

# Giant cells glioblastoma: case report and pathological analysis from this uncommon subtype of glioma

Telmo A.B. Belsuzarri,<sup>1</sup>  
 João F.M. Araujo,<sup>1</sup>  
 Aginaldo P. Catanoco,<sup>1</sup>  
 Maick W.F. Neves,<sup>1</sup> Rodrigo A.S. Sola,<sup>1</sup>  
 Juliano N. Navarro,<sup>1</sup> Leandro G. Brito,<sup>1</sup>  
 Nilton R. Silva Junior,<sup>1</sup>  
 Luis Otavio C. Pontelli,<sup>1</sup>  
 Luiz Gustavo A. Mattos,<sup>1</sup>  
 Tiago F. Gonçalves,<sup>1</sup> Wolnei M. Zeviani,<sup>1</sup>  
 Renata M.B. Marques<sup>2</sup>

<sup>1</sup>Department of Neurosurgery and

<sup>2</sup>Department of Pathology, Maternity Hospital of Celso Pierro, Pontifical Catholic University of Campinas, São Paulo, Brazil

## Abstract

Glioblastoma multiforme (GBM) is the most common glial tumor of the brain system; nevertheless, the giant cell (GC) subtype is uncommon. Recent reviews report for an incidence of 1% in adults and 3% in children. The GCs usually have a better prognosis than GBM and also an increasing long-term survival rate. It is known that the diagnosis of this tumor is due to its histological findings and patterns, such as the unusual increased number of giant cells. Unfortunately, due to its rarity, the immunohistochemical and cytogenetical analysis of this tumor is not well known. Some authors also suggest that there are few subtypes of GCs and their patterns of aggressiveness could be due to cytogenetical markers. It is recognized that maximum safe resection treatment and adjuvant radiotherapy can improve survival rate (5-13 months) similar to GBM patients.

## Introduction

Glioblastoma multiforme (GBM) is a high-grade glioma of the central nervous system associated with high morbidity and/or mortality. According to the WHO classification of brain tumors, there are two subtypes of GBM: the giant cells and the gliosarcomas. Giant cell glioblastoma (GC) is an uncommon subtype of GBMs accounting for 1% of them. Due to the rarity of the cases, epidemiology, natural history and follow up, it is not well defined. It has been hypothesized that GC has a better out-

come and higher survival rates than GBM, due to several reasons, such as the age of diagnosis, histopathological and genetic differences etc.. The standard treatment for GBM is the Stupp protocol with maximum safe resection, adjuvant radiotherapy and temozolamide. Nevertheless, due to its rarity, the clinical and prognostic significance of the treatment with Stupp protocol and the extent of resection (EOR) is not well known. However, there is evidence to suggest that EOR and adjuvant therapy serve as prognosticators for long-term survival.

A literature review was made by searching in several databases (Pubmed, Bireme and Cochrane) the following key words: glioblastoma multiforme, giant cell glioblastoma, genetic, immunohistochemical, long-term survivals

The objectives of this study are i) to report a case of giant cell glioblastoma with clinical, radiological and histology analysis, ii) review the immunohistochemical and genetic findings in GC to be compared to GBM, iii) to discuss the possible reasons of different outcomes.

## Case Report

A 58-year-old white male, with a history of complete right hemiparesis associated with Broca's aphasia, was referred to our hospital, without family suspicion of stroke. At initial examination, patient had a Glasgow:12, with motor deficit and aphasia. Computed tomography (CT) scan was performed: it showed a 3-cm-diameter mass lesion with edema, enhancement with contrast and midline deviation of 5 mm. A magnetic resonance imaging (MRI) was also performed, showing an extended lesion with infiltration of the pre/pos central gyri, the posterior limb of the internal capsule with a heterogenic surface, small cysts and apparent necrosis inside (Figure 1A-C). After examination patient was diagnosed with GBM and surgery was performed.

After surgery, the patient had a worsening of the motor deficit, remaining with the motor aphasia and therefore underwent another CT scan (Figure 1D). The pathology conclusion was a GCG (Figure 2). He was then referred for adjuvant radio/chemotherapy, with 10 months follow up.

## Discussion

Glioblastoma multiforme is the most common primary brain tumor, but the GC subtype is uncommon and also has a different prognosis. In a recent review was found that only 1%

Correspondence: Telmo Augusto Barba Belsuzarri, Av. John Boyd Dunlop s/n. Campinas, São Paulo 13060-803, Brazil.  
 Fax: +55.193.343.8600.  
 E-mail: telmobelsuzarri@hotmail.com

Key words: glioblastoma multiforme, giant cell glioblastoma, genetic, immunohistochemical, long-term survival.

Contributions: TABB, design of the work, data acquisition and analysis; JFMA and APC, critical revision; MWF, RASS, JNN, LGB, NRSJ, LOCP, LGAM, TFG, WMZ, RMB, data collection.

Conflict of interest: the authors declare no potential conflict of interest.

Received for publication: 12 September 2014.

Revision received: 17 December 2014.

Accepted for publication: 18 December 2014.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright T.A.B. Belsuzarri et al., 2015  
 Licensee PAGEPress, Italy  
 Rare Tumors 2015; 7:5634  
 doi:10.4081/rt.2015.5634

of 16,430 cases were GCs,<sup>1</sup> which is also proved by other authors.<sup>2,3</sup> Some other studies account for 5% of GBM,<sup>4,5</sup> In the literature there are less than 100 cases reported.<sup>6</sup>

The mean age is 51 years, 11 years less than GBM, and about 27.5% of GCs occur in patients with less than 40 years. The most common location are the frontal and temporal lobe, and rarely the multifocal.<sup>1</sup> At pediatric age group GBM is about 5-10% of all intracranial neoplasms and GC's are 3% of GBM's at this age group.<sup>7</sup>

Even though both tumors have poor outcomes and overall survival rate, an increased median survival is observed in GC, with 11 months compared to 8 months in GBM. Also, long term survival (5 years) is more frequent in GC (12,3%) than GBM (3,4%).<sup>1,4</sup> Taemin and Rutkowski reported a recent series of 20 patients,<sup>8</sup> with a median age of 47.9 years and a median survival of 15.4 months, congruent to other reports.<sup>1</sup> As firstly described by Meyer,<sup>9</sup> in histological analysis GBM has a predominance of multinucleated giant cells with abundant cytoplasm, which can reach up to 500 nm with abundant reticulin fibers, and it was used to be called monstrocellular brain tumor.<sup>7</sup> Its pathology diagnosis is made by morphology and histological architecture. However, recent studies have also shown that among GC, there are immunohistochemical differences that could lead to GCs subtypes, and that could maybe explain the increased survival rate in

some cases.<sup>10,11</sup> At immunohistochemical analysis, both giant cells/non-giant cells are positive for glial fibrillary acidic protein (GFAP), S100 protein and vimentin; in giant cells nuclei are positive to proliferation of cell nuclear antigen (PCNA) and Ki-67;<sup>12</sup> so there is no specific immunohistochemical for this kind of tumor. At cytogenetic and molecular genetic analyses, microsatellite instability is more frequent in GC than GBM (30% vs 7.8%), TP53 mutation is observed in 83.3%, but epidermal growth factor receptor is uncommon (8.3%). Chromosome 10 deletion is found in all non-giant cells of the GC; at GBM it is found

in 45%. GC has more p53 mutations than GBM, but p16 deletion, MD2M and CD4K amplifications are rare.<sup>10,11,13,14</sup>

Long-term survival (LTS), considered as more than 3 years survival, has been reported in about 3-5% of all GBM. Kraus *et al.* found that about 25% of all LTS were actually mistaken with anaplastic oligodendroglioma. The LTS is associated with the disease free period, suggesting that are different grown factors and courses.<sup>15-17</sup>

The giant cell variety is associated with the presence of giant cell subtype in LTS patients,<sup>2</sup> in almost 30% of the cases.<sup>3,14,18</sup> Some authors

suggest that extremely long-term survival case series could have been misclassified with the pleomorphic xanthoastrocytoma, which is most common in younger patients and has better outcomes; but in a recent review, it was proved that excluding patients with less than 40 years, the survival median rate was unchanged.<sup>14</sup>

There are several hypothesis for the increased survival rate and number of LTS patients. Some authors suggest that the increased survival rate is due to younger presenting age in patients with GC. Others suggest that the margins and circumscription of the GC lesion are more visible and this could lead to better resection.<sup>1</sup> However, Taemin and Rutkowski found a overall mortality of 75% and a median time to death of 13.1 months for gross total resection, and a mortality rate of 93% and a median time to death of 15.4 months in the subtotal resection, which could not reach statistical significance.<sup>8</sup>

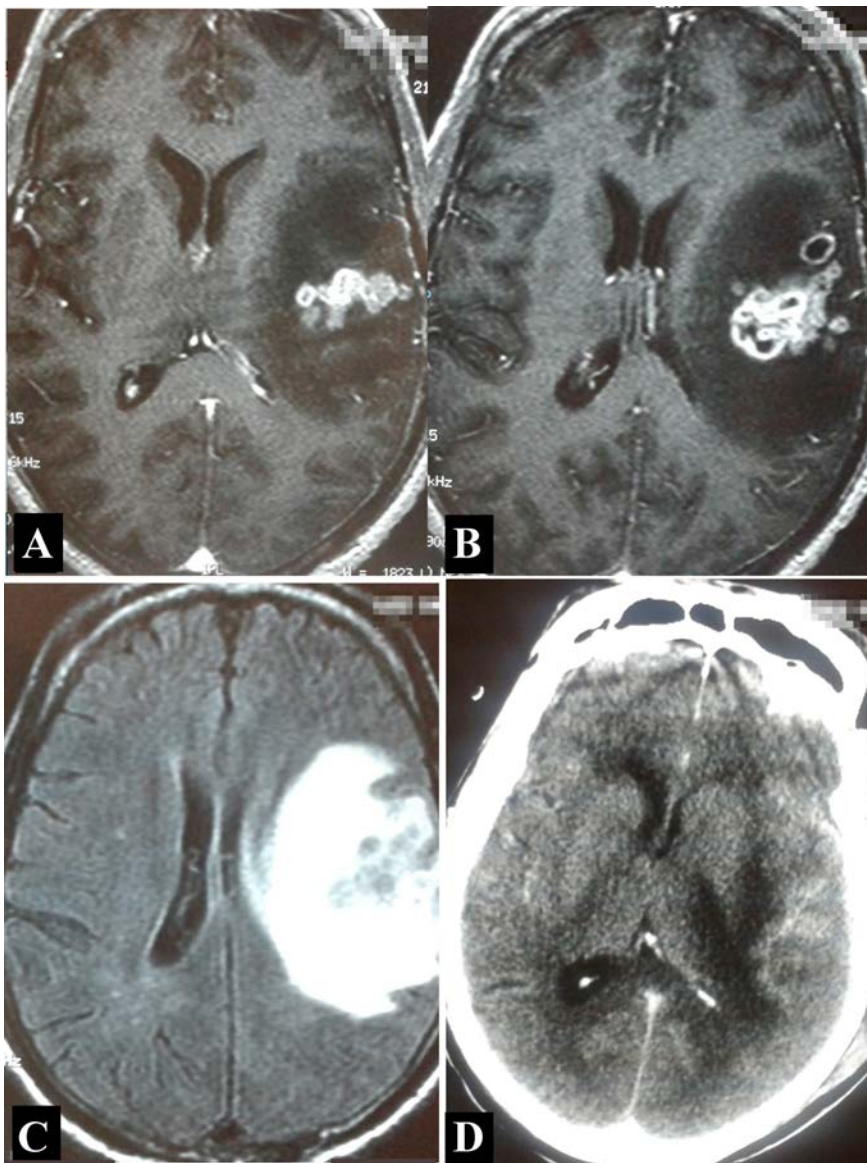


Figure 1. A,B) Magnetic resonance imaging (MRI) T1 with contrast demonstrating the heterogeneity of the tumor and cerebral edema, with contrast enhanced cysts. C) MRI T2 FLAIR demonstrating the heterogeneity of the tumor and cerebral edema, with multiple cysts inside. D) Post-operative computed tomography with contrast showing no contrast enhanced lesion.

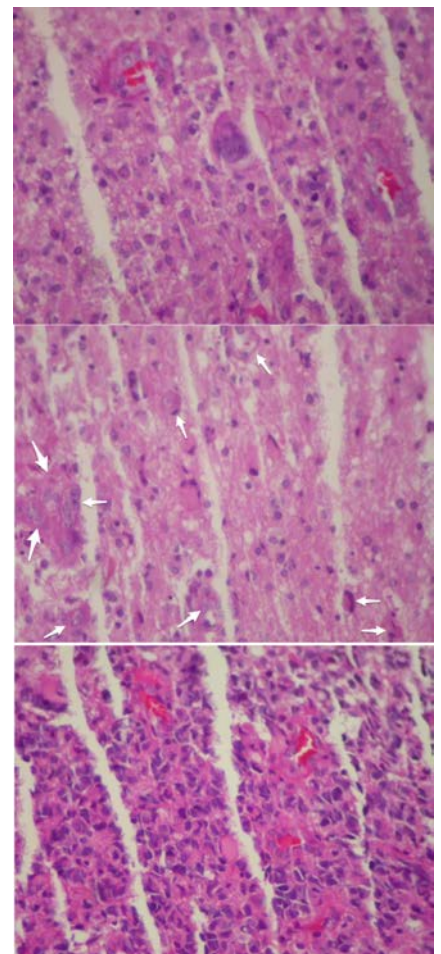


Figure 2. Histology: a giant cell and an increased number of giant cells (arrows) and pleomorphic zone with more aggressive component.

On the other hand, it is believed that the immunohistochemical and genetic differences, as discussed before, could lead to a better prognosis.

The surgical management is still uncertain due to the rarity of these cases, but it is known that maximum safe resection treatment and adjuvant radiotherapy can improve survival rate from 5 to 13 months, similarly to GBM patients.<sup>1</sup>

## Conclusions

Giant cell glioblastoma is a rare subtype of classic GBM with different pathology, genetic and immunohistochemical markers and a better prognosis, but it is still under study. Due to its rarity, case series and reports are necessary to understand the tumor behavior. Recent retrospective reviews have shown an increased survival rate of GCG and maximum safe surgical treatment associated with adjuvant radiotherapy seems to be the best choice.

## References

1. Kozak KR, Moody JS. Giant cell glioblastoma: a glioblastoma subtype with distinct epidemiology and superior prognosis. *Neuro Oncol* 2009;11:833-41.
2. Burger PC, Vollmer RT. Histologic factors of prognostic significance in the glioblastoma multiforme. *Cancer* 1980;46:1179-86.
3. Shinjima N, Kochi M, Hamada JI, et al. The influence of sex and the presence of giant cells on postoperative long-term survival in adult patients with supratentorial glioblastoma multiforme. *J Neurosurg* 2004;101:219-26.
4. Folgueral JMV, Mascarenhas L, Costa JA, et al. Giant cell glioblastoma: review of the literature and illustrated case. *Neurocirugía (Astur)*.2008 19:343-9.
5. Palma L, Celli P, Maleci A, et al. Malignant monstrocellular brain tumors: a study of 42 surgically treated cases. *Acta Neurochir (Wien)* 1989;97:17-25.
6. Ohgaki H, Peraud A, Nakazato Y, et al, ed. World Health Organization classification of tumours: pathology and genetics of tumours of the nervous system. Lyon: IARC Press; 2000. pp. 40-41.
7. Borkar SA, Lakshmi Prasad G, Subbarao KC, et al. Giant cell glioblastoma in pediatric age group: report of two cases. *J Pediatr Neurosci* 2013;8:38-40.
8. Oh T, Rutkowski MJ, Safaei M, et al. Survival outcomes of giant cell glioblastoma: institutional experience in the management of 20 patients. *J Clin Neurosci* 2014;21:2129-34.
9. Meyer O. Ein besonderer Typus von Riesenzellengliom. *Frankf Z Pathol* 1913;14:185-203.
10. Temme A, Geiger KD, Wiedemuth R, et al. Giant cell glioblastoma is associated with altered aurora b expression and concomitant p53 mutation. *J Neuropathol Exp Neurol* 2010;69:632-42.
11. Martinez R, Roggendorf W, Baretton G, et al. Cytogenetic and molecular genetic analyses of giant cell glioblastoma multiforme reveal distinct profiles in giant cell and non-giant cell subpopulations. *Cancer Genet Cytogenet* 2007;175:26-34.
12. Katoh M, Aida T, Sugimoto S, et al. Immunohistochemical analysis of giant cell glioblastoma. *Pathol Int* 1995;45:275-82.
13. Kraus JA, Wenghoefer M, Schmidt MC, et al. Long-term survival of glioblastoma multiforme: importance of histopathological reevaluation. *J Neurol* 2000;247:455-60.
14. Naydenov E, Bussarsky V, Nachev S, et al. Long-term survival of a patient with giant cell glioblastoma: case report and review of the literature. *Case Rep Oncol* 2009;2:103-10.
15. Filippini G, Falcone C, Boiardi A, et al. Prognostic factors for survival in 676 consecutive patients with newly diagnosed primary glioblastoma. *Neuro Oncol* 2008;10:79-87.
16. Mineo JF, Quintin-Roue I, Lucas B, et al. [Glioblastomas: clinical study and search for prognostic factors]. *Neurochirurgie* 2002;48:500-9. [Article in French].
17. Chandler KL, Prados MD, Malec M, Wilson CB. Long-term survival in patients with glioblastoma multiforme. *Neurosurgery* 1993;32:716-20.
18. Deb P, Sharma, MC, Mahapatra, AK, et al. Glioblastoma multiforme with long term survival. *Neurol India* 2005 53:329-32.