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Case Report

A 58-Year-Old Woman with Left-Sided Weakness and a History of a Pediatric Brain Tumor: A Case Report

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Keywords
Cerebral sarcoma · Glioblastoma multiforme · Meningioma · Radiation-induced glioma · Radiation therapy

Abstract
Background: An uncommon but well-established complication of cranial irradiation is secondary neoplasm. This case presentation documents a radiation-induced malignant glioma 55 years after being diagnosed with "cerebral sarcoma," now defined as atypical meningioma. This not only represents the longest reported latency period for a patient initially receiving over 30 Gy, but also provides a valuable historical perspective of neuro-oncology. ***Clinical Presentation:*** A 58-year-old female presenting with progressive left-sided upper and lower extremity weakness with a past medical history significant for "cerebral sarcoma" was diagnosed with glioblastoma multiforme. This patient had previously been treated with resection and adjuvant radiation therapy via a 280-kVP orthovoltage machine and received 3,390 rad to the posterior three-quarters of the skull for "cerebral sarcoma." ***Conclusion:*** A comprehensive investigation of the past medical history helped uncover a mysterious pediatric diagnosis, helped drive the management 5 decades later, and serves as a reminder that seemingly safe interventions may still cause harm.

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Background

"Cerebral sarcoma" was defined in the literature as a neoplasm of the meninges prior to 1979, when the World Health Organization classified several subtypes of typical (grade I), atypical (grade II), and anaplastic (grade III) meningioma [1]. Given long-term toxicity risks, the utilization of radiotherapy in meningiomas remains controversial while postoperative radiotherapy is no longer indicated in pediatric populations [2].

This is largely because an uncommon but well-established complication of cranial irradiation is a secondary neoplasm [3, 4]. Notably, 1.3% of glioblastoma cases are associated with a previous exposure to radiation, with a median latency period of 9 years [5, 6]. Some studies suggest that doses greater than 30 Gy puts the patient at higher risk for malignancy compared to lower doses (less than 18 Gy), although others suggest that there is no threshold dose [3, 5].

We present the case of a radiation-induced glioblastoma multiforme (GBM) in a 58-year-old female who was treated for a "cerebral sarcoma" 55 years earlier, for which the original records were obtained.

Clinical Presentation

Past Medical History

An otherwise healthy 58-year-old female revealed that in 1962 as a 3-year-old child she had been treated for a "cerebral sarcoma" with surgery and radiation. At the time, she presented with a headache and was diagnosed with an intracranial tumor via a ventriculogram. Excision of the lesion was described as "completely or nearly completely resected," and per the pathology report was described as a "cerebral sarcoma or meningiosarcoma." Adjuvant radiotherapy was requested by the neurosurgeon and the administering radiologist reluctantly agreed, noting that "meningiomas are not ordinarily treated with radiotherapy although some may respond, and sarcomas are certainly not radioresponsive. However, careful radiation therapy cannot do any harm and probably may do some good" (Fig. 1).

The patient was treated with a 280-kVP orthovoltage machine with 2 lateral fields, prescribed to 14 cm depth on the right and 6 cm depth on the left. She ultimately received 3,390 of a planned 4,000 rad for 39 days in 1962 to the posterior three-fourths of the entire skull. Treatment was discontinued due to an intensely erythematous scalp, although no other toxicities or neurologic deficits were noted.

Examination

The patient presented with a 1-week history of progressively worsening left-sided upper and lower extremity weakness, described as an inability to hold objects in her left hand and frequent falls secondary to a left foot drop. The weakness eventually culminated in an episode where the patient fell out of bed and could not get up. Physical examination demonstrated stable vital signs, diffuse 3/5 strength in the left upper and lower extremities, and a right frontal craniotomy scar with surrounding soft tissue fibrosis (Karnofsky performance status 70).

Pathological Findings

A contrast-enhanced brain MRI demonstrated a 3 × 3 cm right frontoparietal resection cavity surrounded by a 5 × 4 cm area of heterogeneous contrast enhancement extending to

the right corona radiata and periventricular white matter with associated cerebral edema (Fig. 2). The mass was not technically resectable due to location and biopsy was consistent with GBM, wild-type isocitrate dehydrogenase and unmethylated O^6-methylguanine DNA methyltransferase (MGMT), with an MIB-1 index of 50% (Fig. 3).

Outcome

It was determined that further maximal safe resection would not provide a beneficial therapeutic value, therefore definitive full-dose chemoradiation was recommended. Citing a declining performance status and discontent with the role radiation played in causing her malignancy, the patient ultimately declined treatment. Since identifying information was not used in the context of this case, informed consent for this case presentation was not required.

Discussion

"Meningiosarcoma" or "cerebral sarcoma" are no longer considered histopathological diagnoses, but our patient likely had a variant of meningioma, which would have an approximately 90% chance of local control in such a scenario [7]. To this day, the role of radiotherapy in the management of typical and atypical meningiomas remains controversial, although several treatment paradigms have been established since the patient originally presented in 1962 [8]. For instance, there is virtually no indication for postoperative radiotherapy for meningioma in the pediatric population given the long-term toxicity risks [2]. As was the case for most radiation therapy in that era, the dose was limited by developing erythema of the scalp, an acute toxicity of little consequence, unlike the late and at that time unknown effect of secondary malignancy.

Cahan et al. [9] defined parameters of radiation-induced malignant gliomas (RIGMs) as follows: tumors localizing to where radiotherapy was applied, an adequate latency period measured in years, a histology different than that of the original tumor, and the patient should not have an underlying pathology favoring the growth of tumors. In this case, all four parameters were met. Although 80% of patients have a typical latency period within 15 years prior to the development of a secondary malignancy, the longest reported latency period includes a female who was treated for tinea capitis, presumably at a small dose, 61 years preceding the onset of a secondary malignancy [5, 10]. Prior to this case, the longest latency period between exposure of at least 30 Gy and induction of high-grade glioma was 37 years [11].

Histologically, radiation-induced GBMs are no different than de novo GBMs; however, there have been conflicting reports of whether RIMGs have greater homogeneity of gene expression [3, 12, 13]. With a median survival of 11 months, the prognosis for radiation-induced glioblastomas is comparable to that of GBMs with the unmethylated MGMT promoter gene, suggesting that perhaps they are associated with less favorable tumor biology [14, 15]. It should be noted that the vast majority of reported RIMGs were published before MGMT status testing became commonplace and before adjuvant temozolamide was established as the standard of care [16]. However, the median survival of RIMGs since 2007 was still 11.5 months [5].

The ideal management for de novo or secondary GBM in a medically fit patient includes gross total resection followed by adjuvant chemoradiation at a total dose of 6,000 cGy in 30 fractions with concurrent and adjuvant temozolomide [16]. The risk of neurotoxicity such as

brain necrosis theoretically increases in the setting of reirradiation, which may be why only approximately 40% of patients with radiation-induced GBMs received reirradiation as part of their treatment [15]. Nevertheless, the risk of radionecrosis is minimal with reirradiation to the brain so long as the cumulative dose is less than 100 Gy at 2 Gy per fraction [17–19]. Furthermore, Paulino et al. [15] demonstrated that among 85 cases of RIMGs, the 35 patients who underwent reirradiation at a median dose of 50 Gy (range 30–76 Gy) had a median survival of 13 months compared to 8 months of those who were not reirradiated, without additional toxicity. It should be mentioned that potential long-term toxicity of reirradiation to the brain may not have been observed because most patients do not survive long enough to develop it.

Conclusion

This case illustrates how past medical history, going back even 50 years, is instrumental to workup and management. Two uncommon and valuable pieces of information include the patient's knowledge of her pathology as a 3-year-old and medical records dating back to 1962, both of which helped determine the diagnosis and treatment. The medical records also provide a rare window as to how medicine was practiced 5 decades ago and how it has evolved since then. Importantly, they serve as a humble reminder that there are many aspects of medicine still unknown to clinicians, including the possibility that a seemingly safe therapeutic intervention can still cause harm.

Statement of Ethics

We ensure the accuracy, quality, and integrity of this case report. No identifying patient information was disclosed.

Disclosure Statement

The authors of this paper would like to disclose that they have no financial or other conflicts of interest in relation to this case study and publication.

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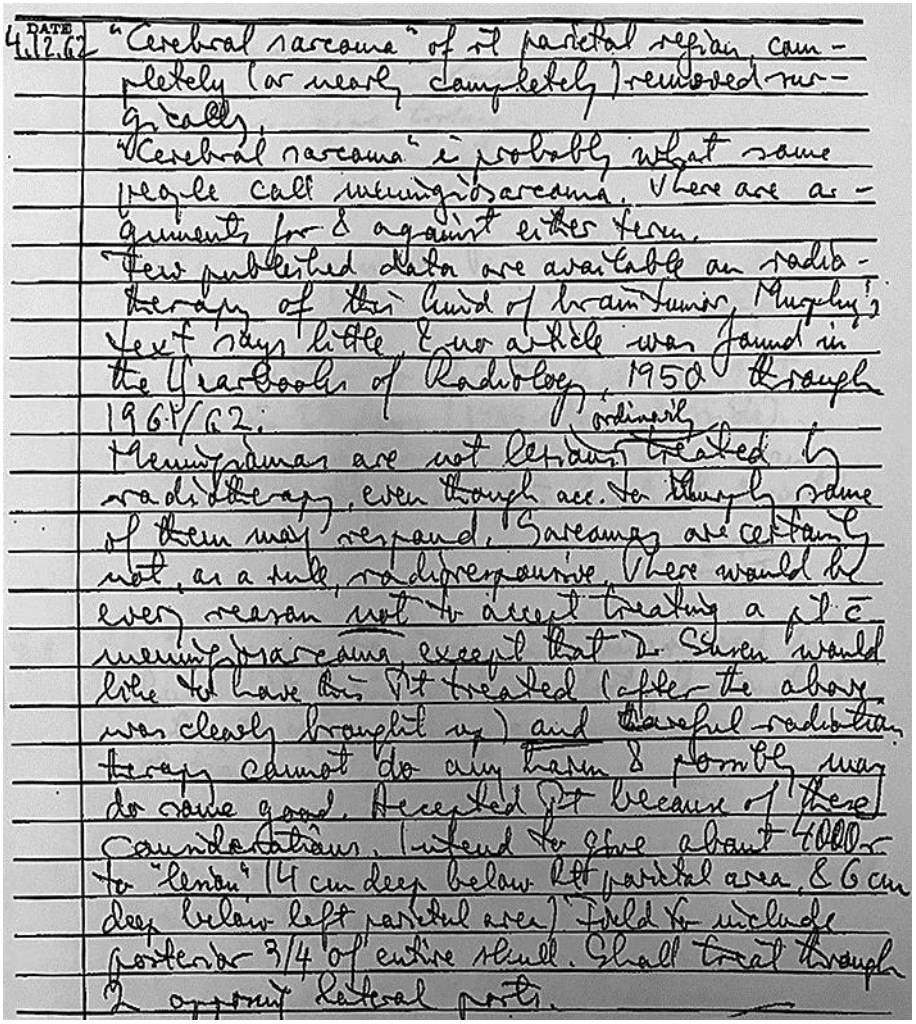
DATE
4.12.62
"Cerebral sarcoma" of rt parietal region, completely (or nearly completely) removed surgically.
"Cerebral sarcoma" is probably what some people call meningiosarcoma. There are arguments for & against either term.
Few published data are available on radiotherapy of this kind of brain tumor. Mugglin's text says little, & no article was found in the Yearbooks of Radiology, 1950 through 1961/62.
Ordinarily
Meningiomas are not [illegible] treated by radiotherapy, even though acc. to theory some of them may respond. Sarcomas are certainly not, as a rule, radiosensitive. There would be every reason not to accept treating a pt w meningiosarcoma except that Dr. Shaw would like to have this pt treated (after the above was clearly brought up) and careful radiation therapy cannot do any harm & probably may do some good. Accepted pt because of these considerations. Intend to give about 4000 r to "tenon" (4 cm deep below rt parietal area, & 6 cm deep below left parietal area) field to include posterior 3/4 of entire skull. Shall treat through 2 opposing lateral ports.

Fig. 1. Assessment and plan of the treating radiologist from 1962.

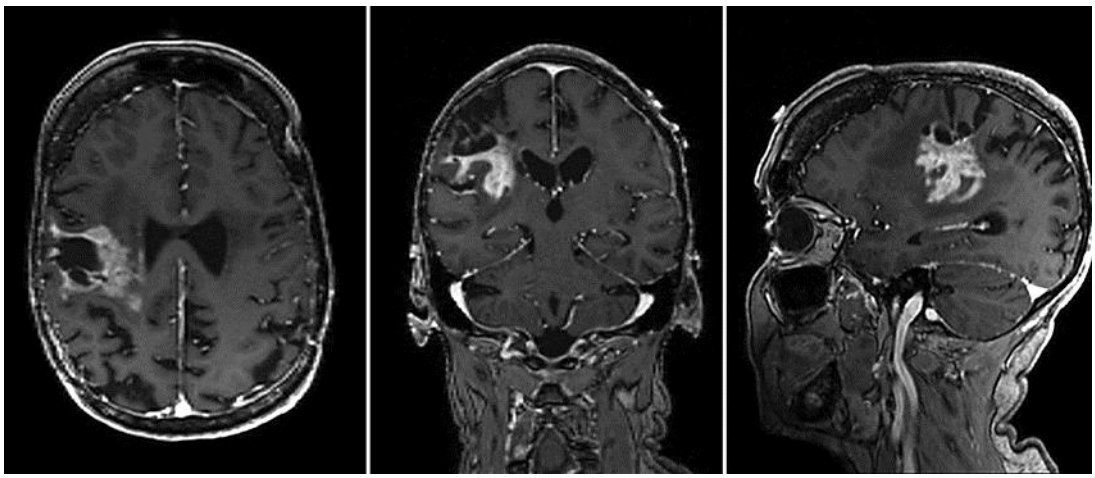

Fig. 2. T1-weighted brain MRI with contrast at the time of diagnosis of radiation-induced glioblastoma multiforme.

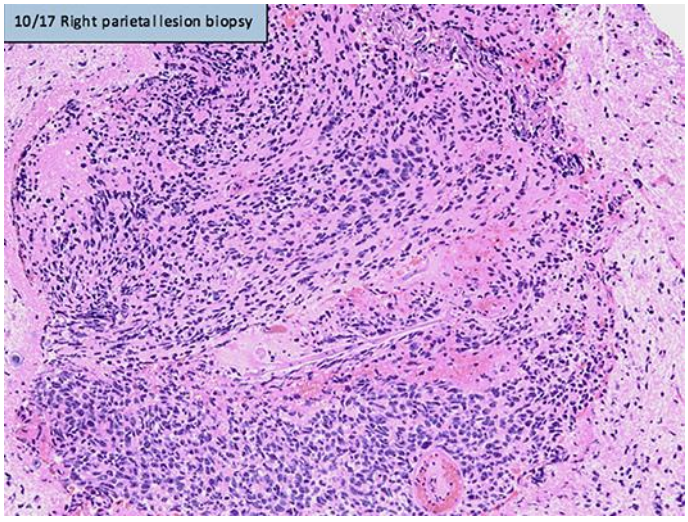

Fig. 3. Radiation-induced glioblastoma multiforme demonstrating increased cellularity with marked nuclear atypia, necrosis, and vascular endothelialization.