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SURGICAL NEUROLOGY INTERNATIONAL
SNI: Cerebrovascular, a supplement to Surgical Neurology International
OPEN ACCESS
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Editor: James I. Ausman, MD, PhD University of California, Los Angeles, CA, USA

Radiotherapy-related intracranial aneurysms: A role for conservative management

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Received: 25 January 16 Accepted: 18 March 16 Published: 03 June 16

Abstract

Background: Radiotherapy-related intracranial aneurysms are a recognized but rare phenomenon and often present following rupture leading to subarachnoid hemorrhage. Treatment poses a particular dilemma and both endovascular, and surgical approaches have been used with varied success. We present the case of a radiotherapy-related aneurysm treated conservatively with a favorable outcome.

Case Description: A 37-year-old man was diagnosed with a left temporal lobe mass for which he underwent an uneventful craniotomy and debulking. Histology revealed Grade III anaplastic astrocytoma following which he received radiotherapy. Three years later, he presented with subacute headache and transient dysphasia. Computed tomography and catheter angiography revealed a fusiform aneurysm of the supramarginal branch of the left middle cerebral artery with probable intra-aneurysmal thrombus. Adjacent vessels also showed mild vasculitic changes. Trial balloon occlusion of the parent vessel resulted in profound dysphasia and was therefore abandoned. Bypass surgery or stent placement was deemed to have too high a risk of neurological deficit, and keeping in mind, the diagnosis of anaplastic astrocytoma, conservative management was pursued with partial thrombosis noted on serial imaging and stable appearances subsequently at 42 months' follow-up.

Conclusion: Conservative management can be pursued in selective cases of radiotherapy-related aneurysms, particularly if the risk of treating is too high and in the context of intracranial malignancy with limited lifespan.

Key Words: Fusiform aneurysm, intracranial aneurysm, radiotherapy

Access this article online
Website: www.surgicalneurologyint.com
DOI: 10.4103/2152-7806.183496
Quick Response Code:

CASE REPORT

A 37-year-old man presented in April 2009 with seizures. Magnetic resonance imaging (MRI) brain showed a minimally enhancing left temporal lobe mass. He underwent left temporal craniotomy and debulking of tumor in May 2009 and made an uneventful postoperative recovery. Follow-up scans showed a significant reduction in tumor volume. Histology revealed the lesion to be a Grade III anaplastic oligoastrocytoma, and the patient subsequently underwent radiotherapy using conformal technique receiving 60 Gy in 30 fractions over 6 weeks in July 2009. This was delivered in two phases. The first phase delivered 54 Gy to the whole planning treatment volume

How to cite this article: Parag S, Arif Z, Chittoor R. Radiotherapy-related intracranial aneurysms: A role for conservative management. Surg Neurol Int 2016;7:S387-90.
http://surgicalneurologyint.com/Radiotherapy-related-intracranial-aneurysms:-A-role-for-conservative-management/

in 27 fractions [Figure 1]. The second phase (shielding out critical organs such as brainstem, optic chiasm) was delivered with 6 Gy in three fractions. There was no specific "boost" to the tumor resection cavity/bed. Routine follow-up MRI in August 2010 showed improvement in tumor status with no visible enhancement.

MRI in June 2011 showed a few areas of nodular enhancement within the primary tumor. This was deemed to be disease progression and chemotherapy using temozolomide was commenced. A routine follow-up MRI in April 2012 showed an entirely new area of enhancement in the left Sylvian cortex adjacent to two prominent vessels thought initially to be further tumor progression [Figure 2].

A few days after this MRI, he presented with subacute headache and acute dysphasia, the latter improving rapidly. Computed tomography (CT) brain showed a small 2 mm hyperdensity in the insular cistern corresponding to the new enhancement which had been noted on the recent MRI. CT angiography [Figure 3] showed a very irregular fusiform aneurysm of a Sylvian branch (supramarginal) of the left middle cerebral artery (MCA) with the hyperdensity thought to be either intra-aneurysmal thrombus or mural/perimural hemorrhage. Digital subtraction angiogram confirmed the large, irregular fusiform aneurysm involving the posterior Sylvian branch of the left MCA [Figure 3]. There was a very short "normal" segment at the origin of the Sylvian branch expanding over a long segment, followed by a short relative stenosis and then a very irregular aneurysmal pouch which tapered to a normal appearing vessel with a runoff supplying the region of the inferior parietal lobule. The adjacent MCA branches showed subtle variation of calibre suggestive of mild vasculitis. MRI brain showed a cap of thrombus around the distal part of the aneurysm suggesting intraluminal or intra-mural thrombus. There was no clear evidence of extraluminal hemorrhage [Figure 4]. These appearances were almost similar to the MRI done a few days before the patient's presentation.

Endovascular occlusion of the aneurysm was considered the best treatment option, provided vessel occlusion was tolerated clinically. Awake catheter angiography was performed to trial balloon occlusion. Placement of a balloon microcatheter, without inflation, into the origin of the MCA branch was sufficient to arrest flow [Figure 5]. The patient immediately developed profound dysphasia; consequently, the procedure was abandoned.

The patient was discussed with neurovascular surgeons and interventional neuroradiologists at two other specialist centers regarding bypass, flow diverters, or stent placement. However, these were deemed to be exceptionally difficult technically with a very high risk of leaving the patient with the permanent

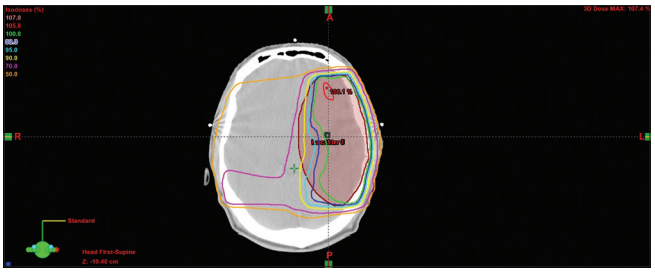

Figure 1: Conformal radiotherapy plan showing the dose distribution where the planning treatment volume is the shaded red contour, and the isodoses are given as a percentage of 60 Gy

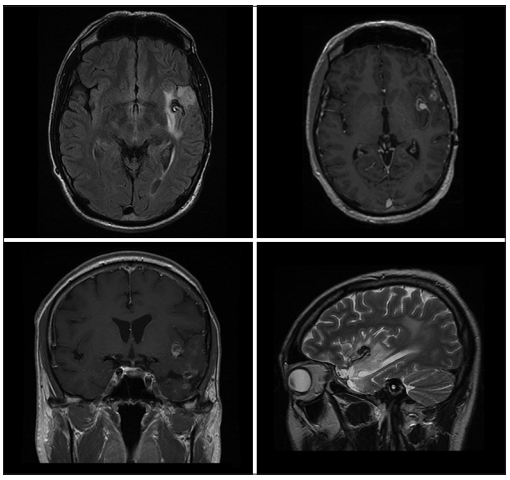

Figure 2: Magnetic resonance imaging brain performed a few days before aneurysm presentation. It shows small intensely enhancing area closely related to left insula showing unusual peripheral ring of enhancement (top right and bottom left) and strikingly low signal on T2-weighted imaging (bottom right). This was initially thought to be tumor progression but later retrospectively recognized as corresponding to the fusiform aneurysm

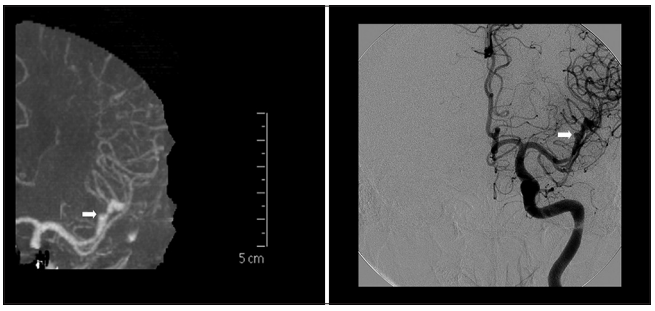

Figure 3: Computed tomography angiogram (left) and corresponding digital subtraction angiogram (right) images confirming the fairly long irregular fusiform dilatation (indicated by the white arrows)

neurological deficit. The patient's underlying diagnosis of Grade III oligoastrocytoma and the possibility of generalized vascular fragility due to radiotherapy/vasculitis also served as a detriment while considering the option of bypass or stenting. After detailed counseling, the patient also opted for conservative treatment.

MRI, 3 months later [Figure 6], revealed narrowing and partial thrombosis of the aneurysmal segment and

the patient remained asymptomatic. Regular follow-up MRI and MR angiography over a period of 42 months has shown stable appearances of the aneurysm and the patient has remained asymptomatic. Unfortunately, the tumor has now started showing signs of radiological progression, and the patient has now been commenced on procarbazine, CCNU, vincristine chemotherapy.

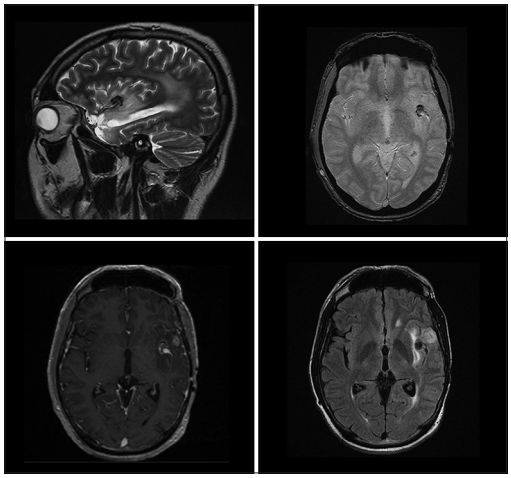

Figure 4: Magnetic resonance imaging brain performed after patient presented with symptoms related to the aneurysm.T2-weighted fast spin echo (top left), gradient echo (top right), T1 with gadolinium (bottom left), and axial flair (bottom right) images confirmed the fusiform aneurysm with a cap of thrombus around its distal part, likely to be either intraluminal or intramural thrombus.There was no evidence of extraluminal hemorrhage

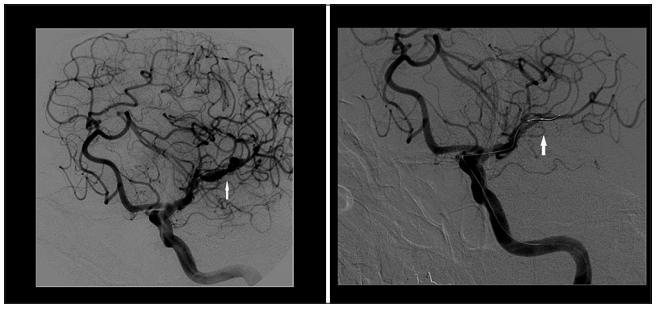

Figure 5: Awake catheter angiogram/digital subtraction angiogram performed during trial balloon occlusion showing the fusiform aneurysm (left) and loss of flow in the middle cerebral artery branch when the balloon microcatheter was deployed even without inflation resulting in profound dysphasia (right)

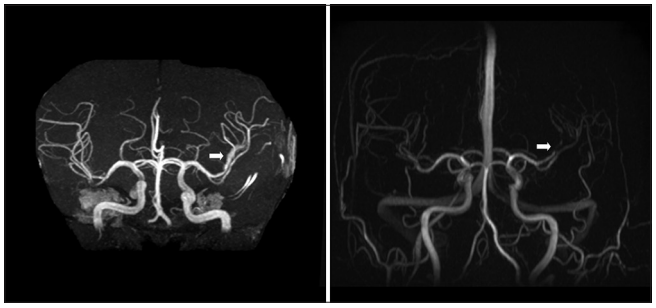

Figure 6: Initial magnetic resonance angiogram (left) showing the fusiform aneurysm. Three-month follow-up magnetic resonance angiogram (right) showing partial thrombosis of the fusiform aneurysm

DISCUSSION

Aneurysm formation following radiotherapy is a rare but recognized phenomenon with the first identified radiotherapy-related intracranial aneurysm being reported in 1984.[2] These should be differentiated from the few, recently reported cases of radiosurgery-induced aneurysms, which are probably more likely due to the high dose of radiation delivered to a focused field.[8] Cases have been described anywhere between 2 and 21 years following radiotherapy with some patients having received treatment in early childhood.[5,7] Median lag time between radiation and aneurysm diagnosis is 9 years for whole brain radiotherapy and 6 years for stereotactic radiosurgery. There are eight reported cases with radiotherapy given for intracranial malignancy, with only two in the context of a malignant glioma.[5]

Radiotherapy-related aneurysms are often discovered when they rupture causing subarachnoid hemorrhage. Besides, subarachnoid hemorrhage, they can also present with nonspecific neurological symptoms, epistaxis, otorrhagia and occasionally as incidental findings.[3,5] The presentation in our patient is unique. He presented with headache and transient neurological deficit rather than acute hemorrhage with most of the imaging pointing toward a mural thrombus-induced transient deficit.

The pathophysiology of radiation-induced aneurysms is not fully appreciated. Acute injury associated with radiotherapy has been long recognized; however, chronic vasculopathy and aneurysm formation are poorly understood. It has been postulated that endothelial damage is most commonly responsible for these changes with capillaries and small arteries mainly affected; however, large vessel involvement has also been documented.[6,8] Studies have revealed vascular injury to start 48 hours after radiation exposure with endothelial damage occurring first. Subsequently, fibrosis of the media and adventitial hemorrhage and inflammation was observed. Aneurysm formation is postulated to result from weakness in the media and/or internal elastic lamina. Studies have also revealed that intimal fibrosis can prevent aneurysm formation.[3] Our patient did not have any other risk factors for aneurysm formation.

In our patient, the aneurysm was deemed to be secondary to radiotherapy as the margin of surgical resection during the initial surgery did not reach the Sylvian fissure, ruling out possible vascular injury as an etiology. Furthermore, the follow-up MRI scans up to 3 years after the surgery did not reveal any abnormality, enhancement, or vascular changes in the insular region. A new area of Sylvian enhancement picked up on the MRI [Figure 1] in April 2012 (3 years after surgery) was initially thought to be

tumor progression but the subsequent presentation of the patient and angiography revealed that this corresponded to the aneurysmal segment and there were mild vasculitic changes in the adjacent MCA branches, further proof of *de novo* aneurysm formation after radiotherapy.

The dose of radiation given to each patient reported to have a radiotherapy-related aneurysm has been comparatively similar with most papers reporting a dose of 50–60 Gy.[5,7] Our patient received 60 Gy in 30 fractions using a conformal technique. Other techniques such as intensity-modulated radiation therapy and radiosurgery which deliver a higher dose may carry a higher risk of delayed vascular changes. Most reported aneurysms are saccular in nature and have been reported to occur in larger intracranial vessels, with 69% occurring in the anterior circulation, 27% in the posterior circulation, and 4% of the aneurysms appearing in association with arteriovenous malformations.[5] Our case is distinctive in that we report a fusiform aneurysm of a small distal branch occurring in an M3 segment of the MCA.

Treatment of these aneurysms poses a particular challenge and coiling, stenting, clipping, and wrapping with or without arterial bypass have all been used with varied success. It must be noted however that quite a few of the reported cases were published in the 1980s and 1990s before the recent advances in endovascular techniques. However, the perceived radiation-induced frailty of the parent vessels poses a challenge for endovascular techniques. Outcomes reported from this condition range from excellent recovery to high neurological morbidity and mortality, with the latter not uncommon.[3,4] The challenges with their surgical and endovascular treatment are well-demonstrated in a recent report where the authors had to abandon surgery, and endovascular trapping was also fraught with difficulties with eventual poor neurological outcome.[4]

In our case, the patient's underlying diagnosis played a significant role in decision-making. Although Grade III oligoastrocytoma has been shown to have a better prognosis than other high-grade gliomas, reported median survival is approximately 60 months. This had an obvious impact on our choice of decision.

Our literature search revealed only one case where the aneurysm was conservatively managed with subsequent spontaneous occlusion of the vessel and no significant morbidity.[6] Whether the favorable prognosis after spontaneous occlusion is due to already present collateral circulation or as a result of neovascularization is debatable. However, in our case, the partial thrombosis and subsequent stable appearances may be related to the fibrosis induced by radiotherapy.

Our case report demonstrates the treatment dilemmas associated with certain radiotherapy-related aneurysms. This is particularly relevant in the context of radiotherapy for intracranial malignancy. The vast majority of the previously reported such cases have been reported in nonmalignant conditions which had a more favorable overall long-term prognosis and therefore prompting aggressive treatment.

Some authors believe that these aneurysms are more prone to rupture than typical aneurysms. It may be the case that radiotherapy-related aneurysms are under-reported as authors may be discouraged to publish similar cases once the novelty of the condition has disappeared, and hence, one can only speculate about the true incidence and natural history.[1] We therefore believe that reporting this case of conservative management is important to highlight that these aneurysms can also remain stable on long-term follow-up.

We demonstrate that conservative management can be considered as a feasible option for complex and difficult-to-treat aneurysms wherein the treatment is likely to be offset by a high risk of morbidity and mortality and also in the context of intracranial malignancy with limited lifespan. Serial imaging may subsequently provide clues regarding spontaneous resolution as against radiological or symptomatic progression which would then necessitate intervention.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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