

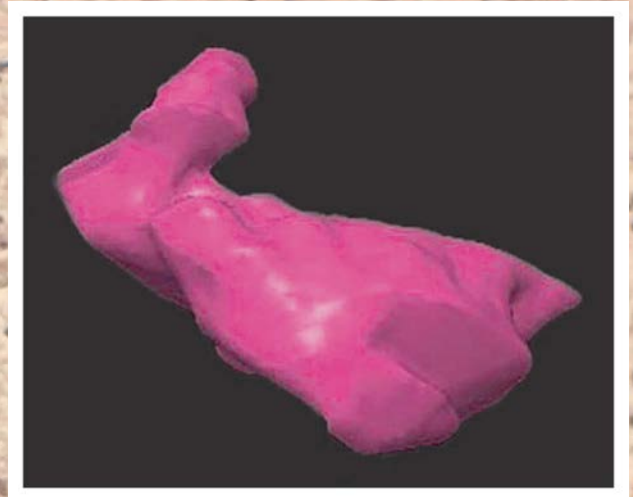
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**Case Report: Low-Grade Glioma
Refractory Epilepsy, VPA
Encephalopathy, and Chemotherapy
Supporting Seizure Control: A
Complex Case**

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Low-Grade Glioma, Refractory Epilepsy, VPA Encephalopathy, and Chemotherapy Supporting Seizure Control: A Complex Case

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■ Introduction

Seizures in patients with low-grade glioma are frequent and the most common leading symptom. Treatment of seizures in such patients can be challenging and sometimes a combination of several antiepileptic drugs is necessary.

We report on a patient with a long history of a low-grade glioma and seizures who developed a life-threatening complication of antiepileptic drug therapy.

■ Case Report

A 73-year-old male suffered from a fibrillary astrocytoma (WHO 2) of the left frontal lobe since 1989. Initial diagnosis was confirmed by biopsy. After surgery, focal radiotherapy with a dose of 60 Gy was performed. Initial focal seizures were controlled with phenytoin for a few years, but antiepileptic drug treatment had to be switched to carbamazepine and clonazepam due to seizure recurrence. In 2002, levetiracetam was added. The patient was followed up at other hospitals until July 2010, therefore seizure control could not be assessed. At this time, first radiological signs of progression of the tumour with new contrast enhancement lead to re-operation with partial resection. Post-OP histological diagnosis showed pure necrosis.

Over the next 16 months, seizure frequency increased and in February 2012, the patient was admitted to our centre due to frequent, daily focal seizures with and without impairment of consciousness. At this time, medication consisted of levetiracetam 3000 mg/d, topiramate 450 mg/d, and phenytoin 200 mg/d. Phenytoin was discontinued as it was suspected to worsen the patient's gait disturbance, which was primarily attributed to post-radiation white matter changes. Lacosamide and subsequently valproic acid were added without any effect on seizure frequency. MRI at this time showed a residual tumour with no clear signs of tumour progression. As a consequence of intractable seizures despite triple AED therapy, chemotherapy with temozolomide was recommended but not initiated due to acute deterioration of the clinical condition. Surgery was not recommended due to the risk of causing neurological deficits. Almost 2 weeks after the start of valproic acid at a dose of 1000 mg/d the patient became somnolent to stuporous with swallowing difficulties and developed aspiration pneumonia. Due to an elevated ammonium level of 69 $\mu\text{mol/l}$ (normal: 12–47 $\mu\text{mol/l}$) and continuous generalized slowing in the EEG, valproate-induced hyperammonemic encephalopathy was diagnosed. After abrupt discontinuation of

valproic acid and with antibiotic therapy the patient recovered. Triple therapy consisting of levetiracetam, topiramate, and phenytoin was again reintroduced and the seizures were well controlled until September 2012. At this time the patient experienced new seizure aggravation combined with cognitive decline. MRI now indicated tumour progression with signs of malignancy (Figure 1). Chemotherapy with temozolomide (dose-dense one week on/one week off [120–150 mg/m²]) was started and after one month seizures disappeared completely. Neurological status indicated no focal deficit, but moderate cognitive impairment, mild gait disorder, and a Karnofsky Performance Score (KPS) of 60.

■ Conclusions

Seizures are sometimes difficult to treat in patients with low-grade glioma. Multiple antiepileptic drug therapies harbour the risk of serious side effects as demonstrated in our patient. Valproate-induced encephalopathy is a rare but serious complication especially in older people. An increased risk in the

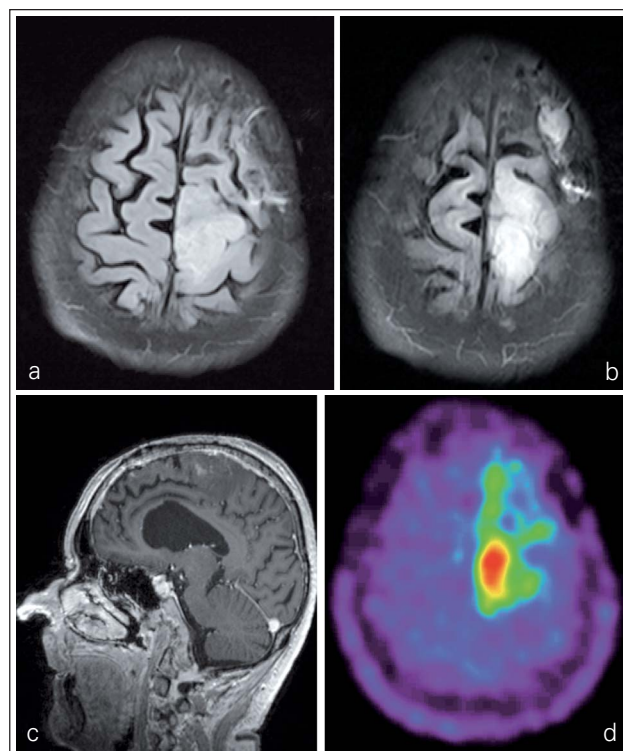


Figure 1: (a, b) MRI: FLAIR; (c) T1 with contrast media showing hyperintense cortical and subcortical signals with contrast enhancement at the left central region. (d) FET-PET increased FET metabolism in the left central region.

presence of topiramate is reported and may be a causative factor in this case [2].

Chemotherapy can positively affect seizure control in low-grade gliomas with or even without radiological signs of tumour response [1, 3, 4]. This treatment option can be taken into account especially in patients with uncontrolled seizures.

Some remarks on this case are necessary. Nowadays, early radiotherapy of low-grade glioma is not the standard of care. Moreover, today 50 Gy are recommended in low-grade glioma in order to reduce late toxicity as occurred in our patient with a high dose of 60 Gy (radionecrosis and white matter changes after 21 years). Surveillance at a centre with both epilepsy and neuro-oncology expertise is crucial in such patients.

During treatment with temozolomide, cognition as well as gait improved and the patient has been on therapy for 2 months with a KPS of 70.

References:

1. Van Breemen MS, Rijnsman RM, Taphoorn MJ, et al. Efficacy of anti-epileptic drugs in patients with gliomas and seizures. *J Neurol* 2009; 256: 1519–26.
2. Noh Y, Kim DW, Chu K, et al. Topiramate increases the risk of valproic acid-induced encephalopathy. *Epilepsia* 2013; 54: e1–e4.
3. Sherman JH, Moldovan K, Yeoh HK, et al. Impact of temozolomide chemotherapy on seizure frequency in patients with low-grade gliomas. *J Neurosurg* 2011; 114: 1617–21.
4. Hu A, Xu Z, Kim RY, et al. Seizure control: a secondary benefit of chemotherapeutic temozolomide in brain cancer patients. *Epilepsy Res* 2011; 95: 270–2.

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