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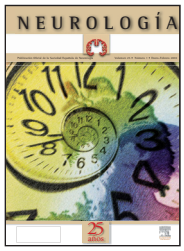

ORIGINAL ARTICLE

# Use of Bevacizumab for neurological complications during initial treatment of malignant gliomas

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**KEYWORDS**
High grade glioma;
Radiation necrosis;
Tumour progression;
Oedema;
Corticosteroids;
Bevacizumab

**Abstract**
*Introduction:* High grade gliomas are the most common primary malignant brain tumours. Treatment with chemoradiation and adjuvant chemotherapy with Temozolomide may prolong survival but some patients develop complications during or soon after therapy due to radiation necrosis, oedema or tumour progression.
*Patients:* We report the use of Bevacizumab in four patients with newly diagnosed high grade gliomas who developed cerebral oedema due to tumour progression or radiation necrosis that did not respond to corticosteroids, and who were not candidates for surgical debulking.
*Outcomes:* All four patients had a rapid response to treatment with bevacizumab, tolerating a decrease of the dose of corticosteroids, and were able to continue their standard therapy.
*Conclusions:* Bevacizumab is effective in controlling some of the neurological complications from oedema, radiation necrosis, or rapid tumour progression during the initial treatment of malignant gliomas.


**PALABRAS CLAVE**
Glioma de alto grado;
Radionecrosis;
Progresión tumoral;
Edema;

**Utilización de bevacizumab en las complicaciones neurológicas durante el tratamiento inicial de los gliomas malignos**

**Resumen**
*Introducción:* Los gliomas de alto grado son los tumores malignos más frecuentes del sistema nervioso central. El tratamiento con quimiorradioterapia y quimioterapia adyu-

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Corticoides;
Bevacizumab

vante con temozolomida puede prolongar la supervivencia, pero algunos pacientes desarrollan complicaciones durante o poco después de acabar el tratamiento debido a radionecrosis, edema o progresión tumoral.

*Pacientes y métodos:* Presentamos el uso de bevacizumab en 4 pacientes que desarrollaron edema cerebral en relación con radionecrosis o progresión tumoral durante la fase inicial del tratamiento, con respuesta inadecuada a los corticoides y que no eran subsidiarios de tratamiento quirúrgico por la localización de la lesión o la mala situación clínica.

*Resultados:* Los cuatro pacientes presentaron una rápida respuesta al tratamiento con bevacizumab, lo cual permitió reducir la dosis de corticoides y continuar el tratamiento estándar.

*Conclusiones:* Bevacizumab es efectivo en el control de algunas complicaciones neurológicas debidas a edema, radionecrosis o rápida progresión de tumores no extirpables durante el tratamiento inicial de los gliomas malignos.



## Introduction

High grade gliomas, including multiform glioblastoma (MGB) and anaplastic astrocytoma (AA), are the most frequent primary cerebral tumours. Mean survival varies with the histological grade: 14 months for MGB and 36 months for AA. Treatment of AA consists in surgery and radiation therapy whereas for MGB, surgery, chemoradiation therapy (temozolomide [TMZ] associated with external radiation therapy on the surgical bed) and 6 cycles of adjuvant chemotherapy with TMZ.[1] The treatments are generally well tolerated, which has contributed to an improvement in patients' quality of life. In some clinical situations, however, as in cases of extensive tumours in which it has not been possible to perform ample resection, or due to the development of radionecrosis during treatment, patients may present clinical deterioration that does not always respond to corticosteroids or that obliges the use of high doses causing intolerable side effects, all of which prevents the continuation of standard anti-tumour treatment. In such situations, the use of bevacizumab, a monoclonal antibody targeting the vascular endothelial growth factor (VEGF) that normalizes vascular patency[2,3] may be of therapeutic benefit. Furthermore, in 2009, the Food and Drug Administration (FDA) accelerated the approval process of this drug for the treatment of recurrent MGBs due to the good results in phase II studies.[4-6]

We report here on 4 patients with high-grade gliomas in which the clinical complications, including oedema, radionecrosis or tumour progression, prevented the continuation of the standard treatment. The use of bevacizumab quickly improved the patients' condition and allowed them to finish treatment.

## Patients

### Case 1

Male, 44 years old, diagnosed in September, 2009, as having left temporal AA after presenting several partial epileptic seizures. Sub-total extirpation was performed due to the location of the tumour. Following surgery, he presented right hemicorporal weakness and discreet aphasia. Six weeks after the surgical procedure, while he was in the first week of chemoradiation therapy, the patient presented deterioration in strength and language in connection with the oedema caused by the treatment, as well as tumour progression, neither of which improved with increased doses of corticosteroids (8 mg of dexametasone/day) (fig. 1). It was decided to start treatment with bevacizumab, which stabilized his clinical condition and allowed his corticosteroid to be clinical trial to one half of the dose, thus enabling him to finish the chemoradiation therapy with minimal morbidity (fig. 1).

### Case 2

Male, 39 years old, diagnosed in January, 2009, as having right fronto-parietal MGB after several episodes of partial seizures. Total extirpation of the tumour was performed and 4 weeks after the procedure he started treatment with radiation therapy. Chemotherapy was delayed by two weeks due to problems with his insurance. Four weeks after starting with radiation, the patient presented repeated epileptic seizures and, after a magnetic resonance image (MRI) showed it was a recurrence of the tumour, he received additional surgery. He subsequently had to be re-admitted due to an abscess in the surgical area for debriding and antibiotic treatment, so the chemoradiation therapy was suspended for a few weeks. Treatment was begun again with radiation therapy while he was receiving antibiotic treatment and the start of the chemotherapy was delayed until his antibiotic treatment was completed. On conclusion of the antibiotic treatment and radiation therapy, the patient presented mild left hemiparesis and an intact cognitive situation. Two weeks after finishing radiation therapy and before starting the 6 cycles of TMZ, while still under treatment with 24 mg of dexametasone per day, he was admitted for motor impairment and signs of mental confusion. An imaging test revealed a major cerebral oedema (fig. 2) and, since he had not responded to corticosteroid treatment, it was decided to use bevacizumab. A considerable improvement was observed within 48 hours and he could be discharged in 5 days (fig. 2). The week after the first dose of bevacizumab, the patient was able to attend the clinic visit by walking independently.