

Intracranial papillary endothelial hyperplasia (Masson's tumour) following gamma knife radiosurgery for temporal lobe epilepsy

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ABSTRACT

We present a rare case of intracranial papillary endothelial hyperplasia, or 'Masson's tumour,' following gamma knife radiosurgery for epilepsy. A 59-year-old woman presented with a 4-month history of escalating headaches and progressive neurological deficit. MR scan of brain showed enlargement of an enhancing right temporal lobe lesion, midline shift and obstructive hydrocephalus. She had previously undergone non-curtative gamma knife radiosurgery at the age of 44 years for medically refractory complex partial seizures. Postprocedure imaging had shown signal change and enhancement within the right temporal lobe consistent with radiation necrosis, which remained stable over the next decade. Now, 15 years following radiosurgery, we suspected an intrinsic high-grade neoplasm, but surgical excision instead found a benign pseudoneoplasm. Papillary endothelial hyperplasia should be considered in the differential diagnosis for mass lesions following gamma knife radiosurgery, particularly as resection can be curative. Remarkably, she has become seizure free.

CASE HISTORY

A 59-year-old woman with normal birth, development and scholastic record presented at age 30 years with stereotyped episodes of up to 20 times per month, heralded by a 'strange warmth' in the torso and an 'odd taste' for 30 s. This would be followed by 5–10 min of altered awareness with a vacant expression, repetitive chewing, non-sensical speech and aimless wandering. In retrospect, intermittent episodes from adolescence closely resembled the aura phase and, 2 years previously, she had experienced a collapse consistent with a

generalised convulsion while on holiday. She was diagnosed with partial-onset seizures with secondary generalisation.

MR scan of brain and electroencephalogram (EEG) at age 33 years were reported as normal, although repeat imaging 5 years later showed right hippocampal sclerosis and repeat EEG showed occasional right frontotemporal region sharp waves. She took various antiepileptic medications alone and in combination, including carbamazepine, sodium valproate, phenytoin, lamotrigine, vigabatrin and gabapentin, although with no sustained improvement despite good adherence. She remained independent but the toll of refractory seizures and pharmacotherapy subjectively affected her attention and memory.

We referred her for possible epilepsy surgery at age 39 years. MR imaging was unchanged, although brain positron emission tomography (PET) identified bilateral temporal hypometabolism. Conventional EEG now showed bitemporal epileptic discharges while invasive foramen ovale telemetry suggested right temporal onset with rapid bilateral spread. An amygdal test suggested left hemisphere dominance for language and adequate memory function residing in both hemispheres with superior left-sided function.

She was offered excision of the right anterior temporal lobe but after informed consideration of the risks, she elected instead for gamma knife radiosurgery. At age 44 years, she received a single unfractionated dose of 25 Gy using the stereotactic Leksell Gamma Knife. There were no immediate complications and



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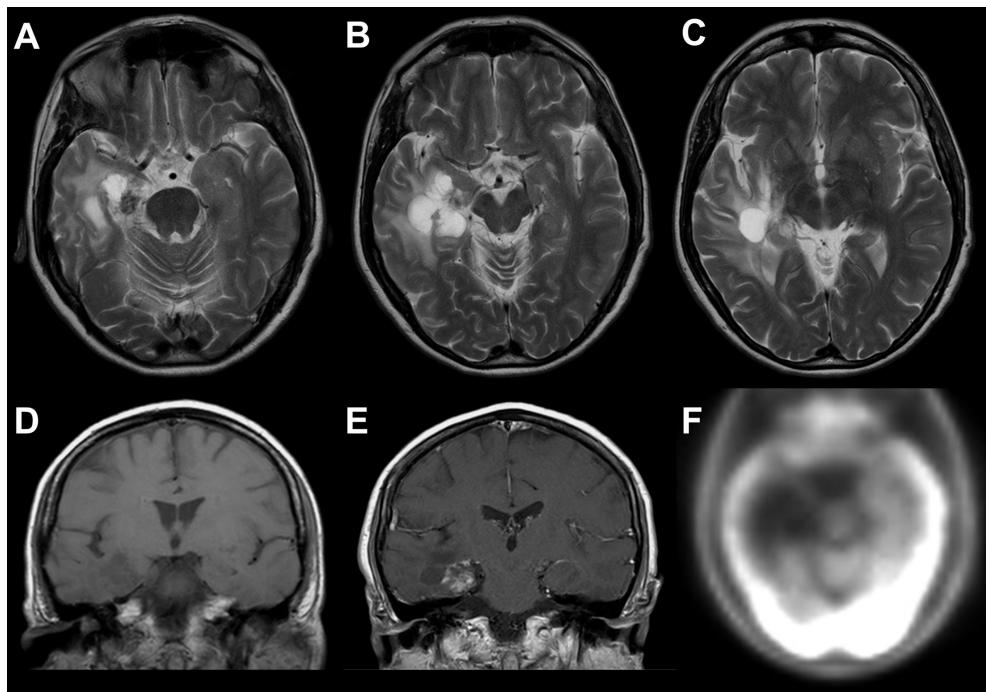


Figure 1 Surveillance MR brain imaging in 2010 continued to show a T2 hyperintense (A–C) and T1 hypointense (D) right anterior temporal multifocal cystic lesion with irregular gadolinium enhancement centrally (E). Positron emission tomography scanning shows the corresponding right anterior temporal lobe hypometabolism (F).

MR brain imaging 10 months later was unchanged. Her complex partial seizures initially continued at 20 per month, but within 15 months it had reduced to 1–5 per month.

Two years after the gamma knife surgery, she was admitted with postictal psychosis, comprising emotional outbursts, auditory hallucinations and paranoia, which resolved completely after several days. MR scan of brain at this time showed a new T2 hyperintensity with cystic areas, peripheral ring enhancement and surrounding oedema within the right medial temporal lobe, highly suspicious for intrinsic tumour. Serial re-imaging over 24 months showed regression and stabilisation, favouring a diagnosis of radiation necrosis, but she remained clinically unchanged.

Surveillance imaging at age 54 years identified a smaller and far less oedematous lesion but with continued irregular enhancement (figure 1). Exhaustive multidisciplinary discussion considered neoplastic disease although repeat brain PET showed lesional hypometabolism; thus, the favoured diagnosis was still a lesion resulting from radiotherapy. Moreover, the patient and we did not feel that the risks of undertaking explorative surgery were warranted.

At age 59 years, following five further years of medically refractory seizures, she developed a gradually worsening headache with morning predominance over several months, with left-sided weakness, gait ataxia and intermittent diplopia. MR scan of brain showed significant extension of the

temporal lesion causing midline shift and obstructive hydrocephalus secondary to marked vasogenic oedema. There was a haemorrhagic component, necrotic change and heterogeneous nodular pathological enhancement without restricted diffusion (figure 2). Neurosurgical and multidisciplinary opinion was divided between intrinsic neoplasm and delayed radiation necrosis. She underwent surgical excision via a right temporal craniotomy. A 70×60×50 mm solid component, including the amygdala and medial hippocampal gyrus, was dissected *en bloc* from adjacent gliotic-appearing brain tissue while the cystic component was aspirated.

Histology showed a well-defined, circular, highly vascular mass surrounded by a pseudo-capsule and a thin layer of compressed brain tissue. The lesion contained predominantly necrotic material and fibrin-rich blood clot along with a close network of ‘frond-like’ thin-walled blood vessels lined with a single layer of endothelium that stained positive for the endothelial marker CD34 on immunohistochemistry (figure 3). There was no evidence of radiation necrosis or angisarcoma. The appearances were consistent with papillary endothelial hyperplasia, otherwise known as Masson’s tumour.

Remarkably, she has remained seizure free postoperatively and weaned on to levetiracetam monotherapy. Her memory and thinking have subjectively improved, with neuropsychometry showing slowed information processing, poor facial recognition and

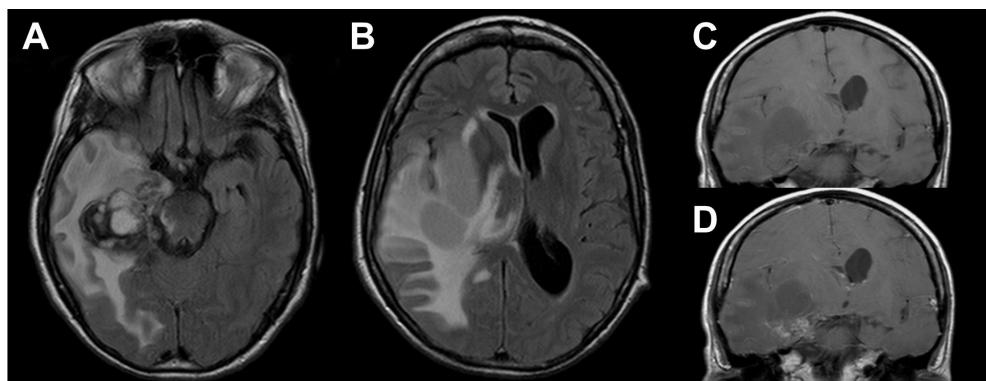


Figure 2 MR brain imaging 2015 shows mass effect, midline shift and obstructive hydrocephalus from enlargement of the right temporal lesion. Fluid attenuation inversion recovery sequences (A, B) show significant surrounding oedema with the lesion itself hypointense on T1 (C) with ongoing patchy gadolinium enhancement (D).

mild delayed recall impairment for visual and verbal information. She has no radiological signs of recurrence after 18 months.

DISCUSSION

This patient's management posed several challenges. Temporal lobe epilepsy that remains steadfastly resistant to adequate trials of pharmacotherapy is not uncommon, particularly with hippocampal sclerosis. Resective surgery offers up to 60% of patients the prospect of seizure freedom at 10 years, although referral for surgery may be underused.¹ Gamma knife was a far less established option to treat epilepsy 20 years ago, although in this case it was led by informed patient choice. Indeed, Régis *et al*'s small multicentre European study using single fraction gamma knife in patients with hippocampal sclerosis who had similarly decided against conventional surgery—which was towards the end of recruitment when our patient received her treatment—reported transient increases in seizure activity in all patients after 9–12 months before a universal decrease, with overall seizure freedom in 65% at 2 years.² A recent meta-analysis of radiosurgery techniques (X-rays or gamma radiation) in patients with hippocampal sclerosis not offered open surgery found this group's seizure freedom rates were almost as good as with temporal lobe resection, albeit after a 14-month mean delay.³ However, there

are no randomised clinical trials directly comparing efficacy and side effect profiles of invasive versus non-invasive surgical methods. Régis reported MR imaging changes consistent with radiation necrosis in all their subjects, peaking at around 1 year after gamma knife and thereafter decreasing up to the end of the 24-month follow-up.² This is reflected by the tempo of imaging evolution in the present case, with stabilisation 2 years after radiosurgery and persistent (if not even less-conspicuous) appearances up to 10 years postoperatively.

Unfortunately, our patient did not achieve seizure freedom and our second challenge was management of refractory focal epilepsy, given that the wide spectrum of older and newer antiepileptic drugs in combination had proved ineffective. Moreover, it only became clear during recent weaning just how much these treatments had affected her cognition and alertness.

An intriguing question is at what point did the papillary endothelial hyperplasia arise and, also, was it responsible for the ongoing seizures? It is possible that the MR brain scan changes that provoked so much multidisciplinary discussion actually represented radiation necrosis all along, and that papillary endothelial hyperplasia only became relevant in line with the latest rapid deterioration at the age of 59 years. Indeed, the stopping of seizures following the anterior

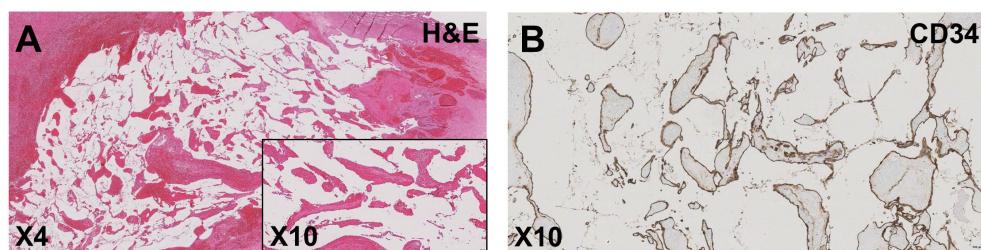


Figure 3 Histopathology of the lesion. There are frond-like papillary structures within intravascular organising thrombus (A) lined by a single layer of hyperplastic endothelium (inset), confirmed by CD34 immunohistochemistry (B).

temporal lobe excision may be explained by removal of the original epileptic focus within this region that had not been eradicated by gamma knife. Since the seizure frequency remained largely unchanged for nearly 15 years, it might be tricky to attribute them to the papillary endothelial hyperplasia, unless an early focus suddenly enlarged.

Papillary endothelial hyperplasia is a rare, benign and usually slow-growing mass of vascular origin.⁴ Pierre Masson first described (1923) the characteristic protuberances of endothelial overgrowth within a thrombosed haemorrhoidal vein, and hence the eponym Masson's tumour. There are three categories of papillary endothelial hyperplasia: a primary type arising inside a normal blood vessel (more often a vein than artery); a secondary or 'mixed' type associated with a vascular malformation; and an extravascular type.⁴ Each seems to arise after disproportionate organisation of thrombus with haemodynamic and angiogenic signalling factors playing roles in pathogenesis.^{4,5}

Papillary endothelial hyperplasia can occur anywhere, most commonly within skin and subcutaneous tissues of the head, neck, trunk and upper limbs.⁶ It is much rarer in the central nervous system (CNS), with tumours affecting the parenchyma, meningeal layers or venous sinuses.^{4,7} Appearances on MR imaging can resemble malignant neoplastic lesions. Although there are no defined imaging characteristics, T1 hypointensity, T2 hyperintensity and varying degrees of contrast enhancement can also occur in other intracranial papillary endothelial hyperplasia cases.^{5,8} While many appear to have developed spontaneously, papillary endothelial hyperplasia may develop as a complication of previous external beam radiotherapy or stereotactic radiosurgery, such as gamma knife, for other mass lesions and arteriovenous malformations.^{4,7} Of the nine CNS cases from one department, six followed radiosurgery with presentation up to 25 years following exposure.⁷ Both vascular-associated and extravascular subtypes can occur,^{4,7} but mechanisms by which radiosurgery might trigger the tumour's development are unknown. It may arise as a direct consequence of radiation or be facilitated through tissue damage, such as radiation necrosis or haematoma formation.⁶

Complete excision of papillary endothelial hyperplasia, if warranted, can be curative,^{4,5} but recurrence occurs after subtotal resection.⁸ Ironically, residual papillary endothelial hyperplasia has been successfully reduced by gamma knife radiosurgery itself,⁹ and potentially establishes a bizarre paradox of cause and effect. However, it may only transpire that a mass lesion is papillary endothelial hyperplasia mid-operation or following histological analysis, and thus clinicians need a high index of suspicion to minimise

potential hazards such as severe haemorrhage during biopsy.

Key points

- Papillary endothelial hyperplasia is a benign entity of vascular origin.
- Mass lesions resembling malignant neoplasia at target sites of previous radiosurgery should prompt consideration of papillary endothelial hyperplasia.
- Clinicians need a high index of suspicion before surgical intervention to minimise risk of haemorrhage.
- Complete surgical resection of papillary endothelial hyperplasia can be curative.

Contributors AWB performed a literature search and review of the literature, and constructed the article. AM contributed to the figure panels and histological information. PE provided surgical management and critical appraisal of the article for submission. JA provided case management and critical appraisal of the article for submission.

Competing interests None declared.

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