CASE REPORT

Rare case of radiation-induced trigeminal schwannoma occurring in a long-term glioblastoma multiforme survivor

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SUMMARY

Glioblastoma multiforme (GBM) is a high-grade primary brain tumour with a notably poor prognosis. Research demonstrates a median survival of just over 1 year following aggressive treatment. Long-term survival is notably rare. Cranial radiotherapy and postexcisional prophylactic treatment is associated with the development of second, histologically distinct tumours in rare cases. Radiation-induced intracranial schwannomas are uncommon, with only a small number of cranial nerve schwannoma cases reported in recent decades. To our knowledge, this is the first reported case of a radiation-induced benign trigeminal schwannoma occurring following long-term survival from glioblastoma. Here we present (1) a rare case of 14-year survival following treatment of a right parietal glioblastoma and the development of a radiation-induced benign trigeminal schwannoma in a 35-year-old man, and (2) a review of radiation-induced schwannoma cases reported in the existing literature.

BACKGROUND

Glioblastoma multiforme (GBM) is the commonest and most aggressive type of glioma. Gliomas are a type of central nervous system tumour that arise from the glial cells of the brain. Despite its high prevalence and ongoing research trials into improving outcomes, it continues to exhibit the poorest prognosis of all gliomas.

GBM treatment includes surgical resection, radiotherapy and/or chemotherapy. Recurrence is inevitable, however, it is not currently possible to predict when this will occur. Multimodal approaches to treatment are associated with the best possible outcomes,¹ however, median overall survival is still poor, ranging between 12.2 and 15.9 months.²

Our case presents a rare occasion whereby the patient has survived free of progression for over a decade, but has developed a benign trigeminal schwannoma in line with the previous radiotherapy treatment. In the context of a primary GBM tumour, the benign trigeminal schwannoma uniquely manages to fulfil the criteria for a radiation-induced tumour described in the existing literature.³

CASE PRESENTATION

A 19-year-old man presented in 2001 with a 4-week history of headaches associated with nausea and occasional neck pain. A CT of the head

revealed the presence of a right parietal intra-axial space-occupying lesion that was subsequently excised. The histological diagnosis was GBM.

The patient was then treated with radiotherapy (figures 1 and 2) at the standard dose (table 1).

In the years following initial treatment, the patient began to experience occasional seizures but remained otherwise well, with no significant psychological sequelae.

INVESTIGATIONS

The patient had yearly CT of the brain scans followed by the first MRI scan in 2004. These were all unremarkable. An MRI head scan performed on 7 July 2014 showed a 4 mm enhancing extra-axial mass in the left ambient cistern, just superior-lateral but separate from the intracranial component of the left trigeminal nerve (figure 3A). This was not present on previous images. An MRI head scan in May 2015 showed the enhancing lesion in the left ambient cistern superior to the intracranial component of the left trigeminal nerve, measuring 8 mm in diameter (figure 3B).

DIFFERENTIAL DIAGNOSIS

Following imaging in July 2014, the top differential was a radiation-induced meningioma. The lesion appeared to be attached to the petrous dura.

Figure 1 Orthogonal planning films of the lateral radiotherapy field arrangement.

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Figure 2 MRI with overlay of original dose distribution in phase 1 (left) and phase 2 (right).

No compression of adjacent brainstem was seen and the 5/6/7/8th cranial nerve complexes appeared separate from the lesion. The patient did not have any impairment of the cranial nerves.

Following this, a rescan in May 2015 ([figure 3B](#)) showed the lesion to have grown from 4 mm to 8 mm in size.

TREATMENT

In light of the quick progression of the lesion despite the patient remaining asymptomatic, the options of stereotactic surgery and surgical resection were discussed with the patient.

The patient chose to undergo surgical resection.

The patient was treated in May 2015 with a posterior fossa craniotomy and a left retrosigmoid approach for the removal of the known lesion in the cerebellopontine angle with intraoperative monitoring of the cranial nerves. The patient went home 2 days following surgery with no new neurological deficit. The immediate postoperative MRI showed complete removal of the lesion ([figure 3C](#)).

Table 1 Radiotherapy treatment regimen

Phase I	46 Gy in 23 fractions using anterior posterior and right lateral fields
Phase II	14 Gy in 7 fractions to a reduced volume

The patient was treated with 60 Gy in 30 fractions in two phases.

OUTCOME AND FOLLOW-UP

The postoperative course was uneventful. Histology showed the lesion to be a grade A schwannoma.

Review of the first histological results was performed and diagnosis of GBM was again confirmed.

DISCUSSION

Newly diagnosed patients with GBM undergo aggressive treatment with maximal surgical resection, radiotherapy and/or chemotherapy. However, only 3–5% of GBM patients survive more than 3 years after initial diagnosis⁴ and there is no current evidence that this figure is increasing.

Research has attempted to identify important prognostic factors in GBM survival. These include age, radiotherapy treatment and extent of tumour resection. Gross-total tumour resection is associated with longer survival than subtotal resection,⁵ but a resection threshold level for maximum survival is yet to be defined.⁶ Other prognostic factors include preoperative Karnofsky performance status score, biochemical tumour markers, degree of tumour tissue necrosis and the level of enhancement found on preoperative imaging.⁵

Radiation-induced tumours are a rare but important complication following radiotherapy treatment. The radiotherapy method used depends on the type of lesion concerned. Some tumours are treated with radiosurgery. This procedure is usually reserved for metastatic lesions or lesions deemed unsuitable for

Figure 3 (A) July 2014 axial head MRI. A 4 mm mass is seen in the left ambient cistern, superior-lateral to the intracranial component of the left trigeminal nerve. (B) May 2015 preoperative axial head MRI. The previously reported 4 mm mass now measures 8 mm in maximal diameter. (C) May 2015 postoperative axial head MRI. Postoperative imaging shows successful removal of the lesion.

Table 2 Summary of reported cases of radiation-induced intracranial benign schwannomas

Study (year)	Sample	Radiation dose (Gy)	Indication for radiotherapy treatment	Diagnosis	Interval (years)
Salvati <i>et al</i> (2003) ¹³	5	1. 5 2. 24 3. 5 4. 25 5. 4	1. Tinea capitis 2. ALL 3. Tinea capitis 4. Skin haemangioma 5. Tinea capitis	1. VS 2. VS 3. VS 4. VS 5. VS	1. 23 2. 15 3. 20 4. 22 5. 18
Schneider <i>et al</i> (2008) ¹⁴	43	5.24 (mean)	Enlarged tonsils and adenoids	VS	20 (earliest)—55 (latest)
Loeffler <i>et al</i> (2003) ¹⁵	1	104	Acromegaly	VS	19
Rubinstein <i>et al</i> (1989) ¹⁶	1	Unknown	Retinoblastoma	Schwannoma (subtype unknown)	26
O'Malley <i>et al</i> (1997) ¹⁷	1	60	Medulloblastoma	Trigeminal schwannoma	24

ALL, acute lymphoblastic leukaemia; VS, vestibular schwannoma.

surgical resection. In GBM and other high-grade tumours, radiotherapy as a postsurgical prophylactic treatment is used to prolong survival and improve outcomes. Cranial radiotherapy is sometimes used in the treatment of other pathologies including benign skin conditions such as tinea capitis, or in the prevention of CNS relapse of childhood malignancies such as acute lymphoblastic leukaemia.⁷

Several important factors are associated with the development of radiation-induced tumours. These include age at exposure and the radiation dosage received. The most commonly reported radiation-induced brain tumours include malignant gliomas and meningiomas.^{7, 8} Several cases of radiation-induced GBM have been previously reported. However, in patients with GBM, the incidence of radiation-induced second tumours is unknown. This is largely due to the short survival rate in patients and, therefore, any second malignancy that does occur would not meet the criteria for a radiation-induced tumour. These criteria³ were first described by Cahan, in 1948, and include: (1) that the new tumour occurs at the irradiated site at least 5 years after treatment, (2) that the new tumour is of a different pathological type from the initial tumour, (3) the absence of a second tumour at the time of initial radiotherapy, and (4) the absence of a pathology associated with increased susceptibility to tumour development.

Fukushima *et al*⁹ described a case of a radiation-induced cavernous angioma in a long-term GBM survivor. Goyal *et al*¹⁰ reported a case of a sinonasal carcinoma occurring 1.5 years post-GBM radiotherapy treatment and outside the radiation field, however, in that case, due to the short interval time, radiation therapy was unlikely to be the cause of the second malignancy and therefore the malignancy did not meet Cahan's criteria. The case we have described here presents a rare event whereby the criteria for a radiation-induced tumour were met, due to the patient surviving significantly longer than would otherwise be expected following surgical treatment of GBM. Cahan's criteria were described in relation to sarcomas arising in previously irradiated bone. With advancing knowledge and clinical practice, there is a clear need for an updated, more uniform approach to defining radiation-induced tumours.

After vestibular nerve schwannomas, trigeminal schwannomas are the second commonest subtype of schwannomas. Peak incidence is in the third and fourth decades of life.¹¹ Primary benign trigeminal nerve schwannomas are very rare and comprise only 0.2–0.4% of all intracranial tumours.¹² Most reported schwannoma cases relate to primary schwannomas or malignant progression of primary benign schwannomas. Radiation-induced benign intracranial schwannomas have scarcely been reported in the literature.^{13–17} We have summarised these cases in the table below (table 2). To our

knowledge, no cases of schwannomas arising after GBM treatment have previously been reported.

Radiation-induced tumours remain a rare but significant long-term complication following tumour resection and radiotherapy treatment. Long-term surveillance is of utmost importance following radiotherapy, regardless of whether or not a tumour with a high recurrence rate is diagnosed. It is, therefore, key for clinicians to remain vigilant and maintain stringent follow-up in patient groups. In particular, younger patients with good prognostic markers may be at increased risk, and should be closely monitored and made aware of the importance of reporting new symptoms.

Learning points

- Positive prognostic factors for glioblastoma multiforme (GBM) survival include gross-total tumour resection and multimodal treatment approaches, but overall survival rates remain short and recurrence is inevitable.
- The incidence of radiation-induced tumours following GBM is unknown.
- An updated approach to defining radiation-induced tumours is needed.
- Surveillance is of vital importance following radiotherapy treatment in long-term GBM survivors.

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