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Teaching Case

Stereotactic Radiation Therapy for an Arteriovenous Malformation of the Oral Tongue: A Teaching Case

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Introduction

Arteriovenous malformations (AVMs) are congenital vascular anomalies resulting in a direct connection between feeding arteries and draining veins. This results in a high-flow nidus, which is commonly progressive and can become life-threatening.[1] Over 90% of AVMs are intracranial.[2] Head and neck AVMs represent almost 50% of extracranial AVMs[3] and most commonly occur within the face or mandible. Lingual AVMs are quite rare.[4]

Management of head and neck AVMs typically includes conventional surgery and endovascular interventions, with a goal of complete resection or blockade of the nidus.[1] However, recurrence rates after resection of up to 80% are reported.[5,6] Incomplete treatment of AVMs can induce aggressive regrowth, complicating further management.[4,7] Stereotactic radiation therapy (SRT) is used with good efficacy to obliterate and reduce the risk of hemorrhage in intracranial AVMs.[8] Experience with SRT for head and neck AVMs, and particularly tongue AVMs, is limited.[9-11]

Here, we describe use of frameless SRT for a patient with a high-flow AVM of the oral tongue.

Methods and Materials

Case presentation

A 21-year-old woman presented with a tongue ulcer 10 months postpartum. Several attempted biopsies resulted in bleeding events requiring transfusion. On referral to otolaryngology at our institution, she was found to have prominent vessels with palpable thrill on the ventral surface of the tongue. Angiography demonstrated an extremely high-flow and diffuse AVM involving the anterior two-thirds of the bilateral tongue (Fig 1A). Given the extensive nature of the lesion, she proceeded with tracheotomy for airway protection, near-total glossectomy, ligation of the bilateral lingual arteries and left facial artery, and reconstruction with a perforator-based anterolateral thigh free flap. Angiogram 3 days postoperatively showed

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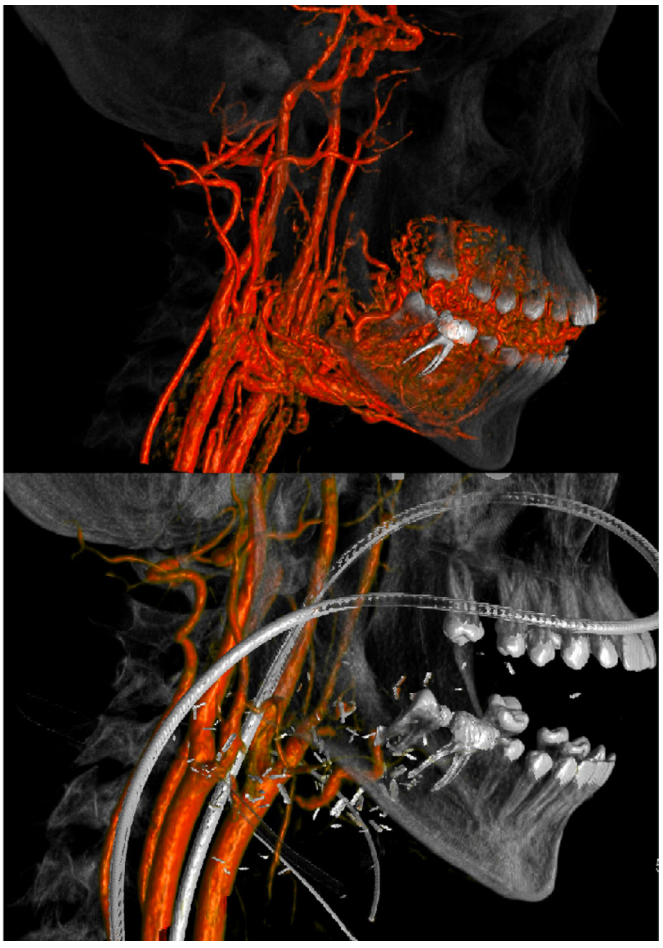

Figure 1 A, Preoperative angiography image showing a high-flow arteriovenous malformation diffusely involving the bilateral anterior two-thirds of the oral tongue. B, Angiography image 3 days postoperatively showing no evidence of residual arteriovenous malformation.

no evidence of residual AVM (Fig 1B). However, angiogram 3 months later demonstrated slightly early venous drainage of the right lingual artery, suggesting a possible small residual shunt. Six months postoperatively, she began to experience recurrent episodes of bleeding. Targeted next-generation sequencing revealed a somatic KRAS mutation, and she subsequently began therapy with trametinib. The patient represented with a massive bleed approximately 1 year after resection, requiring intubation, transfusions, and tracheotomy for airway protection. Computed tomographic angiography (CTA) and magnetic resonance angiography demonstrated a large AVM recurrence, essentially replacing the entirety of the free flap reconstruction tissue at the tongue base. Angiography was performed and did not show an arterial source amenable to embolization. Her case was discussed at multidisciplinary conference, with recommendation for SRT and a dose increase of trametinib.

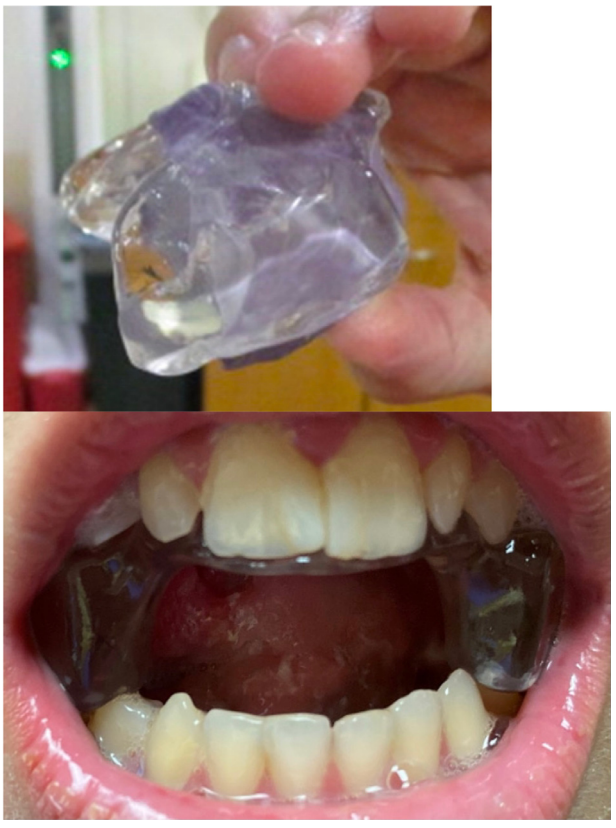

Figure 2 Custom oral fixation bite piece created by prosthodontist, including acrylic component for impression of the jaws/teeth and central component made of impression material to depress residual tongue.

Results

Radiation therapy planning and treatment

A prosthodontist created a custom oral fixation bite piece, consisting of an acrylic component for impression of the jaws/teeth and a large central component made of impression material, to depress the residual tongue, encourage interfraction reproducibility, and minimize intrafraction motion of the tongue and mandible (Fig 2). With the bite piece in place, the patient underwent simulation in our department using CTA. Antimuscarinic agents were prescribed to reduce secretions and associated motion, including a scopolamine patch to be used for several days before simulation and atropine drops administered sublingually just before simulation. A custom thermoplastic face mask and head sponge were created, according to our institutional frameless SRT protocol. Intravenous iohexol contrast (Omnipaque 300 mg/mL, GE Healthcare) was administered at a flowrate of 4 mL/s over 25 seconds. An arterial phase was acquired 4 seconds after contrast bolus tracking in the aortic arch. Images were acquired in a caudocranial direction with the

following parameters: slice thickness of 1 mm, pitch of 0.5, rotation time of 0.5 seconds, collimation of 0.6 mm × 128, x-ray tube potentials of 120 kVp, and a field of view of 50 cm. A BR38 filter kernel was used for image reconstruction with iMAR (Siemens Healthineers), an iterative metal artifact reduction. After the initial scan, the mask and mouthpiece were disassembled and then replaced, and another CT scan was obtained to estimate the magnitude of potential interfraction motion. After rigid registration to account for gross patient positioning differences, a manually guided deformable registration of the patient's residual tongue (MIM Software) revealed scan-to-scan deformations averaging 1.0 mm, with a maximum of 2.0 mm as quantified using a target registration error metric.[12]

Using the simulation CTA, the AVM nidus was contoured under the guidance of the radiation oncologist and interventional neuroradiologist. An expansion of 2 mm was performed to determine the final planning target volume (PTV) (Fig 3). PTV volume was 112.5 mL. SRT treatment planning was then performed to determine the optimal treatment field setup parameters to achieve appropriate dose coverage of the target and minimize dose to surrounding healthy tissues, including the mandible, teeth, soft palate, lips, spinal cord, and brain stem. The resulting plan used 5 noncoplanar volumetric modulated arc therapy applications (4 arcs within ± 20° of the axial plane and 1 limited span sagittal arc) and was optimized to maximize dose falloff outside the treatment volume (Fig 4). Material override of the bite piece and dental hardware was performed. A total dose of 22 Gy given in 2 fractions spaced 5 days apart was prescribed. On the final plan, 96.5% of the PTV received 22 Gy, and 99.5% of the PTV received 20.2 Gy. Prescription isodose volume-to-target volume ratio was 1.00. Dose gradient[13] index (50% Rx isodose volume/100% Rx isodose volume) was 2.79. The maximum dose to 0.1 cm^3 was 27.5 Gy, centered in the residual tongue (Fig 5). Trametinib was held for 48 hours before and after SRT.

Before treatment, a scopolamine patch and sublingual atropine drops were again administered, along with lorazepam. A verification cone beam CT simulation scan was performed, and soft tissue alignment was excellent. Optical surface monitoring (AlignRT; Vision RT Ltd) was used throughout the treatment to ensure minimal intrafraction motion on our SRT treatment unit (TrueBeam STx; Varian Medical Systems, Inc).

Patient outcome

The patient had a nasogastric feeding tube placed prophylactically to ensure adequate oral intake. She developed oral pain, odynophagia, and mucositis consistent with grade 3 toxicity, which peaked from 3.5 to 5 weeks after completion of SRT. The patient was seen in clinic 6 weeks after completion of SRT, at which time symptoms had almost completely resolved. The patient did

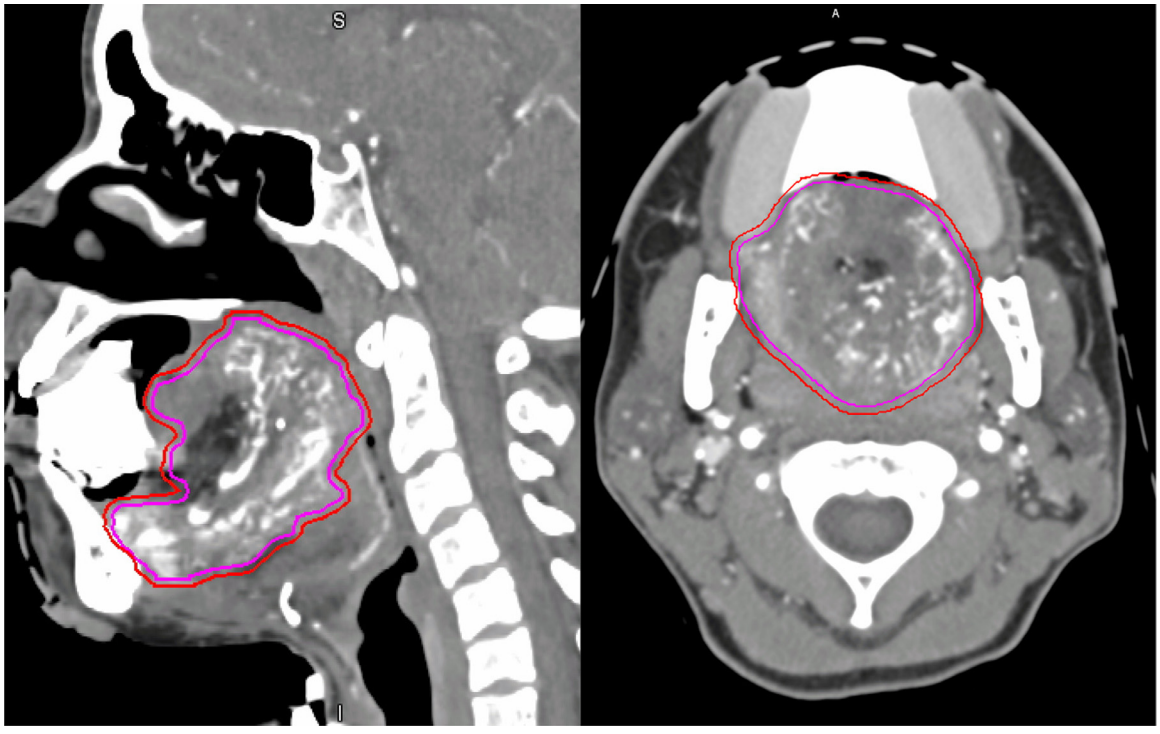

Figure 3 Simulation computed tomographic angiogram permits excellent delineation of the arteriovenous malformation nidus, which was contoured (pink) and then expanded by 2 mm to determine the final planning target volume (red).

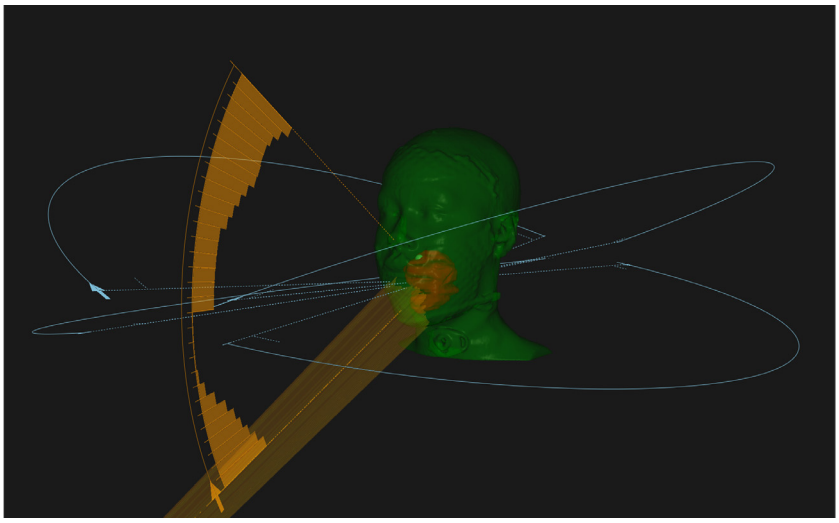

Figure 4 The stereotactic radiation therapy plan used 5 noncoplanar volumetric modulated arc therapy applications (4 arcs within ± 20° of the axial plane and 1 limited span sagittal arc).

experience a bleeding event requiring transfusion and hospitalization approximately 3 months after SRT.

Discussion

We report a case of SRT to treat an AVM of the oral tongue. Based on the aggressive natural history of head and neck AVMs[5,6] and potentially serious functional limitations after extensive resections in the region, noninvasive approaches such as SRT are attractive. However, to our knowledge, there are only 2 case reports describing SRT for tongue AVMs,[10,11] and tissue motion and toxicity to healthy tissues in the oral cavity are serious concerns. We describe details of the procedure, including novel techniques and treatment planning considerations.

Motion in the current study was limited by use of a custom bite piece, thermoplastic face mask, medications to limit secretions, and surface guidance during treatment. This permitted us to use a PTV expansion of 2 mm, and reproducibility of setup was affirmed at the time of simulation. The use of CTA on the CT simulator additionally eliminated inaccuracy introduced by image fusion from a separate diagnostic scan.

Given acute toxicity risks associated with radiation to the oral tongue, which is less of a concern in the setting of SRT for brain AVMs, we elected to fractionate into 2 fractions. The selected dose of 22 Gy in 2 fractions of 11 Gy results in a biologic equivalent dose to 16 Gy in 1 fraction, according to the linear quadratic equation using an α/β of 2. SRT doses for brain AVMs typically range from 16 to 25 Gy, with 16 Gy resulting in an obliteration rate of approximately 70%.[14,15] Although doses up to 20 Gy have been shown to result in higher obliteration rates,[15] based on the large target size of 112.5 mL and the AVM location, we did not feel the benefits of dose escalation would outweigh the risks in the current case. Escalation to 20 Gy biologic equivalent dose may be considered for future head and neck AVMs with smaller targets located further away from critical structures. Saito et al and Koyfman et al prescribed doses of 22 Gy in 2 fractions daily and 24 Gy in 3 fractions once weekly, respectively, for tongue AVMs.[10,11] Notably, Saito et al prescribed to the 49% isodose line, allowing for a maximum dose of 45 Gy. We were able to achieve adequate target coverage with less heterogeneity and opted for this approach given concerns about toxicity with higher maximum doses in the tongue. We additionally elected for an interval of 5 days between fractions with a goal of reducing acute toxicities by allowing time for oral mucosa repopulation, and because tumor repopulation was not a concern in a benign disease.

The patient did have mucositis that developed approximately 3.5 weeks after treatment, consistent with turnover time of the oral mucosa.[16] In the future, we would attempt to limit mucositis further with a longer bite piece to push the tongue away from the soft palate, which was not possible in the current case due to the shape of the patient's residual tongue.

Regarding efficacy, complete angiographic obliteration and major improvement on CT angiogram several years after SRT were noted in the above case reports.[10,11] Our patient did experience a bleeding event 3 months after SRT. Although there is some reduction in bleeding risk during the approximately 2-year latency period after SRT for intracranial AVMs, the major decrease in bleeding risk occurs after AVM obliteration.[8] Thus, it remains too early to assess overall treatment efficacy in our patient, and this is a limitation of the current report.

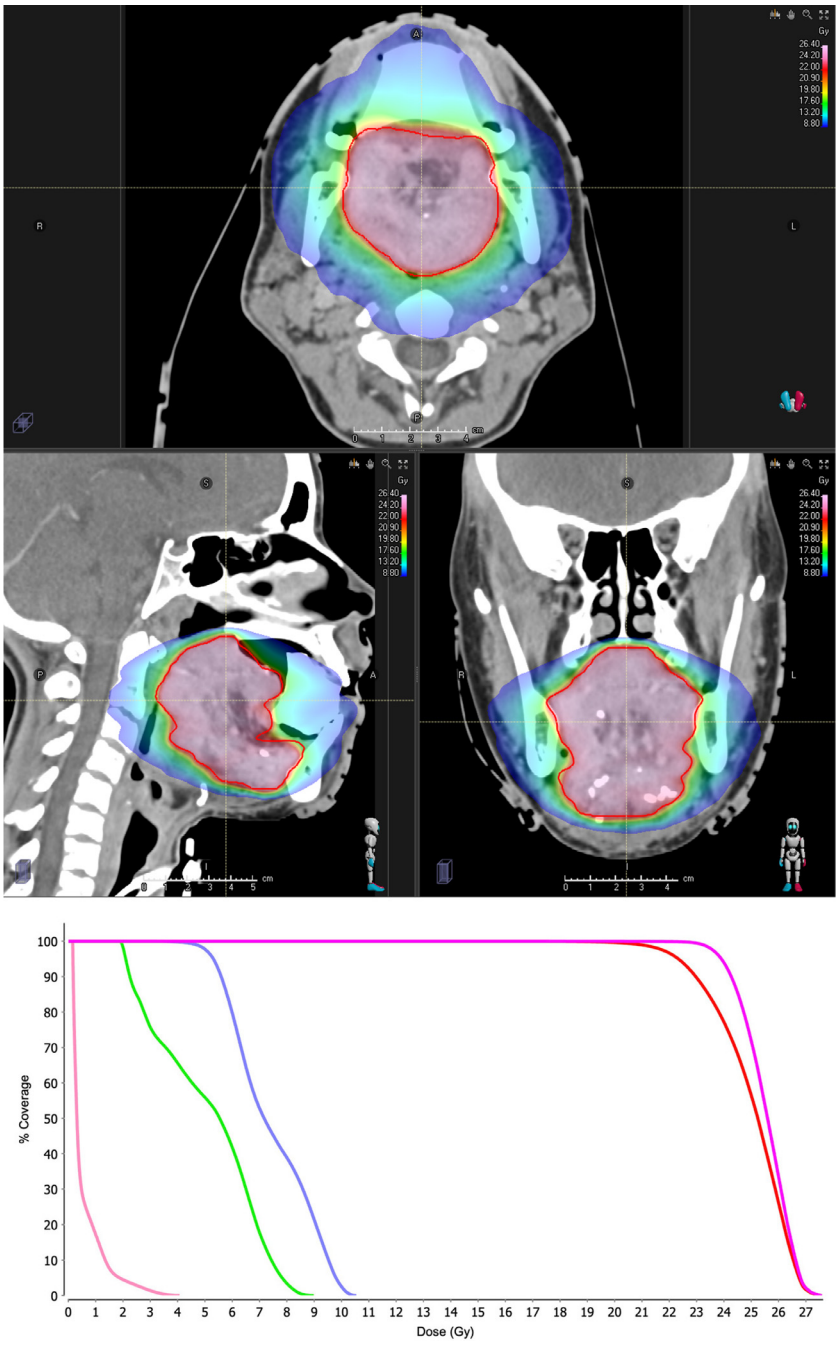

Figure 5 Final treatment plan consisted of 22 Gy in 2 fractions spaced 5 days apart, as shown, with isodose lines in color wash. Dose volume histogram demonstrates coverage of the arteriovenous malformation (pink) and planning target volume (red), and organs at risk doses including lips (blue), spinal cord (green), and brain stem (pink).

Conclusion

We report the procedural details for performing SRT to an AVM of the oral tongue. Given that this is feasible and well tolerated, SRT should be considered for patients with head and neck AVMs and limited surgical or endovascular options. We hope this publication increases awareness of this treatment option and serves as a practical guide to those performing SRT for head and neck AVMs.

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