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Case Reports & Case Series

Symptomatic radionecrosis of cerebral arteriovenous malformation post-stereotactic radiosurgery: Report of 2 cases

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ABSTRACT

Stereotactic radiosurgery (SRS) is an effective and non-invasive modality for the treatment of cerebral arteriovenous malformation (cAVM). Delayed radionecrosis may occur in a small percentage of them, with the majority of their symptoms being transient. We present 2 patients who developed persistently symptomatic radionecrosis lesions post-SRS of their cAVMs. Currently, causative factors underlying this phenomenon remain unelucidated. In addition, there are no biological markers to identify patients at risk of developing progressive lesions. Given the infrequency of such cases, the disease is discussed in corroboration with current literature and management strategies.

1. Introduction

A cerebral arteriovenous malformation (cAVM) is a congenital collection of abnormal blood vessels in the central nervous system. In present times, stereotactic radiosurgery (SRS) for cAVM has become a well-established management strategy with good outcomes [1]. Delayed symptomatic radionecrosis occurs in up to 9% of cAVM patients treated with SRS, with the majority being transient [2]. In this group of patients, the phenomenon of cyst formation post-SRS of cAVMs is uncommon, and may have a relatively long latency mean period of up to 6.5 years [3]. We present 2 patients who developed with persistently symptomatic radionecrosis lesions post-SRS of their cAVMs. Given the infrequency of such cases, the disease is discussed in corroboration with current literature and management strategies.

2. Case report

2.1. Case 1: Spetzer-Martin grade II corona radiata cAVM

A 26-year-old female presented with an onset of right-sided weakness secondary to a Spetzer-Martin Grade II left corona radiata-centred cAVM that haemorrhaged (Fig. 1). She recovered with good function post-neurorehabilitation. In view of the close proximity of the lesion to the motor cortex, the patient elected for SRS. She received a total dose of 23 Gy in a single fraction from a purpose-built linear accelerator (LINAC) system (Novalis, BrainLAB) to her cAVM nidus. However, approximately 18 months later, the patient re-presented with complaints of weakness in her right upper and lower limbs. Magnetic resonance imaging (MRI) of her brain reported a 3.5 × 3.8 cm heterogeneously enhancing lesion in the region of the patient's previous cAVM. There was extensive perilesional oedema involving left frontal and parietal white matter, with associated mass effect with midline shift of 1.1 cm. Angiography sequences were unremarkable and did not show recurrence of her previous cAVM. Follow-up spectroscopy scans showed that the left frontal lesion demonstrated raised lactate with no choline peak; hence, favouring radiation necrosis over a malignant tumour (Fig. 2). Despite her symptoms, the patient elected for conservative management. An interval MRI brain performed 12 months later did not show significant size reduction of the lesion and there was minimal improvement of her left-sided weakness. However, she was still not keen for surgical intervention.

2.2. Case 2: Spetzler-Martin grade I frontal cAVM

A 62-year-old male was diagnosed with an incidental Spetzler-Martin Grade I right frontal cAVM during workup for liver transplant

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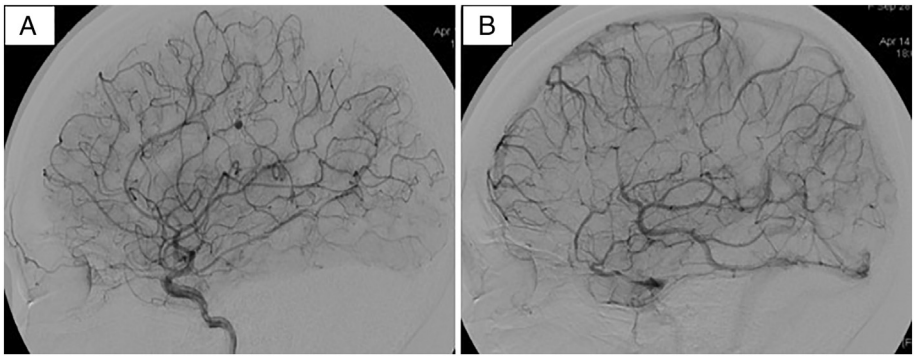

Fig. 1. (A) Lateral view of left internal carotid angiogram in arterial phase. This shows a small slow flow cAVM with a 3.6 mm diameter pseudoaneurysm supplied by an enlarged lenticulo-striate artery in the left corona radiata. (B) Lateral view of left internal carotid artery in venous phase. This shows there is venous drainage of the cAVM into the superior sagittal sinus.

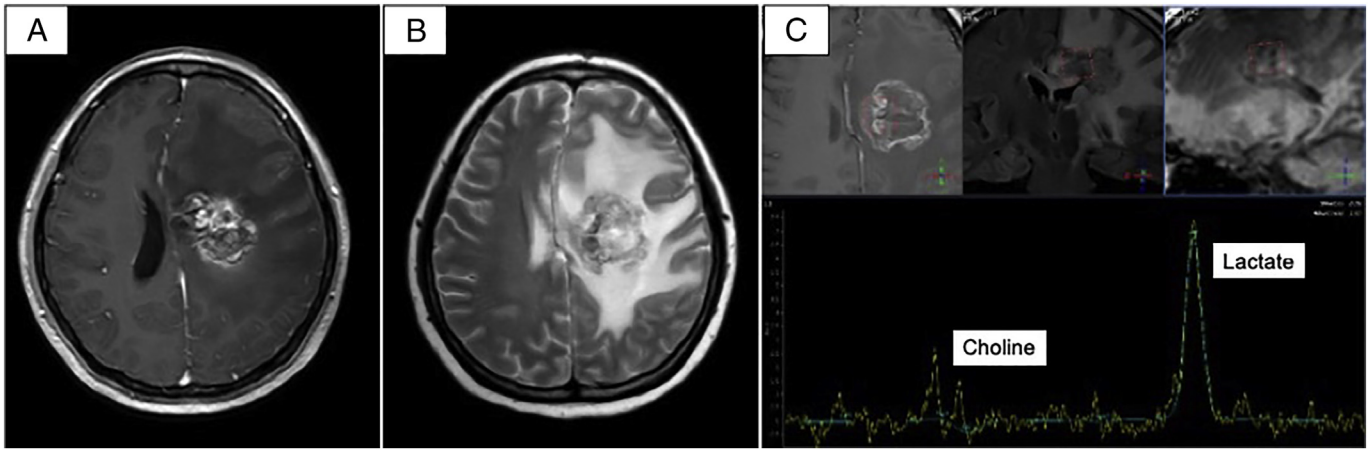

Fig. 2. (**A**) Representative post-contrast T1-weighted image in axial view. There is a heterogeneously enhancing lesion centred in the region of the patient's previous left cAVM. This lesion is associated with local mass effect and midline shift. (**B**) Representative T2-weighted image in axial view. This image demonstrates the extensive white matter changes secondary to perilesional oedema. (**C**) Metabolic changes of the MRS show a low choline levels and high lactate peak in the lesion of interest.

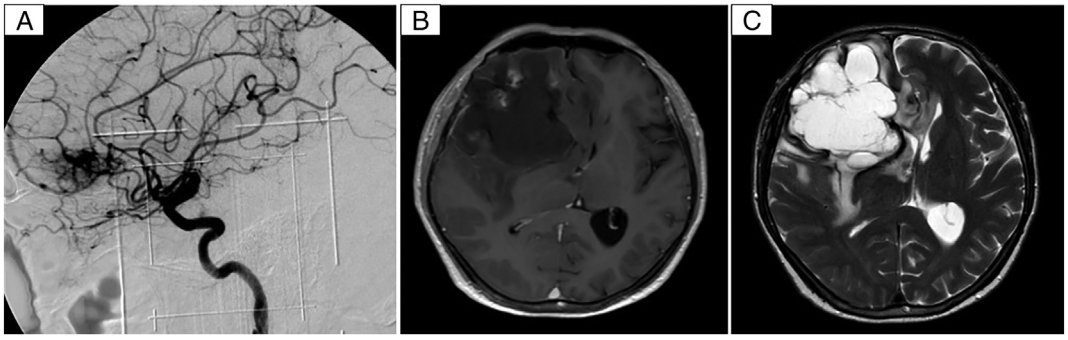

Fig. 3. (**A**) Lateral view of right internal carotid angiogram in arterial phase. There is a basifrontal cAVM with no deep venous drainage. Representative post-contrast T1-weighted (**B**) and T2-weighted (**C**) images of in axial view. Both images show a large, heterogenenous multi-loculated cystic area with a small, solid component within the lesion. This lesion is centred in the right frontal lobe where the cAVM previously was. This lesion has causative mass effect, perilesional oedema and midline shift.

surgery. The patient elected for SRS treatment after discussion with the neurosurgical team. He received 22 Gy in a single fraction (Novalis, BrainLAB) to his lesion's nidus. An interval cerebral angiogram 2 years post-SRS demonstrated obliteration of his cAVM. However, about 4 years post-SRS, the patient presented with headaches associated with vomiting. Magnetic resonance imaging of his brain reported a right frontal, multi-loculated cystic lesion with nodular enhancing areas centred in the region of his previous cAVM (Fig. 3). Further MR angiography sequences did not show recurrence of the cAVM. Decision was made for surgical excision of the cystic lesion. Histopathology reported chronic inflammatory regions with reactive gliosis changes (Fig. 4 and Fig. 5). No malignancy was detected. Post-operatively, the patient recovered well, and has been asymptomatic since.

3. Discussion

Cerebral arteriovernous malformation is postulated to be caused by defects during the development of blood vessels; and they are characterized by an arteriovenous shunt without a capillary bed, but with the presence of an arterial nidus [4,5]. Owing to the risk of intracranial haemorrhage, the goal of all therapies in cAVMs is obliteration of the malformation [4,5]. In particular for cAVMs at high surgical risk, radiosurgery is an useful option with good outcomes. Current data demonstrates that SRS is a safe and effective management approach

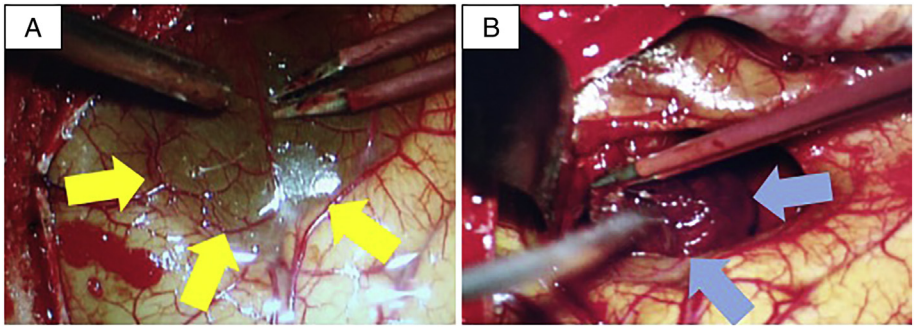

Fig. 4. Intra-operative photos of the cystic area of the intraparenchymal lesion marked with yellow arrows (**A**), and reddish, nodular component within the lesion marked with blue arrows (**B**). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

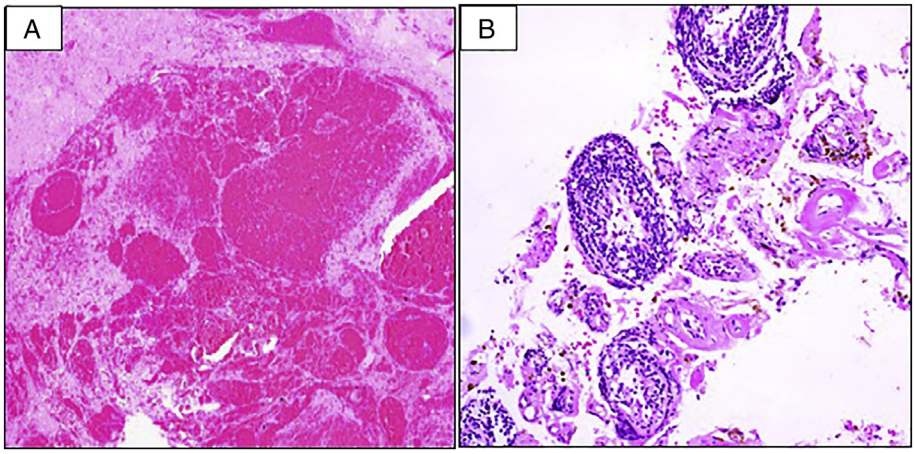

Fig. 5. (**A**) A haematoxylin and eosin stain photomicrograph showing large calibre blood vessels with congestion and surrounding brain parenchymal haemorrhage with associated necrosis (magnification ×200). (**B**) A haematoxylin and eosin stain photomicrograph showing blood vessels with hyalinized vessel walls and perivascular chronic inflammatory infiltrates (magnification ×400).

that is applicable for cAVMs [1]. Overall, the incidence of radionecrosis after SRS has been reported to be 5–20% [6]. Furthermore, the use of Gamma Knife compared to LINAC radiosurgery has not been shown to affect outcomes, with similar obliteration rates being reported between the two modalities in a prior study [7].

Late adverse effects of radiosurgery are uncommon [1]. Delayed symptomatic radionecrosis occurs in up to 9% of cases, with the majority being transient [2]. Broadly speaking, most cAVM post-SRS radionecrotic lesions are usually asymptomatic, and can be managed conservatively [3]. However, for patients with persistent and, or worsening neurological sequelae, there are no established guidelines for clinical management. In addition, it is difficult to predict which cohort of affected patients will have higher risk of symptom progression. Interestingly, patients with prior bleeds were observed to have delayed cyst formation, giving raise to the hypothesis that residual iron deposition in the brain tissue may have served as a radiation sensitizer that could potentiate the effects of radiosurgery on a long-term basis [1]. However, this theory has not been biologically validated; and in the context of our second patient, does not apply.

Under such circumstances, the use of adjunct imaging such as MRS may be helpful in this subset of patients. Radionecrosis post-radiation treatment being confused with a malignant tumour on MRI is a known phenomenon [8]. Recently, the use of MRS has been advocated as an increasingly valuable tool for the differential diagnosis of radiation-related reactions, as it provides metabolic and chemical patterns of tissue that reflect ongoing metabolic activity in brain lesions [9]. Nonetheless, all results should be interpreted with caution in context with the clinical scenario to avoid misdiagnosis. Most importantly, it should be emphasized that the use of MRS should be supplementary to conventional imaging, and no therapeutic decision should be based on MRS data alone [9].

In summary, we present 2 unique patients with symptomatic radionecrosis lesions post-SRS of their cAVMs. Both cases emphasize the need for conscientious, long-term follow-up of post-SRS cAVM patients, where this condition can be unforeseeable. In addition, these cases reflect there are knowledge gaps in the prediction of patients at risk of developing persistently symptomatic lesions.

4. Conclusion

Although radionecrosis with or without cyst formation post-SRS for cAVMs has been reported to be a largely benign entity, this case report reflects a subset of cases affected by effects of SRS complications. As clinicians managing these patients, we reiterate the need for more in-depth biological studies to better understand this challenging phenomenon.

Disclosure/conflict of interest declaration

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