

Case report

## Fatal case of intracerebral hemorrhage during gamma knife treatment for metastases

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### Abstract

This case report presents a patient suffering acute fatal intracranial–intratumoral hemorrhage during a gamma knife treatment session. Acute hemorrhage during a radiosurgery session is extremely rare and a plausible cause for this case is discussed along with a literature review of previously reported incidents. The patient was a 71-year-old male presenting with three large intracranial lesions and an underlying primary renal cell carcinoma malignancy. Because of a severe kyphotic deformity resulting from ankylosing spondylitis, the patient was placed in a moderate Trendelenburg position to allow his head to fit into the gamma knife unit during the radiosurgery session. The two left-sided lesions were to be treated with 20 Gy to the 50% isodose line, and the right-sided lesion with 16 Gy to the 40% isodose line. Anesthesia was available throughout the treatment session to aid with pain control. The gamma knife treatment was aborted because the patient suffered a generalized seizure while in the unit. Immediate head CT of the patient revealed large acute hemorrhages into all three intracranial masses. This proved to be a fatal complication. It is likely that this positioning contributed to the hemorrhage. The clinical history of this patient is provided as well as a review of the literature on acute intracranial hemorrhage associated with radiosurgical therapy.

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### 1. Introduction

Radiosurgery is a widely used therapy for the control of solitary and multiple metastatic brain tumors, which is the most common use for this treatment modality [1–3]. In a large series of patients with solitary metastases of mixed sources, radiosurgery provided a median survival of 11 months after diagnosis [1]. Efficacy has also been

demonstrated for specific pathologies such as renal cell carcinoma [4] and non-small cell lung carcinoma metastases [5]. A level of safe tumor control has also been demonstrated for repeat radiosurgery for metastases [6]. Complications of radiosurgery for solitary metastatic lesions include the development of neighboring radiation necrosis, increases in surrounding edema, and tumor hemorrhage (actuarial rate at 1 and 2 years of 7.6% in mixed pathology [1]). In a small group of patients with renal cell carcinoma (52 treated lesions), complications were very rare and none of them suffered a delayed hemorrhage [4], while in a larger series (75 patients with 350 treated lesions), the delayed hemorrhage rate was 12% [7].

Acute bleeding taking place during a radiosurgery treatment session for a metastatic lesion, or in the immediate

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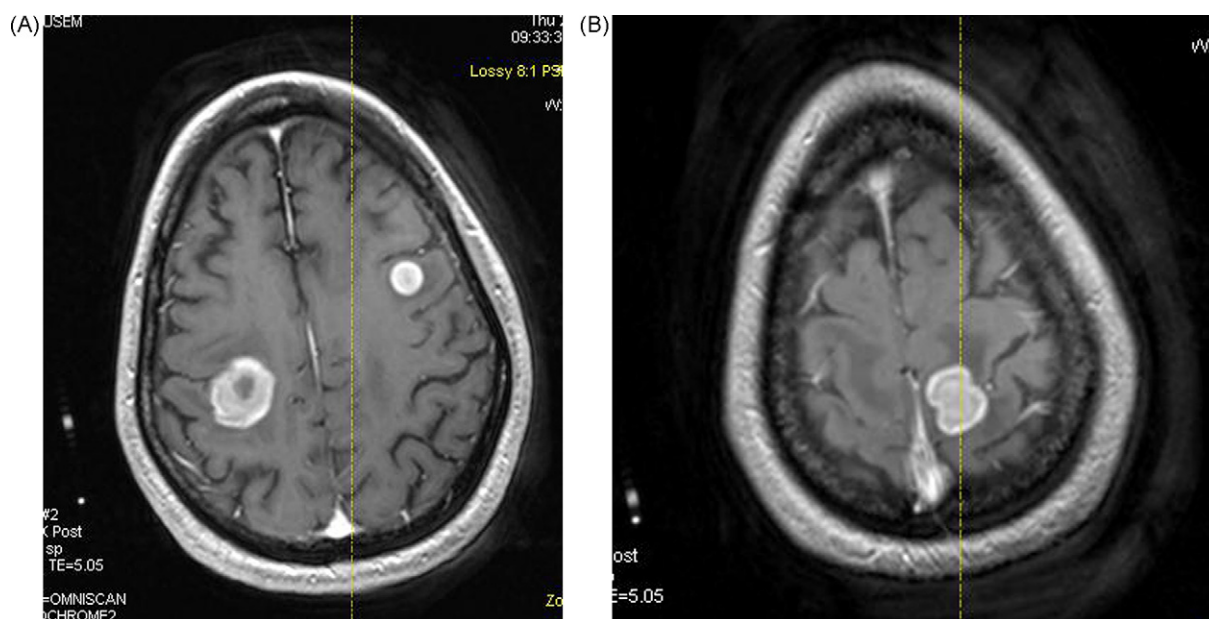


Fig. 1. T1 post-gadolinium contrast axial MRI images demonstrating the location of the three treated metastases.

post-treatment period, is extremely rare. We describe in this case report the occurrence of simultaneous hemorrhage in several metastatic lesions in one patient during a gamma knife treatment session. This individual had a history of ankylosing spondylitis with a severe cervical kyphotic deformity, and had to be placed in Trendelenburg position to allow the head and frame to fit correctly into the gamma knife unit. It is possible that this positioning contributed to the patient's hemorrhagic complication. Two previous patients have been described as having acute onset intratumoral hemorrhage within 24 h after radiosurgical treatment, one at 15 min post-treatment [8], and one at 2 h post-treatment [9]. A description of the current patient suffering a hemorrhage during gamma knife treatment as well as a review of the previous two patients is presented. Discussion of the possible role Trendelenburg positioning and its alteration in venous flow dynamics might have played in this unusual complication is also included.

## 2. Case report

A 71-year-old gentleman with a history of ankylosing spondylitis presented to an outside institution approximately 1 month prior to treatment with new onset left hand weakness. On exam in the emergency room, this consisted of poor hand intrinsic muscle strength, 2/5 biceps weakness, C5 dermatomal hypoalgesia, and a decreased biceps reflex. An MRI performed at that time demonstrated degenerative osteophytic disease from C5-C7 with pronounced cord impingement. Ten days later the patient underwent a C5-6 anterior cervical discectomy and fusion with plated stabilization and allograft with demineralized bone matrix. A brief course of perioperative dexamethasone was instituted.

Immediately after surgery, the patient noted a subjective improvement in left upper extremity strength, but after 3 days this had reversed its course and both the left arm and leg began exhibiting pronounced weakness.

Approximately 3 weeks after presentation, a CT of the brain was performed which revealed three intracranial mass lesions: a right frontal mass measuring 17 mm × 21 mm in greatest axial dimension, a left inferior frontal 6-mm diameter mass, and a second left premotor frontal mass of 11-mm diameter. At that time, an MRI was difficult to obtain because of the patient's severe cervical kyphosis related to the ankylosing spondylitis. After diagnosing these intracranial mass lesions, the patient exhibited a dramatic functional improvement while on dexamethasone. The patient was also placed on phenytoin, and at no time exhibited seizures prior to treatment. A full oncologic staging diagnostic evaluation was performed which additionally revealed a 3-mm right pulmonary nodule and a large left renal mass. A fine needle aspiration of the pulmonary nodule was performed, which revealed metastatic renal cell carcinoma, positive for CD10. A plan was proposed to treat these various malignant lesions, including radiosurgery for the intracranial lesions, possible radiofrequency ablation for the lung nodule, and possible laparoscopic treatment of the renal mass.

A system of sloped pads was slipped under the patient's back to orient the patient's head collinear to the MRI head coil. The preoperative planning images to be used for radiosurgical treatment were obtained (Fig. 1). The same system of pads was also used on the radiosurgery (gamma knife) treatment table, effectively putting the patient into 15–20° of Trendelenburg positioning. The patient had significant cervical discomfort at baseline and an anesthesia team was present to help with positioning and pain management. Because of

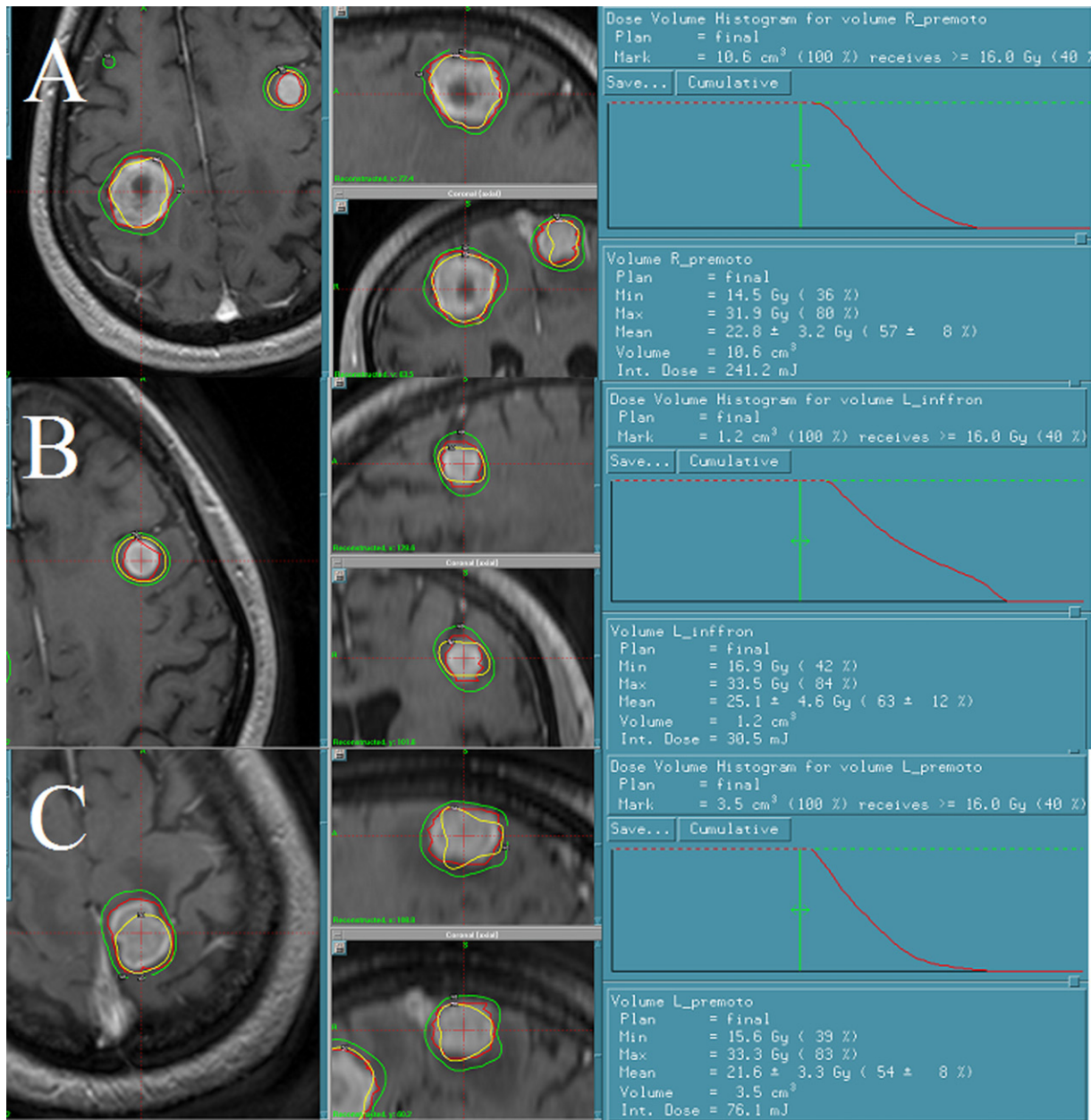


Fig. 2. Gamma plan screen snapshots and dose–volume histograms for the (A) right premotor lesion, (B) left inferior frontal lesion, and (C) left premotor lesion.

concern regarding the stability of the patient’s cervical spine and to accommodate the patient’s wishes, he received only small doses of opiate and was awake and conversant throughout the 1-hour MRI and 3-hour radiosurgery treatment.

The planned dosage was for 20 Gy to the 50% isodose line for both left-sided lesions, and 16 Gy to the 40% isodose line for the right-sided mass. An additional right frontal white matter (<1 cm) lesion discovered during the planning MRI was also to be treated for 20 Gy to the 50% isodose line (maximum dose 40.0 Gy), and a final small (<1 cm) right superior frontal lesion was to be treated for 20 Gy to the 50% isodose line (maximum dose 24.8 Gy). The maximum doses to the three largest lesions were left inferior frontal lesion, 33.5 Gy;

left premotor, 33.3 Gy; right premotor frontal, 31.9 Gy. No unusually excessive “hot spots” were noted in the pretreatment gamma knife plan. The whole brain maximum dose was 40.0 Gy. Screenshots of the Gamma Plan (Elekta AB, Stockholm, Sweden) software during treatment planning as well as dose–volume histograms for the three large lesions are presented in Fig. 2.

During the treatment for the posterior portion of the right frontal lesion and the left superior frontal lesion, the patient suffered a focal motor seizure involving his left foot. The patient became acutely hypertensive during this focal seizure as well. As the patient was pointing toward his foot during treatment he lost consciousness and suffered a generalized





Fig. 3. Head CT without contrast demonstrating intratumoral hemorrhages in the metastatic lesions.

seizure. The patient was immediately removed from the treatment couch and an emergent head CT examination revealed large hemorrhagic lesions at the site of the metastases (Fig. 3). The patient never regained consciousness from this generalized seizure, and his neurologic status gradually declined. Comfort care measures were instituted after extensive discussions between staff and family and he died shortly afterward. No pretreatment coagulation profile was available for the patient, but immediately after the post-treatment CT examination, the prothrombin time was 10.3 s, with an activated partial thromboplastin time of 18.8 s (normal 23.5–34.0 s).

### 3. Discussion

This case report describes a patient with three intracranial metastatic tumors from a renal cell carcinoma source who suffered concurrent hemorrhages in the masses during radiosurgical treatment. A previous case report described by Izawa et al. [8] presents a 46-year-old woman who was being treated for multiple brain metastases from lung cancer. The largest of these metastases had been removed surgically from the left frontal lobe without complication. On postoperative day 4 she underwent gamma knife treatment for the remaining nine intracranial lesions (20 Gy to the 50% isodose line). Per Izawa et al. [8], 15 min post-treatment the patient became unresponsive and the head CT demonstrated a large intraparenchymal hemorrhage in the left cerebellar hemisphere where one of the treated metastases was located. The authors monitored this

patient's blood pressure during treatment, and there were no abnormal values recorded. One case report in the Japanese literature is similar, describing the case of a patient undergoing LINAC radiosurgical therapy for intracranial metastases from a breast cancer primary [8,9]. This patient suffered peritumoral hemorrhage 2 h after treatment. Additionally, in the large series of Wowra et al. [7], one patient with a treated renal cell metastases did suffer an acute hemorrhage 5 h post-treatment. No further details were provided. A comparative table of these four cases is presented in Table 1.

One concerning aspect of our patient's treatment plan involved his positioning on the gamma knife table. He was placed into a relative Trendelenburg position by approximately 15–20° using a system of pads placed under the lower back and legs. This position enabled the head with frame attached to fit appropriately into the collimator helmet, which would otherwise have been impossible due to his severe kyphotic deformity. It is conceivable that this positioning created an adverse venous pressure gradient making the intratumoral vascular system more likely to bleed even during the radiosurgery treatment. Internal jugular venous distention occurs during Trendelenburg positioning, with only 10° of positioning needed to increase the mean internal jugular diameter by 2 mm [10]. In a study 20 healthy volunteers, 25° of Trendelenburg positioning produced the maximum amount of distention [10], which is closer to the angle used during the gamma knife treatment. There are analogous rises in ICP with Trendelenburg positioning as well as decreases with the reverse Trendelenburg positioning, which is often used for its clinical effect [11,12]. We have no definitive evidence that this positioning was the cause of our patient's simultaneous hemorrhage in all three lesions, but given that acute hemorrhages taking place either during the treatment or within a few hours after it have been extremely rare, we feel the positioning was a very likely contributor.

It is not unusual for intracranial neoplasms to undergo spontaneous hemorrhage, whether they are intrinsic brain tumors or metastatic lesions. Prospective series indicate that brain tumors present as hemorrhagic lesions 2–3% of the time [13–16]. Similarly, in prospective series, a given presenting spontaneous intracerebral hemorrhage can be associated with an intracranial tumor approximately 7% of the time [14]. Renal cell carcinoma metastatic lesions in particular have a propensity to undergo spontaneous hemorrhage [17,18]. But they do seem to hold up fairly robustly to gamma knife treatment, with one large prospective series of 350 metastases demonstrating a delayed bleed rate of 12% of treated patients [7]. This further highlights the temporal correla-

Table 1  
Comparison of four reported acute (<24 h) hemorrhage cases after radiosurgical treatment

Patient	Pathology	Post-treatment time to neurologic decline	Outcome
71-Year-old male	Renal cell carcinoma	Occurred during treatment	Fatal
46-Year-old female [8]	Lung adenocarcinoma	Acute neurologic decline 15 min after treatment	Fatal
44-Year-old female [9]	Breast cancer	2 h post-treatment	Recovery to baseline function
NA [7]	Renal cell carcinoma	5 h post-treatment	NA

tion of when our patient's hemorrhage occurred, which we believe supports the patient's positioning as contributing to this morbidity.

It is conceivable that this patient had an underlying coagulopathy which contributed to his acute hemorrhage. No coagulopathic workup was performed for the patient before gamma knife therapy. The prothrombin time and activated partial thromboplastin times were normal for two successive values after the hemorrhage, but this does not rule out all bleeding disorders. Additionally, the patient's cause of hemorrhage might truly have been multifactorial given the predisposition for renal cell metastatic lesions to hemorrhage, the unusual position the patient was placed in, and his concurrent radiosurgical therapy. Some combination of these factors could explain this unfortunate outcome. Preoperative or preprocedure embolization of renal cell carcinoma metastases has been described, particularly in cases of bony metastases or spinal compressive lesions [19,20]. Preoperative embolization is also sometimes used for intracranial hypervascular dural-based masses like meningiomas [21]. This has never been described specifically for intracranial renal cell metastases, and most likely would not have been useful in this patient with multiple lesions involving eloquent brain.

#### 4. Conclusion

Given this patient's severe kyphotic deformity, an alternative radiosurgery treatment device would probably not have helped change the positioning. The patient would still have been placed in Trendelenburg position to mate well with the facemask in the case of a linear accelerator based system. Another possibility would have been the newer gamma knife unit currently being marketed (Perfixion, Elekta AB, Stockholm, Sweden). Its more versatile treatment volume might have been a better choice for our patient if it had been available at our institution, and might not have required such a significant degree of Trendelenburg angle. Patient positioning has always been an extremely important aspect of every neurosurgical operative case, and on its own can produce or protect from surgical morbidity. We believe that this case shows the importance of positioning for radiosurgical procedures as well.

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