Delayed hemorrhage after surgery and radiation in suprasellar pilocytic astrocytomas

Mazda K. Turel, Tim-Rasmus Kiehl¹, Fred Gentili
Division of Neurosurgery, Toronto Western Hospital, ¹Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada

Address for correspondence: Dr. Mazda K. Turel, Division of Neurosurgery, Toronto Western Hospital, 399 Bathurst Street M5T 2S8 Toronto, Ontario, Canada. E-mail: mazdaturel@gmail.com

ABSTRACT

Delayed intracranial hemorrhage is a rare complication of treatment for central nervous system tumors. This may be secondary to malignant transformation of the tumor or vasculopathy related to radiation therapy (RT). While most reports on radiation-induced vasculopathy in children with optic pathway gliomas are associated with ischemic complications, there are only two reports of hemorrhagic complications in these patients. In both cases, the hemorrhage was asymptomatic and remote from the site of the original tumor but within the field of irradiation. We describe a female patient who underwent surgery for an optico-chiasmatic pilocytic astrocytoma (PA) at the age of 12 followed by RT at the age of 17 for tumor progression. The patient was followed with serial magnetic resonance imaging (MRI) scans showing marginal regression and no subsequent evidence of tumor recurrence, including the most recent MRI done only 6 months before the latest presentation. She then developed a symptomatic intratumoral hemorrhage at the age of 32 for which she underwent emergent surgery. To our knowledge, this is the first report of a nonaneurysmal-delayed hemorrhage within the site of previous surgery, several years after RT for a suprasellar PA. We review literature on delayed vasculopathy following the treatment of pediatric optic pathway gliomas and discuss the possible mechanisms of hemorrhage in our case. These long-term follow-up outcomes add significant insight and have implications in patient management.

Key words: Delayed hemorrhage, optico-chiasmatic, pilocytic astrocytoma, radiation, suprasellar, surgery

Introduction

Pilocytic astrocytomas (PAs) are benign, slow-growing World Health Organization (WHO) Grade I, glial tumors that typically occur in children and young adults.¹ Two-thirds of these tumors are located within the cerebellum. Supratentorial PAs are rare, especially in children. While the incidence of spontaneous intracranial hemorrhage in gliomas is reported to be around 5%, this complication is more often seen in higher grade tumors. Low-grade gliomas rarely present with hemorrhage, with only 6 cases of spontaneous hemorrhage in pediatric supratentorial PAs having been reported.²³ Radiation therapy (RT)-induced vascular injury is well-documented in these tumors and often occurs within the first decade of the treatment.²¹ An immature central nervous system vasculature in the pediatric population may predispose these patients to cerebrovascular morbidity. The occurrence

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of Moyamoya disease is more common than intracerebral hemorrhage (ICH). While delayed hemorrhage after surgery and RT for high-grade gliomas are known, there are only two prior reports of the same in an optic nerve and hypothalamic glioma, both remote from the site of surgery. Most other reports describe ischemic complications.

We describe the case of a 32-year-old female who presented with hemorrhage into a suprasellar PA two-decades after surgery and RT. This was unusual since a magnetic resonance imaging (MRI) scan done only 6 months previously had shown a very small residue that had been stable for over 15 years. The possibility of a radiation-induced aneurysmal hemorrhage was excluded. To our knowledge, this is the first report of a nonaneurysmal delayed hemorrhage within the site of previous surgery, several years after RT for a suprasellar PA. The behavior of these tumors after complete or incomplete resection and adjuvant therapy can be unpredictable. We review literature on delayed vasculopathy following the treatment of pediatric optic pathway gliomas.

Case Report

History and examination
We report the case of a 32-year-old female who was diagnosed with neurofibromatosis type 1 (NF-1) at the age of 3 (1986). She underwent subtotal excision of an optico-chiasmatic PA (WHO Grade I) at the age of 12 (1995), followed by fractioned stereotactic radiotherapy for documented growth of her tumor 5 years later (2000). Apart from a residual left homonymous hemianopsia, she was clinically asymptomatic. The patient was followed with serial MRI scans which initially had shown progressive regression of the tumor and over the last 10 years no subsequent evidence of tumor recurrence, including the most recent MRI done only 6 months before her current presentation [Figure 1a-d].

She now presented with a 3-month history of progressive diminution of vision in both eyes, right more than left, significant memory disturbances and headache, worsening over the last month but with no acute deterioration. On examination, she had cutaneous stigmata of NF-1. Her Glasgow Coma Scale (GCS) score was 14/15 (6-4-4) and visual acuity was limited to counting fingers at one foot in both the eyes. Fundi showed bilateral optic atrophy. Extraocular movements were full and there were no motor or sensory deficits in the limbs. Surprisingly, she had no hormonal or endocrinological dysfunction.

Radiology
The computed tomography (CT) [Figure 2a-c] scan showed a large hemorrhagic suprasellar lesion measuring 4 cm in largest diameter with perilesional edema extending along the region of the optic tracts. There was mass effect on the infundibulum, mammillary bodies, and the anterior wall and roof of the third ventricle with resultant hydrocephalus. There were no ischemic infarcts noted.

The MRI [Figure 2d-f] confirmed the CT findings of a 4 cm suprasellar hemorrhagic mass that was hyperintense on T1-weighted imaging, showed mixed intensity of T2-weighted imaging with the gradient echo images showing evidence of hemorrhage within the lesion. There were T2-weighted changes in the midbrain, striatum, and diencephalon. The pituitary gland appeared intact. There was no infarct seen on diffusion-weighted images. A CT angiogram ruled out an aneurysm but showed prominent vascularity within the lesion. The preoperative diagnosis was that of possible malignant transformation of the tumor, with hemorrhage.

Surgery
In view of her clinico-radiological findings and marked visual disturbance, emergent surgery was performed. The lesion was approached using a bifrontal craniotomy and interhemispheric transbasal approach. The lesion was seen in the suprasellar cistern with the anterior communicating artery (ACom) stretched over its anterior surface. Initially, the lesion was internally decompressed; removing large organized clots of fresh blood intermixed with dark altered blood suggestive of older hemorrhage. Areas of more firm viable tissue were also encountered. There were no areas of necrosis or signs of overt malignancy or calcification. A gliotic plane separated it from the thalamus and hypothalamus, from which it could be readily dissected, ultimately entering the third ventricle. A gross total resection was achieved and a large volume of representative tissue was sent to pathology.

Histopathology
Microscopic examination revealed a large acute blood clot, surrounded by an extensive fibroblastic reaction with

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Figure 1: Gadolinium-enhanced (a) axial and (b) coronal magnetic resonance imaging images of the patient 5 years after radiation for an operated optic-chiasmatic pilocytic astrocytoma showing a small suprasellar residue (arrow) Gadolinium-enhanced (c) axial and (d) coronal magnetic resonance imaging images of the patient 10 years after the above-described scan showing stable tumor with evidence of further regression (arrow)
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Figure 2: (a) axial (b) sagittal (c) coronal computed tomography scan showing a well-contained hemorrhage within a suprasellar tumor with surrounding vasogenic edema 6 months after the above-described magnetic resonance imaging in Figure 1c and d. (d) T2-axial (e) T1-sagittal plain (f) gadolinium-enhanced coronal magnetic resonance imaging showing T1-weighted hyperintense lesion with mixed signal intensity on T-2 weighted images and no additional enhancement on gadolinium suggesting a hemorrhage within the tumor.

hemosiderin-laden macrophages [Figure 3a, lower left]. There were frequent collections of hemosiderin, consistent with remote hemorrhage.

Furthermore, present were fragments of neuroglial tissue with abundant inflammation, few eosinophilic granular bodies, and pleomorphic nuclei but no mitosis [Figure 3a, middle and upper right]. A degree of nuclear atypia was present, but no mitotic figures. In addition, there were foci of sclerotic, hyalinized as well as mineralized (calcified) blood vessels with ectasia and fibrosis [Figure 3b]. These fragments were positive for glial fibrillary acidic protein [Figure 3c]. The Mib-1 (Ki-67) proliferation index was very low, estimated at about 1%–2% [Figure 3d]. The findings are best interpreted as being a focus of residual PA with extensive treatment effect although nonneoplastic glial tissue with reactive changes could not be entirely excluded. There was no evidence of a radiation-induced neoplasm.

Postoperative recovery and follow-up

The patient’s postoperative course was complicated with hormonal disturbance including diabetes insipidus, fluctuating sensorium, and pyrexia, which was felt to be of hypothalamic origin. She ultimately made a good recovery, including improvement in her vision to counting fingers at 3 feet in the right eye and six feet in the left eye with a residual left homonymous hemianopia. Her GCS score was 15/15 at discharge. The MRI 1 week after surgery showed postoperative changes with no residual mass [Figure 4]. At 3 months, postoperatively, the patient’s cognitive status had improved further, but she still exhibited disturbance of both central temperature and thirst regulation.

Discussion

Spontaneous hemorrhage in suprasellar pilocytic astrocytoma

Hemorrhage within a PA is exceedingly rare and is seen in only 1%–3% of cases. Only 6 previous cases of spontaneous hemorrhage into a suprasellar PA have been reported in the pediatric age group. The initial presentation of tumors with hemorrhage is similar to subarachnoid hemorrhage or spontaneous intracranial bleeding and is usually catastrophic. Our patient on the contrary presented with subacute visual decline, memory impairment, and headache over a 1-month
The hypothalamic lesion was reported hemorrhage in a suprasellar 13 of 69 (19%) patients irradiated. Some granulation tissue was seen in our case, but there is an increased risk of Moyamoya if a matter of speculation. The causal relationship between traction of the vessels around leading to microhemorrhages whether the tumor regression itself could have caused proliferation, stromal degeneration, and hyalinization. As such, hyalinized vessels with dysplastic capillary beds are more prone to rupture.

Hemorrhage in suprasellar pilocytic astrocytoma after radiation due to aneurysmal formation

Aichholzer et al.\(^\text{[10]}\) reported hemorrhage in a suprasellar PA 9 years after surgery and radiation, caused by an ACom aneurysm that was virtually encased within the tumor. They postulated the cause to be either a neoplastic aneurysm formation (tumorous infiltration with aneurysmal dilation) or bleeding from a de novo aneurysm due to radiation. In our case, no aneurysm was seen on CT angiogram or at surgery. Nanney et al.\(^\text{[10]}\) reviewed a series of 46 patients radiated for various tumors who developed 69 intracranial aneurysms within the irradiated fields over a median period of 12 years. Among these, 55% presented with some form of hemorrhage. Whether a microaneurysm was the cause of hemorrhage in our case, not identified on CT angiography or at surgery is very unlikely. The pathology in our case showed a neuroglial lesion, likely representing residual tumor with treatment effect and hemosiderin, plus a variety of vascular abnormalities such as vascular ectasia and calcification. These changes, separately or in combination, may explain why the hemorrhage occurred.

Radiation-induced vasculopathy

Radiation-induced vasculopathy is well-documented. It is thought to be the result of arteriosclerotic changes of blood vessels within the field of radiation. This can occur early (within weeks to months) due to arterial disruption, or delayed (several years after RT) due to arterial stenosis or occlusion. Other processes, such as disruption of the internal elastic membrane and subacute accumulation of lipids and macrophages may contribute to the pathophysiology of RT-induced cerebro-vasculopathy.\(^\text{[11]}\)

In a review of 77 patients with delayed cerebral vasculopathy following RT for pediatric tumors, 45 had changes of Moyamoya disease while 30 were cases of ICH and two patients had both.\(^\text{[12]}\) There is an increased risk of Moyamoya disease in patients with NF-1. The median interval from radiation to presentation in cases of Moyamoya was 3.3 years, whereas for ICH cases it was 7.5 years. The authors found a significant association between radiation dose and interval from radiation to Moyamoya syndrome. For patients with ICH, this association was insignificant. The authors suggest that Moyamoya may be a factor that predisposes to ICH. Our patient had no evidence of Moyamoya disease on CT angiogram.

In a series by Grill et al.\(^\text{[11]}\), 13 of 69 (19%) patients irradiated for optic pathway gliomas reported occlusive vasculopathy as a cerebrovascular complication within a median interval of 3 years. The major risk factor was NF-1, seen in 30% of these patients who developed the complication compared with only 6% of patients without NF-1. However, all of their patients had ischemic events with no case of hemorrhage.
contrast to the findings of Wang et al. radiation dose was not associated with this complication.[3]

**Long-term follow-up**

In a series of supratentorial PA, 9%–20% of them showed recurrence after 6–12 years and there are several anecdotal reports of late recurrences after a so-called “cure” several decades after the treatment. Hence, it is imperative to follow these patients life-long. Late recurrences are usually caused by malignant transformation of the tumor, but it was not so in our case. In fact, the most surprising feature was that the tumor showed radiologic regression over the years. The overall and progression-free survival of visual pathway gliomas at 10 years is 77% and 39%, respectively.[9] Our patient had a good long-term outcome and successful treatment of her hemorrhage two-decades after surgery and RT.

**Conclusions**

PA can present with spontaneous hemorrhage into the tumor in both children and adults and the presentation can be dramatic. However, while delayed hemorrhage following surgery and RT is known, it is quite rare and may occur remote from the original tumor site. It is important to recognize and treat delayed symptomatic intratumoral hemorrhage acutely after RT, even in the absence of malignant transformation. The pathology showed a neuroglial lesion, likely representing residual tumor with treatment effect and hemosiderin, plus a variety of vascular abnormalities such as vascular ectasia and calcification. These changes, separately or in combination, may explain why the hemorrhage occurred. This case illustrates the need for life-long follow-up for patients with optic pathway PA, especially if they had RT since delayed complications can occur after several decades.

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**Conflicts of interest**

There are no conflicts of interest.

**References**