Case Report

Incidentalomas to glioblastoma multiforme

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In April 1999, a 25-year-old male underwent magnetic resonance imaging (MRI) as a control subject for a multiple sclerosis study. The scan serendipitously revealed two lesions (‘incidentalomas’) in the right frontal lobe. Initially, he was asymptomatic and was monitored with interval MRI scans. After years of monitoring, contact was accidentally lost. He later presented following a witnessed generalized seizure. He was commenced on phenytoin, which was changed to carbamazepine due to side effects. MRI revealed three gliomas and an open brain biopsy confirmed a diagnosis of low-grade astrocytoma. The location and multifocal nature of the gliomas ruled out complete neurosurgical debulking. However, his seizures increased in frequency and in February 2007, the biopsy confirmed malignant transformation to multifocal glioblastoma multiforme. He successfully underwent partial debulking, radiotherapy and adjuvant temozolomide chemotherapy. Currently, he is 6 years post-treatment and asymptomatic.

INTRODUCTION

A 25-year-old male underwent magnetic resonance imaging (MRI) as a control subject for a multiple sclerosis study. Investigators identified two abnormalities (‘incidentalomas’), which returned high T2-weighted and proton density images, in the cortex: one above the insula and the other anteriorly above the ventricles. Contrast dye (gadolinium) imaging was not obtained. Subsequently, the safety committee suggested him to get his general practitioner (GP) to refer him to neuro-oncology.

CASE REPORT

Following the serendipitous discovery of two incidentalomas in his right frontal lobe, the patient’s GP referred him to neuro-oncology as suggested. He presented as an asymptomatic 25-year-old, left-handed male with no significant past medical, drug or family history. The neuro-oncologist found nothing abnormal on neurological examination. No treatment was commenced and he was followed up with 6-month interval MRI scans, which all showed no changes in the initial abnormalities. He remained asymptomatic up until his last appointment in 2001 when contact was lost due to a misunderstanding about the frequency of future appointments and further interval MRI scans were not performed.

In June 2005, he was rushed to the local emergency department after a seizure. Whilst in hospital, he had two further witnessed generalized seizures where he bit his tongue and lost a tooth. He reported feeling drowsy and no abnormalities were detected on neurological examination. He resumed follow-up with neuro-oncology and was commenced on phenytoin 200 mg once daily, which caused bleeding gums and subsequently, he was switched to carbamazepine 200 mg once daily. On T2 weighted and proton density MR images, there were three areas of increased signal in the right hemisphere: one in the frontal region, another near the vertex and a third in the right parietal lobe, extending anteriorly into right centrum semiovale. On T1-weighted coronal scanning, all three areas were of slightly heterogeneous signals with no enhancement post-gadolinium, which was suggestive of slow growing astrocytomas as opposed to infarcts. The multifocal nature of the tumours ruled out a surgical debulking. He underwent a mini-craniotomy with open brain biopsy, which confirmed he had a low-grade astrocytoma (Grade II), as classified by the World Health Organization (WHO). By August 2006, he was battling medical and social issues. He experienced two partial seizures a week and was in a protracted dispute with his insurance.
company regarding critical illness cover. His claim was refused because it was determined that he had an undeclared pre-existing condition: the incidentalomas.

By February 2007, he experienced two to three partial seizures daily. MRI showed tumour enhancement and biopsy confirmed multifocal, right-sided frontal multifocal glioblastoma multiforme (GBM). In March 2007, he underwent neuro-surgical debulking (30% removed) via awake craniotomy. Histology confirmed that the majority of the tumour was low-grade astrocytoma (WHO Grade II) with areas of increased cellularity (WHO Grade IV). Following surgery, he was commenced on 6 weeks of radiotherapy of 55 Gy (30 fractions). Furthermore, he received six cycles of adjuvant temozolomide chemotherapy over 6 months. Carbamazepine was increased to 800 mg twice daily and he was given clobazam 10 mg once daily to control focal seizures. In September 2007, he completed chemotherapy and MRI scans since then have shown no signs of recurrence. Currently, he is 6 years post-treatment for multifocal GBM and has not reported any new symptoms.

**DISCUSSION**

This patient has defied several medical odds from initial detection as part of a study to surviving GBM. A systematic review of 16 studies in 19 559 patients reported the prevalence of incidental neoplastic brain findings in MRI studies as 0.7% with the prevalence of glioma at 0.05% [1]. GBM is the most malignant primary tumour of the central nervous system with an incidence of 5 in 100 000 people every year. Incidence is greater in men, with a median age of 60 at presentation [2]. Gliomas have been categorized as WHO Grades I–IV based on histology, which have associated prognostic and survival correlate. Patients with GBM have a survival rate of 17–30% at 1 year and 3–5% at 2 years with a median survival of 14 months following diagnosis [3]. It is debatable whether he had primary or secondary GBM. The original grade II glioma may have shown high-grade transformation in 2007 or it could be the case that at the time of his presentation with seizures in 2005 he had GBM and the initial biopsy report of a low-grade astrocytoma (II) was due to a sampling error.

Malignant glioblastomas are arguably the most challenging malignancy in neuro-oncology. Surgical resection is mainstay therapy and a key prognostic factor in survival. GBM notoriously infiltrates normal brain tissue, meaning that surgical resection often involves removal of functional brain tissue. Gliomas are not aggressively removed in order to preserve function. This is unlike other tumours such as acoustic neuromas [4] where deficits are tolerated. Instead, glioma treatment is sometimes described as ‘biopsy and radiate’, which may seem like a rather nebulous notion in glioma management [5].

Despite radiological evidence, it is believed that with gliomas, there is widespread dissemination and even microscopic infiltration in brain tissues [6]. Post-mortem studies demonstrate wide dissemination in end stage and many clinicians believe that even low-grade gliomas are widespread at diagnosis [5]. Gliomas are considered incurable due to recurrence as demonstrated in a series of five patients who underwent hemispherectomies in 1928 [7]. As a result, aggressive surgery might be delayed due to reliance on evidence, which could be regarded as statistically trivial and antiquated in terms of current imaging techniques. However, the extent of surgical resection to survival time is also contentious. It may have no effect [8] or show a positive correlation [9]. In this patient, only 30% of the tumour was removed with excellent clinical outcome. However, studies that show a positive correlation between resection and survival time also use radiotherapy and chemotherapy at various points in treatment. As such, the benefit of the extent of surgical resection is wholly uncertain in terms of overall management for each patient. Currently, it remains to be seen what aggressive treatment regimes could accomplish in the future management of gliomas.

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**CONFLICT OF INTEREST**

The authors have no conflict of interests to declare.

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