Second primary cancer in the brain: A longitudinal case study from childhood into adulthood

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**ABSTRACT**

Second cancers occur after the remission of a previous cancer in patients. Due to the increased successful treatment of childhood cancers, these second cancers are more likely to occur for these patients later in life. Risk factors and causes for these second cancers include predisposing genetic factors, exposure to radiation and chemotherapy from initial cancer treatment, and environmental conditions. The most likely reason second cancers occur is multifactorial and involves an interaction between environmental and genetic factors. We present a longitudinal case study following a patient who was treated for an ependymoma at age three and twenty-two years later presenting with symptoms indicative of a second cancer at age 25.

**Keywords:** Second cancer, childhood cancers, brain cancers, neurosurgery, pediatric cancers

**INTRODUCTION**

Patients who have a primary cancer even after they are cured have a higher incidence of developing another primary cancer after their remission. These are called second cancers and account for about 6–10 percent of all cancer diagnoses. The risks related to these cancers are not completely known but are suspected to be multifactorial involving both genetic and environmental factors. As new treatment methods are developed for primary cancers, patients who were able to survive childhood cancers have a substantially greater risk for second cancers later in life.

**CASE**

We present a 25-year-old Hispanic woman with a past medical history of rheumatoid arthritis, diagnosed with posterior fossa tumor in 1998 and treated surgically at age three. Pathology showed ependymoma and was treated with total resection and radiotherapy.

She presented to the neurosurgery clinic at age 25 with a complaint of blurred vision and significant headache. The patient then went to the emergency room to have magnetic resonance imaging of the brain and spine with stealth protocol, stealth T1 and T2, and spectroscopy and perfusion to assess for possible brain lesions (Figures 1 and 2).

Magnetic resonance imaging results showed a posterior fossa mass involving the vermis and medial

![Figure 1. Coronal T2 image demonstrates the posterior fossa mass with minimal surrounding vasogenic edema.](image-url)
aspect of bilateral cerebellar hemispheres with imaging characteristics, suggestive of a glial tumor (Figure 3). There was an elevated choline peak and increased cerebral blood flow (Figure 4). There was an arachnoid cyst along the ventral aspect of the cervical spinal cord at C2–C4 with mass effect on the cervical spinal cord but no drop metastases. No intervention was done due to the lack of neurological symptoms. Previous imaging from the patient's childhood tumor was not available; the patient was discharged until these films could be reviewed two months later.

Figure 2. Axial T1 post contrast images demonstrate minimal peripheral enhancement of the posterior fossa mass.

Figure 3. Axial T2 FLAIR image demonstrates a T2 hyperintense posterior fossa mass involving the vermis and medial aspect of the bilateral cerebellar hemispheres. There is mass effect on the fourth ventricle.

Two months later, the patient was taken to the OR for craniotomy and tumor resection. Pathology results showed a high-grade glioma, glioblastoma multiforme. The pathology suggests radiation induced process or cancer predisposition syndrome requiring additional dissection. The patient was taken to the operating room again for a posterior mass resection. She was discharged to continue radiation treatments in New Mexico. The last contact with the patient was in May 2021, and there has been no follow up since then. The patient gave consent for this case to be published.

DISCUSSION

A second primary cancer is a term described by the National Cancer Institute as a new primary cancer that occurs in a patient who has had cancer in the past. These cancers can occur any time after the original cancer diagnosis, from months to even years after. The risk of a second cancer development is not increased with any specific cancer, and the pathogenesis is complex and multifactorial. However, second cancers are a leading cause of morbidity and mortality...
among cancer survivors worldwide. In adults, environmental exposures and lifestyle factors accumulating over time may have a key role in second cancer development. Survivors of childhood cancers, in particular, are at a substantially increased risk. In fact, approximately 19% of cancer diagnoses today are seen in individuals with previous histories of malignancy. Second cancers are the most common cause of post-treatment death (standardized mortality ratio 15.2, 95% CI 13.9–16.6). For these survivors of childhood malignancies, both genetic susceptibility and radiation treatment of primary cancer likely contribute to the pathogenesis and recurrence of a second cancer.

The most evident examples of genetic predisposition to cancers are gene mutations that lead to inherited dispositions to cancer, such as in Li-Fraumeni syndrome. In this genetic disorder, a mutation in a tumor suppressor gene leads to nearly a 100% chance of developing cancer in a lifetime. Although our patient did not undergo any genetic testing or studies to determine susceptibility to cancer, there are many cases of this in the literature.

Treatment of childhood cancer is often aggressive, using mostly radiation and chemotherapy. Radiation, in particular, has significant carcinogenic potential. Exposure to ionizing radiation causes both single and double strand DNA breaks, leading to gene mutations and malignant transformation. Based on this information, the hypothesis that the treatment of a primary cancer in childhood itself poses a risk for developing a second cancer later in life is understood. One study showed that among 1,230 female survivors’ exposure to radiotherapy showed the incidence of breast cancer to be 30%, with a 35% increase among survivors of Hodgkin’s lymphoma.

Another case control study showed the development of both central nervous system meningiomas and gliomas was associated with radiotherapy, with the risk for glioma highest in children treated with radiotherapy before age five. The patient in this study was treated with radiation for the primary CNS tumor in childhood and developed cancer in the same area 11 years later. The radiation therapy of glioblastoma multiforme is especially aggressive due to the diffusely infiltrative nature of the disease and is associated with significant toxicity. This could support the idea of radiation as a risk factor for the occurrence of her second cancer. Some studies have shown a potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumors.

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**References**


