

Aggressive giant cell glioblastoma with negative p53 expression: case report

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ABSTRACT

Glioblastoma (GBM) is the most common intrinsic brain tumor in adults, accounting for 67% of primary brain tumors. Giant cell glioblastoma (GCG) is a rare variation of GBM, occurring in less than 5% of the cases. GCG has been demonstrated to affect younger patients and have a more indolent course than traditional GBM with longer survival rates. Age, surgical resection, and genetic features are likely related with better prognosis. The presence of a p53 mutation is found in 75% of GCG with this more indolent behavior. We present a case of a 72 years-old female who presented with an extremely aggressive GCG without p53 expression who had an unusually rapid neurological deterioration and tumor regrowth after surgical excision.

KEYWORDS

Glioblastoma, astrocytoma, brain neoplasms.

RESUMO

Glioblastoma de células gigantes agressivo com expressão negativa do p53: relato de caso
Glioblastoma (GBM) é o mais comum tumor cerebral intrínseco em adultos e representa cerca de 67% dos tumores cerebrais primários. O glioblastoma de células gigantes (GCG) é uma variante infrequente dos GBMs, ocorrendo em menos de 5% dos casos. GCGs aparentemente afetam pacientes mais jovens e apresentam um curso mais indolente que os tradicionais GBMs, com taxas mais longas de sobrevivência. Idade, ressecção cirúrgica e características genéticas parecem estar relacionadas com melhor prognóstico. A presença de mutação no gene p53 é encontrada em cerca de 75% dos GCGs com esse comportamento mais indolente. Apresentamos o caso de uma paciente de 72 anos com um GCG extremamente agressivo e sem expressão do p53, que teve incomum e rápida deterioração neurológica e recidiva tumoral após cirurgia.

PALAVRAS-CHAVE

Glioblastoma, astrocitoma, neoplasias encefálicas.

Introduction

Giant cell glioblastoma (GCG) accounts for 0.8% of brain tumors^{1,2} and has distinguished pathological and clinical features from traditional glioblastomas (GBM)² including higher incidence of p53 mutations compared with GBM.^{2,3} We present a case of an older patient that was diagnosed with GCG without p53 gene expression and had unusually rapid disease progression.

Case report

A 72 years-old female presented with impaired speech and right-sided weakness. Computed tomography (CT) showed a left frontal mass with a large cystic component, perilesional edema, midline shift and heterogeneous contrast enhancement suggestive of a high-grade glioma (Figure 1a). The patient underwent surgery through a frontal craniotomy. Maximal debulking was obtained.

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A CT head was done in the immediate post-operative and showed subtotal tumor resection with significant reduction of the mass effect and midline shift (Figure 1b). Additional CT were done three and ten days after surgery showing a large tumor recurrence with significant worsening in the edema and contrast enhancement (Figure 1c). The patient evolved with progressive neurological deterioration, was eventually transferred to palliative care and died less than eight weeks after surgery.

Histological examination showed a densely cellular tumour with abundant, extremely pleomorphic multinucleated giant cells, endothelial proliferation and necrosis (Figures 2a and 2b). The cells expressed GFAP, the Ki67 proliferative index was high, and there was no nuclear reactivity for p53 (Figure 2c). The diagnosis was GCG without p53 expression.

Discussion

Gliomas are the most common primary brain tumors in adults (67% of all brain tumors)⁴ and high-grade gliomas account for only 2% of them but are the

4th cause of cancer-related deaths.⁵ GCG are a subtype of grade IV gliomas accounting for 1%-5% of GBM.^{1,6-8}

GCG are described as being an intermediate tumor between primary (or *de novo*) and secondary GBM (anaplastic transformation of low-grade tumors).⁸ Like secondary GBM, GCG usually affects younger patients (mean age of 42 years compared with 55 years of GB) with 35% occurring in patients under 40.^{1,6,8,9} GCG shared features of primary GBM are a short clinical history, absence of a less malignant precursor lesion and frequent phosphatase and tensin homologue (PTEN) mutations.⁷

In GCG, a slightly higher incidence in males has been reported without significant difference.^{1,5,6} Radiological features are similar to GBM, seen as a contrast enhancing heterogeneous mass with solid and cystic areas sometimes with the appearance of a mural nodule.

GCG are thought to be a less aggressive variation of grade IV gliomas, with longer mean survival rates (8 months for GBM and 11 months for GCG) and also reports of long-term survival been more common in GCG.^{1,9-11} The combination of factors such as age, extension of the surgical resection and genetic features are suggested to be responsible for longer survival.

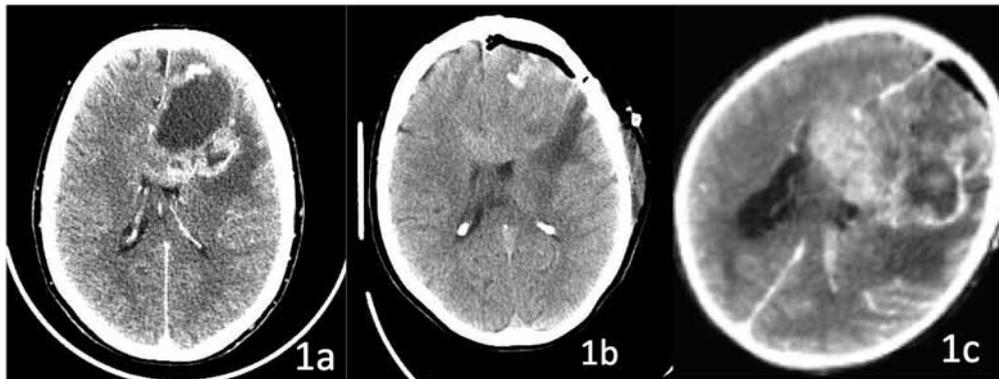


Figure 1 - (a,b) Hematoxylin and eosin stained sections showing multinucleated giant cells, endothelial proliferation and necrosis at 10X and 20X magnification. (c) Immunohistochemistry for p53 (Novocastra (D0-7) at 1:500 dilution) showing no expression at 20X magnification.

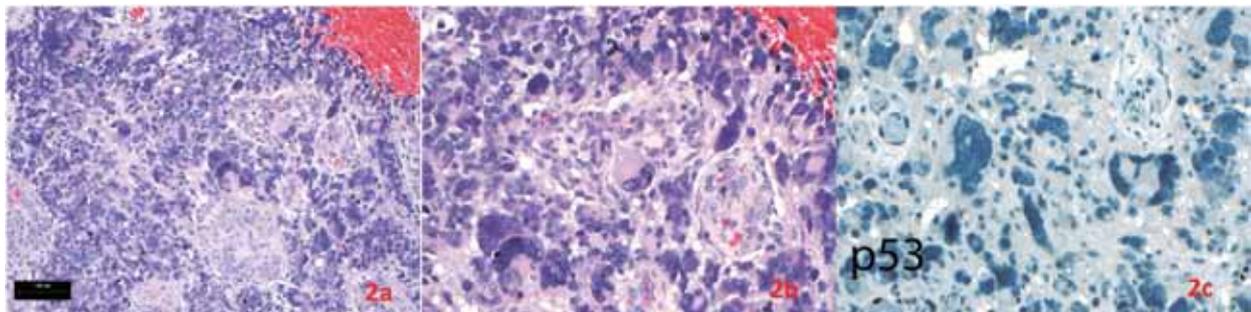


Figure 2 - (a) Preoperative CT showing contrast enhancing mass and cystic component. (b) Immediate postoperative CT showing satisfactory decompression. (c) Postoperative day #10 CT with aggressive regrowth of tumor.

GCG can be more circumscribed than GBM, evidenced by radiology and pathology, which can enable more complete tumor resection.¹ Other factor leading to a more complete resection includes fibrous stroma that may contribute to a better cleavage plan.² Another factor that may influence prognosis is the frequently seen tumor infiltration by leukocytes, which may be indicative of an augmented immune response.²

However, young age and extension of resection do not entirely explain the longer survival in this patient population. Tumor genetics and histology are important factors for prognosis and may explain the divergent clinical course of GCG and GBM. A p53 mutation is present in 75%-90% of GCG patients but only 30% of GBM.^{1,3,8,10,12} Its positivity on immunohistochemistry is a criteria recommended for GCG diagnosis^{2,3,7} and helps to differentiate these tumors from pleomorphic xanthoastrocytoma (PXA), a benign entity with some shared pathology features, plus p53 negative tumors.² Low rates of epidermal growth factor receptor (EGFR) amplification (~5% against 30%-40% of GBM) are another characteristic feature of GCG.^{3,13}

The current treatment strategy for GCG is similar to GBM. Patients benefit from maximal resection and adjuvant radio and chemotherapy.

GCG is an entity described as a less aggressive subtype of GBM with a slightly different genetic profile that preferentially affects younger patients. We presented a case of a patient with unusual characteristics for a GCG such as older age, negative p53 mutation and extremely rapid tumor regrowth. We were unable to find in the literature any evaluation of the p53 status and survival rates but maybe the absence of the p53 mutation, present in up to 75% of GCG, may be related to the aggressive tumor regrowth. Evolution of genetic profiling may help to guide surgical planning and adjunctive therapies in the future.

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