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Stereotactic radiosurgery planning based on time-resolved CTA for arteriovenous malformation: a case report and review of the literature

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Abstract

Stereotactic radiosurgery has long been recognized as the optimal form of management for high-grade arteriovenous malformations not amenable to surgical resection. Radiosurgical plans have generally relied upon the integration of stereotactic magnetic resonance angiography (MRA), standard contrast-enhanced magnetic resonance imaging (MRI), or computed tomography angiography (CTA) with biplane digital subtraction angiography (DSA). Current options are disadvantageous in that catheter-based biplane DSA is an invasive test associated with a small risk of complications and perhaps more importantly, the two-dimensional nature of DSA is an inherent limitation in creating radiosurgical contours. The necessity of multiple scans to create DSA contours for radiosurgical planning puts patients at increased risk. Furthermore, the inability to import two-dimensional plans into some radiosurgery programs, such as Cyberknife TPS, limits treatment options for patients. Defining the nidus itself is sometimes difficult in any of the traditional modalities as all draining veins and feeding arteries are included in the images. This sometimes necessitates targeting a larger volume, than strictly necessary, with stereotactic radiosurgery for treatment of the AVM. In this case report, we show the ability to use a less-invasive and three-dimensional form of angiography based on time-lapsed CTA (4D-CTA) rather than traditional DSA for radiosurgical planning. 4D-CTA may allow generation of a series of images, which can show the flow of contrast through the AVM. A review of these series may allow the surgeon to pick and use a volume set that best outlines the nidus with least interference from

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Compliance with ethical standards

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feeding arteries or draining veins. In addition, 4D-CTA scans can be uploaded into radio-surgery programs and allow three-dimensional targeting. This is the first reported case demonstrating the use of a 4D CTA and an MRI to delineate the AVM nidus for Gamma Knife radiosurgery, with complete obliteration of the nidus over time and subsequent management of associated radiation necrosis with bevacizumab.

Keywords

4D computed tomography angiography; Arteriovenous malformation; Gamma knife radiosurgery; Radiation necrosis; Bevacizumab

Introduction

The gold standard of arteriovenous malformation (AVM) visualization remains digital subtraction angiography (DSA). For radiosurgical treatment, the inherent two-dimensional nature of this modality limits radiosurgical planning. This is particularly problematic in that correct delineation of the AVM nidus is necessary for success in radiosurgical ablation. In fact, Buis and colleagues demonstrated that inter-observer differences in the radiosurgical plan were elevated in cases of treatment failure, illustrating the limitation of DSA in AVM nidus localization and contouring [2]. For this reason, three-dimensional imaging (CTA/MRI) is often implemented for radiosurgery planning purposes [8]. Unfortunately, conventional CTA/MRI loses the temporal advantages associated with DSA, even with the use of timed boluses. To overcome these shortcomings, dynamic CTA and MRA have been developed and implemented at some institutions for the diagnosis and treatment of AVMs. Here we present a case in which we utilized conventional DSA for diagnosis and then time-resolved CTA (4D-CTA) for the design of the radiosurgical approach to treat a high-grade arteriovenous malformation. This case was further complicated by the development of radiation necrosis following treatment that was subsequently managed successfully with bevacizumab.

Case report

The patient, a 43-year-old white male, presented to our institution with left-sided weakness and complaints of numbness/tingling in his left lower extremity. Magnetic resonance imaging and computed tomography of the brain was obtained, revealing a right posterior frontal AVM. The lesion was not felt to be amenable to surgical resection due to the size and location. This was a Spetzler–Martin grade 4 AVM (more than 3 cm, related to the motor strip and with deep drainage). Gamma Knife radiosurgery (GKRS) was recommended and elected by the patient.

DSA was performed for diagnosis where a mask image was obtained and a subsequent contrast enhanced image with 50 cc ioversol 350 mg/ml IV was taken (Fig. 1). The image intensifier and digital subtraction was performed to remove the background. It was determined that the patient had a posterior frontal arteriovenous malformation supplied by the right middle cerebral artery. 4D CTA and contrast-enhanced magnetic resonance imaging were subsequently performed to localize the nidus for GKRS planning (Fig. 2).

4D CTA is performed with the Leksell G frame attached to the patient and the table. A mask image is obtained without contrast. This includes the entire frame and fiducial box. Then a test bolus of 10 to 20 ml of iopamidol 61 % is given followed by a limited timed arterial brain scan. The time it takes for the contrast to show up in the internal carotid artery at the skull base is noted. We then re-inject with 50 to 70 ml of contrast and 50 ml of saline flush. Using the time delay recorded initially, multiple volumetric whole-brain scans are obtained covering the arterial, nidal, and delayed phases of flow through the AVM. Usually a time period 3–4 s before and 1–2 s after the time noted for the bolus to appear at the skull base is used. The acquired volume sets are reviewed and the set that shows the nidus the best is sent to the planning software along with the mask images.

4D CTA provided enhanced temporal resolution due to a decreased sampling interval of 0.275–0.5 s for every $\frac{1}{2}$ of a gantry rotation. Three different time frames were utilized allowing excellent flow dynamic characteristics for the nidus, draining veins, and feeding arteries. Each acquisition was done with parameter ranges of 160 mm, 80 kV, 120 mA, and a time of 0.35 s. Total time in the scanner was 15 s. 4D CTA images from selected series, as the contrast bolus passed through the AVM, are shown in (Fig. 2). These show the calcification in the AVM and the contrast outlining the nidus (Fig. 2b–d) with visualization over time of the feeding arteries and draining veins (Fig. 2b–f). The series that were felt to show the nidus the best (b–c) were imported into the radiosurgery software and merged with the stereotactic MRI obtained after the 4D-CTA. A GKRS plan was then created and approved by the radiation oncologist and radiation physicist (Figs. 3, 4, and 5). The nidus volume was 9.04 cm³. The plan was composed of 4, 8, and 16 mm standard and composite shots for a total of 37 shots. The beam was on for 113.8 min with the nidus of the AVM receiving a dose of 18 Gy to the 50 % isodose line. The patient was positioned on the Gamma Knife unit, and the treatment was delivered without complications.

Three months later, following the completion of GKRS, the patient was admitted to the hospital again for complaints of severe headache and periods of unresponsiveness. The patient was diagnosed with a seizure disorder and anti-epileptic drug therapy was initiated. CT brain also revealed persistence of the AVM with associated FLAIR signal change, believed to be a radiation effect, but without midline shift. At this point, the patient was treated with dexamethasone, 2 mg BID for 21 days. Subsequently, a year later the patient presented with severe hemiparesis and studies identified the development of radiation necrosis that was managed successfully using bevacizumab, similar to cases described previously (Figs. 6 and 7). Bevacizumab was given at 7.5 mg/kg tri-weekly over three cycles. The patient showed significant clinical improvement and radiation necrosis and mass effect from edema resolved completely. Cerebral angiography revealed complete obliteration of the AVM nidus at 15 months (Fig. 8).

Discussion

The gold standard for diagnosing AVMs has been DSA. DSA has also been used with varying success in designing treatment contours. Willems and colleagues recently compared DSA to 4D-CTA, however, and found that 4D-CTA was able to delineate the AVM nidus for diagnosis better than DSA [15]. With a compact AVM the nidus can usually be outlined with

good certainty using MRI. When the nidus is somewhat loose and the AVM has high flow, outlining the nidus can be very difficult. In this scenario, if the demarcation of the nidus is too conservative, the AVM may persist, and if the nidus is characterized too broadly, the patient may not be able to receive an adequate prescription dose to the nidus margin. This may lead to a higher risk of adverse radiation effects. In such cases, 4D-CTA may help in outlining the nidus with more precision than conventional means. Improved nidus demarcation allows for a smaller nidus volume and more focused treatment to the site of vascular pathology [5]. 4D-CTA has several advantages over DSA for treatment planning in that the fast gantry rotating speed and enhanced post-processing interval increases temporal resolution [9]. The improved temporal resolution is useful for distinguishing collateral vascular flow and feeding vessels for the AVM to avoid excess radiation administered outside of the nidus [13]. 4D-CTA is therefore useful for surgical planning for the treatment of AVM [19]. We show in this report that 4D-CTA can be used to establish stereotactic radiosurgery contours for the treatment of an AVM. DSA was again later used to confirm treatment success, but was not used for treatment planning. A post-treatment angiogram was obtained 15 months after GKRS for our patient, and this showed complete resolution of the AVM (Fig. 8).

4D-CTA has recently been used in designing treatment approaches for AVM-related aneurysms [3]. It has been used in designing therapeutic approaches for vascular shunts and dural AV fistulas [4, 19]. It has even been employed in the treatment of ischemic and hemorrhagic stroke [10]. We report for the first time the use of 4D-CTA for GKRS. The temporal resolution and 3D imaging capability make it an ideal modality for mapping contours. The GKRS successfully treated the AVM in the case above. GKRS is always well tolerated initially, but adverse radiation effects may be seen in up to 30 % of patients with 10 % having clinically significant symptoms. A smaller target volume may lead to a decrease in the adverse radiation effects. 4D-CTA may therefore be used to optimize GKRS delivery and decrease the target volume with conformal contouring of the nidus [1]. A potential outcome following GKRS is radiation necrosis. Radiation necrosis is reported in ~12 % of patients by one year [14]. Our patient did develop radiation necrosis at the site of the treatment and was successfully treated with bevacizumab, to avoid prolonged steroid use.

Recent advances in medical management have made the treatment of radiation necrosis feasible. A recent double-blind placebo-controlled clinical trial showed class 1 evidence that bevacizumab is efficacious for the treatment of radiation necrosis in the central nervous system [11]. Sheehan and colleagues showed that it was effective for radiation necrosis caused by stereotactic radiosurgery for an AVM [16]; 7.5 mg/kg of bevacizumab administered bi-weekly over three cycles has provided excellent results in patient recovery [6]. The effect appears to be independent of the underlying etiology [17]. Radiation necrosis is proposed to occur due to vascular damage and proliferation, therefore bevacizumab, an angiogenesis inhibitor, treats the underlying cause of symptom manifestation [12]. Bevacizumab has been shown to reduce angiogenesis in patients thereby limiting edema and proteinopathies around the radiation site [18]. Bevacizumab can limit prolonged dexamethasone therapy. It works by preventing vascular endothelial growth factor from reaching leaky capillaries damaged by radiation [7]. In our patient, bevacizumab was successful in alleviating clinical symptoms allowing a full functional recovery.

Conclusions

DSA has been the gold standard for diagnosing AVMs. It is limited by 2D resolution, and potential risk of an invasive modality, making it a poor choice for treatment planning. We present a case showing the successful use of 4D-CTA in outlining an AVM nidus and designing GKSR contours in combination with a MRI. We believe that the use of the 4DCTA allowed us to minimize the nidus volume, allow successful single volume therapy, and was ultimately helpful in the complete obliteration of the nidus. Although the treatment was successful in obliterating the AVM, it was complicated by radiation-induced necrosis. The angiogenesis inhibitor, bevacizumab, was used to treat the radiation necrosis with full recovery. 4D-CTA should be considered as a useful planning tool for treating AVMs radiosurgically.

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Fig. 1. Digital subtraction angiography (DSA) demonstrating presence of AVM on antero-posterior (a) and lateral (b) views. Magnetic resonance imaging confirms the presence of the AVM (c-d)

Fig. 2.
Examples of AVM nidus visualization over time on 4D CTA, **a** Standard head CT, **b** time 0 s, **c** time 0.87 s, **d** time 1.73 s, **e** time 6.52 s, and **f** time 10 s

Fig. 3.
Nidus delineation on MRI (a) and with 4D CTA (b)

Fig. 4.
Sample MRI planning images from *Leksell GammaPlan®*

Fig. 5.
Sample 4D CTA planning images from *Leksell GammaPlan®*

Fig. 6. Pre (a–b) and post bevacizumab (c–d) MRI scans, showing increased permeability and edema, with resolution following therapy

Fig. 7. Radiation necrosis on: **a** T1 with contrast and **b** FLAIR images after Gamma Knife radiosurgery. Treatment with bevacizumab resolved the radiation necrosis as evident on **c** T1 with contrast and **d** FLAIR imaging

Fig. 8.
Fifteen-month post-treatment angiography (a–b) and MRI (c–d) show complete resolution of the AVM