present an atypical case of high-grade, isocitrate dehydrogenase (IDH) wildtype glioma with limbic system infiltration, mimicking the clinical and radiographic features of an AE/ALE, in order to emphasize this unusual and confusing clinical presentation.

Case report:

A previously active 50 -year-old woman was brought to the emergency room (ER) with generalized convulsive status epilepticus, requiring admission to the intensive care unit (ICU). After successful status treatment, anterograde amnesia, disorientation and a mild motor deficit in the upper right limb persisted. The brain MRI exam showed bilaterally temporal, left thalamic and left insular posterior parietal occipital lesions, hyperintense on T2-weighted and FLAIR images (Fig. 1 A and B) without contrast enhancement.

Fig. 1: Bilaterally temporal, left thalamic and left insular posterior parietal occipital lesions, hyperintense on T2-weighted and FLAIR images (A), without contranst enhancement (B)

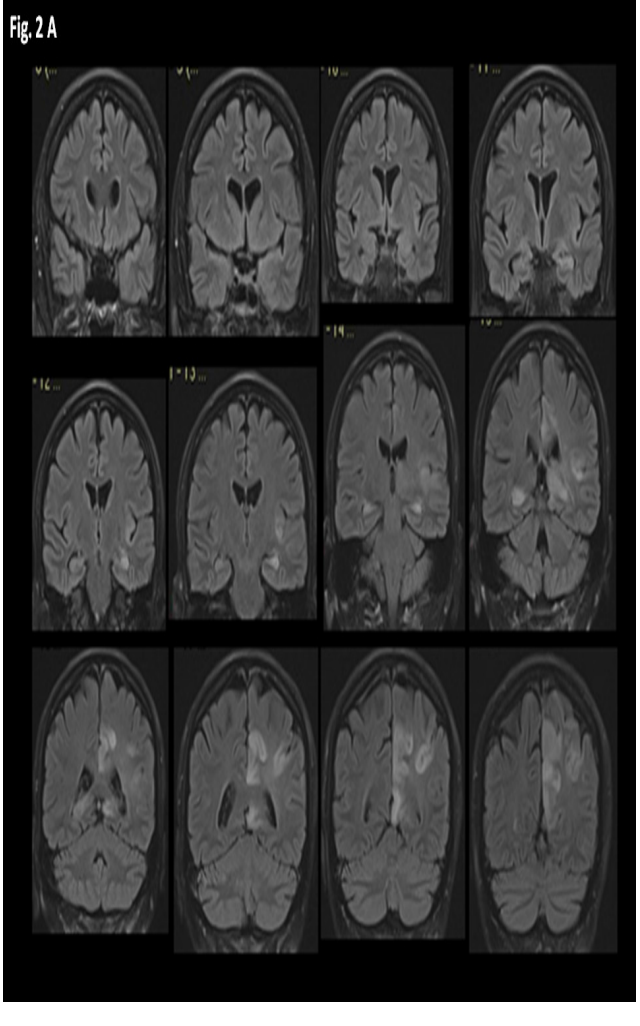


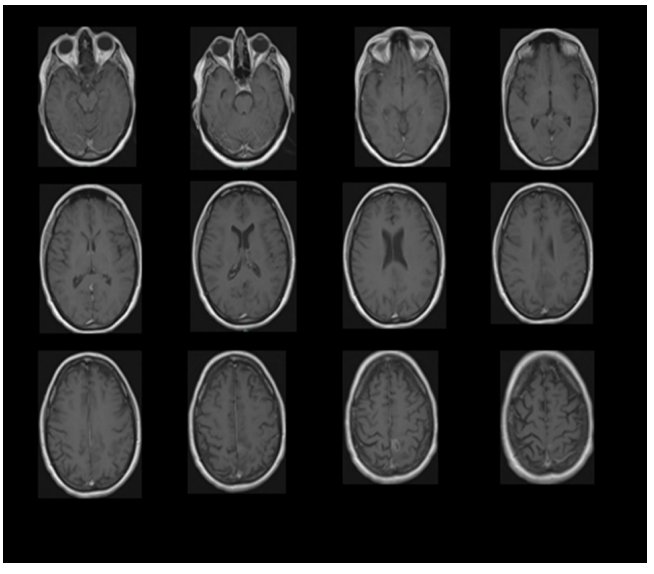
A lumbar puncture revealed clear CSF with normal cell count and glucose level, a protein level of 38 mg/dl without oligoclonal bands (OCBs).

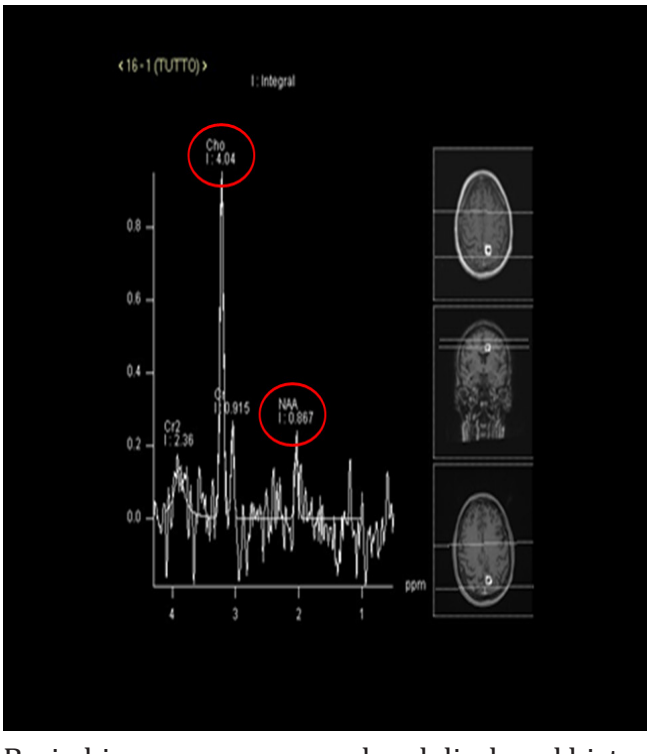
Cite this article: Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report. Am J Bra Dis and Tum. 2019; 3(1): 01-05.

Considering the patient's age and the clinical presentation, a preliminary diagnosis of autoimmune encephalitis was made and treatment with steroid bolus and antiepileptic drugs were administered with a noticeable improvement in symptoms improvement. Immunohistochemisty and cell-based assays for antibodies against cell surface or synaptic proteins were performed in CSF, with negative results. 25 days later, after symptom onset, on control brain MRI, the initial lesions were confirmed and a lesion enlargement was detected in left posterior parietal occipital region, showing the classic ring shape enhancement and a central necrotic area. Increased Cho/NAA ratio Cho/Cr ratio and a Lip/Lactate peak were detected on MR spectroscopy (Fig. 2A, B and C).

Fig. 2: The initial lesions were confirmed (A and B) and a lesion enlargement was detected in left posterior parietal occipital region, showing the classic ring shape enhancement and a central necrotic area. Increased Cho/NAA ratio Cho/Cr ratio and a Lip/Lactate peak were detected on MRI spectroscopy (Fig. 2 B and C).







Brain biopsy was proposed and disclosed histologic evidence of highly aggressive GBM (isocitrate dehydrogenase, IDH1 and IDH2 wild type, without 1p19q codeletion and without promoter methylation of the methyl-guanine methyl transferase (MGMT) gene.

Discussion:

The early identification of a subset of GBM patients with an AE-like presentation is of utmost importance, for both therapeutic and prognostic implications. In the present case report, we demonstrate that GBM can incorrectly suggest an AE/ALE and that to identify this condition, a high index of suspicion and close MRI follow-up are needed. We found bilaterally MRI signal changes

Cite this article: Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report. Am J Bra Dis and Tum. 2019; 3(1): 01-05.

in hippocampal regions. Although bilateral temporo-mesial involvement on brain MRI is largely considered as strongly suggestive of an inflammatory or infectious process, Vogrig. A. et al. (1) found that up to 54% of the patients with an AE-like presentation of GBM had bilateral involvement. These data suggest that bilateral involvement should not lead to the exclusion of alternative diagnosis, particularly neoplastic causes. Bilateral distribution within the hippocampi in our case, parallels the fact that nearly 9% of high-grade gliomas can present initially with unilateral findings which become multifocal over time. Tumor spread is hypothesized to occur via white matter pathways between lesions (2). Careful re-evaluation of initial FLAIR sequences disclosed a modest mass effect in the deep thalamic region and in the posterior parietal region of the left hemisphere. However some degree of edema and even amygdala enlargement is frequently described in AE patients. Moreover our patient presented with prolonged seizures and status epilepticus, which could potentially cause hippocampal MRI abnormalities on FLAIR and diffusion-weighted imaging (DWI) sequences related to seizure-induced neuronal injury. In our patient the initial brain MRI study did not show contrast enhancement while a control brain MRI—performed 1 month after the first admission—showed the unprecedented appearance of left posterior parietal contrast enhancement with the classic ring shape enhancement and a central necrotic area. An increased Cho/NAA and Cho/Cr were detected on MR spectroscopy, in favor of a neoplastic hypothesis. We acknowledge that one possible reason for the misinterpretation of GBM imaging findings as AE was the absence of MR spectroscopy on initial imaging. In the literature, there is one report on MR spectroscopy findings in NMDAR-encephalitis demonstrated atypical features. Vogrig et al. (1) had the same experience with one case that expresses extensive demyelination. This is in agreement with the known difficulty to differentiate high-grade gliomas and acute demyelinating lesions (e.g., in multiple sclerosis) using spectroscopy alone. The presence of contrast enhancement reflects blood brain barrier disruption and its occurrence is not sufficient to distinguishbetween neoplastic and inflammatory lesions.

In a series of 50 patients with paraneoplastic limbic encephalitis, 25 patients had temporal lobe abnormalities on T2-weighted sequences and 5 showed contrast enhancement (3). Vogrig et al. (1) found that five patients exhibited slight, patchy, contrast enhancement, but none of them showed the classic ring shape enhancement, with a central necrotic area, which is more indicative of GBM. This pattern was in fact observed only in the advanced stage of the disease. The absence of isocitrate dehydrogenase (IDH) mutation, like in the study of Vogrig et al. is consistent with a classical primary GBM and not with a secondary evolution of a low-grade glioma. The absence of contrast enhancement at the initial stage as well as the CSF inflammation could be related to a specific unknown molecular characteristic of these GBMs as reported in oligodendrogliomas. Immunohistochemisty and cell-based assays for antibodies against cell surface or synaptic proteins were performed in CSF of our studied patient, with negative results. However while the detection of autoantibodies can establish a diagnosis of ALE, it is not needed in the current diagnostic criteria. Testing for autoantibodies remains clinically important to help clarify the possibility of a paraneoplastic process and prognosis. Furthermore, the detection of a relevant autoantibody in those patients that do not fully meet the formal diagnostic criteria can help establish a diagnosis. Although, as in our case , the criterion of bilateral brain abnormalities highly restricted to the medial temporal lobes is highly suggestive of an autoimmune etiology rather than glioma. In conclusion, an alternative diagnosis of glioblastoma should be considered in all patients presenting initially as AE, especially if they are middle-aged/ elderly with a poor clinical evolution despite initial improvement presenting with limbic lesions and seizures, not only male, unlike suggested by Vogrig A. et al. (1). Brain biopsy should be considered in indeterminate cases. Future larger scale studies are needed to confirm the potential role of MR spectroscopy in differentiating AE from glioma lesions. In everyday practice, our recommendation is to implement the use of advanced MRI techniques in the approach of patients with suspected encephalitis and to perform a close MRI follow-up to avoid diagnostic pitfalls.

Cite this article: Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report. Am J Bra Dis and Tum. 2019; 3(1): 01-05.

Referances

1) Glioblastoma as differential diagnosis of autoimmune encephalitis. Vogrig A, Joubert B, Ducray F, Thomas L, Izquierdo C, Decaestecker K, Martinaud O, Gerardin E, Grand S, Honnorat J. J Neurol. 2018 Mar;265(3):669-677. doi: 10.1007/s00415-018-8767-1. Epub 2018 Jan 30. PMID: 29383516

2) Glioblastoma as an autoimmune limbic encephalitis mimic: A case and review of the literature. Macchi ZA, Kleinschmidt-DeMasters BK, Orjuela KD, Pastula DM, Piquet AL, Baca CB. J Neuroimmunol. 2020 Mar 7;342:577214. doi: 10.1016/j.jneuroim.2020.577214. [Epub ahead of print] PMID:32182452).

3) Gultekin SH, Rosenfeld MR, Voltz R, Eichen J, Posner JB, Dalmau J (2000) Paraneoplastic limbic encephalitis: neurological symptoms, immunological findings and tumour association in 5 patients. Brain 123(Pt 7):1481–1494

Cite this article: Multiform Glioblastoma with a mimicking limbic autoimmune encephalitis-like onset: evaluation of clinical and MRI changes in a case report. Am J Bra Dis and Tum. 2019; 3(1): 01-05.