Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Case report

Metachronous medulloblastoma and glioblastoma: Implications for clinical and technical aspects of re-irradiation

Vivek Verma[a], *Rajesh R. Kulkarni*[a], *Abhijeet R. Bhirud*[a], *Nathan R. Bennion*[a], *Rodney D. McComb*[b], *Chi Lin*[a,*]

[a] *Department of Radiation Oncology, University of Nebraska Medical Center, Omaha, NE, USA*
[b] *Department of Pathology, University of Nebraska Medical Center, Omaha, NE, USA*

ARTICLE INFO

Article history:
Received 25 April 2015
Received in revised form
24 July 2015
Accepted 15 October 2015
Available online 21 November 2015

Keywords:
Medulloblastoma
Glioblastoma
Re-irradiation
Brainstem tolerance
Toxicity

ABSTRACT

A seven-year-old male underwent surgical resection and chemoradiation for average risk medulloblastoma; twelve years later, the presence of a necrotic and infiltrative mass in the same area and invading the brainstem prompted a subtotal resection. Pathology was indicative of glioblastoma. He was then treated with concurrent temozolomide and using biologically effective dose calculations for gross residual tumor tissue in the brainstem as well as brainstem tolerance, a radiotherapy dose of 3750 cGy was chosen, fractionated in twice-daily fractions of 125 cGy each. The gross tumor volume was expanded with a 5 mm margin to the planning target volume, which was also judiciously subtracted from the normal brainstem. He completed his radiotherapy course with subsequent imaging free of residual tumor and continued adjuvant temozolomide and remains under follow-up surveillance. This case underscores the rarity of metachronous medulloblastoma and glioblastoma, of which only five known cases heretofore have been described. We discuss the technicalities of radiotherapy planning in this patient, including common hurdles for radiation oncologists in similar patients.

1. Background

Metachronous brain tumors are defined as the development of at least two histologically distinct primary intracranial neoplasms, not related to local recurrence of the initial tumor. Local recurrences are often difficult to differentiate from a *de novo* tumor.[1] Sometimes, the development of a second primary brain tumor is a result of previous radiation, especially in pediatric patients.[2,3] The presence of certain risk factors, such as familial cancer syndromes, may increase the chance of developing secondary neoplasms after radiotherapy.[4]

While many radiation-induced intracranial neoplasms have been reported within fifteen years of radiotherapy,[2,3]

* *Corresponding author at*: Department of Radiation Oncology, University of Nebraska Medical Center, 987521 Nebraska Medical Center, Ground Floor, Clarkson Tower, Omaha, NE 68198, USA. Tel.: +1 402 552 3844; fax: +1 402 552 3013.
E-mail addresses: vivek.verma@unmc.edu (V. Verma), clin@unmc.edu (C. Lin).

http://dx.doi.org/10.1016/j.rpor.2015.10.002
1507-1367/

other studies have seen the occurrence of secondary tumors as late as 20–25 years after radiation.[5,6] However, as the interval between initial and second tumor occurrence increases, it is often difficult to ascertain whether the second tumor was caused by radiotherapy or *de novo*.

Metachronous primary intracranial neoplasms are relatively scarce in the literature, especially in pediatric patients. Although there have been reports of metachronous glioblastomas, medulloblastomas and anaplastic astrocytomas in adults,[5–7] there are rare reports on metachronous medulloblastoma and glioblastoma to date.[8] Re-irradiation to the posterior fossa and brainstem for secondary glioblastoma after radiotherapy for medulloblastoma has even fewer cases reported to guide treatment. We report a case of glioblastoma in a pediatric patient after chemoradiotherapy for medulloblastoma, and discuss technical issues of radiotherapy planning and treatment for re-irradiation.

2. Case presentation

A 7-year-old otherwise healthy male experienced several days of severe bioccipital headaches with nausea and a few episodes of non-bloody emesis. He had no significant past medical history and received all appropriate immunizations. Physical examination was remarkable for papilledema on fundoscopy, and the absence of neurologic deficits. Initial computed tomography (CT) scan of the head revealed a large mass in the posterior fossa (Fig. 1). It measured 5 cm in the greatest dimension and displaced the fourth ventricle anteriorly, causing secondary hydrocephalus in the lateral and third ventricles. It was highly suspicious for medulloblastoma. Lumbar puncture did not show any evidence of tumor cells. Modified Chang's staging of the tumor was T3a, M0. He underwent gross total resection without residual disease evident on postoperative imaging (Fig. 2A). Pathology revealed a classic/biphasic medulloblastoma with focal anaplasia (Fig. 2B). There was vague neuroblastic nodule formation without internodular desmoplasia. Synaptophysin immunostaining

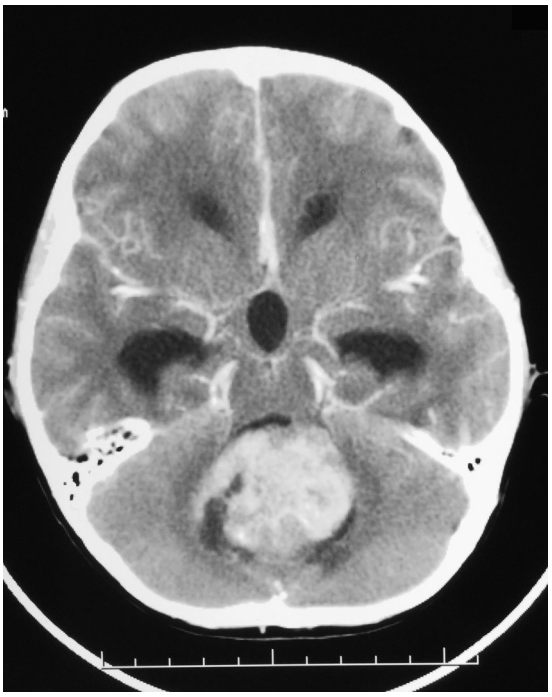

Fig. 1 – Head CT scan with contrast of patient on initial presentation.

was positive. He was then classified as standard (average) risk given the absence of visible residual disease, initial M0 status, and the age of 7 years.

The patient then underwent postoperative chemoradiation on the Children's Cancer Group A9961 protocol[9] which consisted of concurrent vincristine and cranio-spinal irradiation (CSI) to 2430 cGy followed by a posterior fossa (PF) boost to 5580 cGy, and adjuvant cisplatin, vincristine, and lomustine. Radiation was performed at another hospital using two-dimensional treatment planning (Fig. 3). He lost tactile sensation on the left half of his face and tongue from the time of surgery and developed continually worsening sensorineural

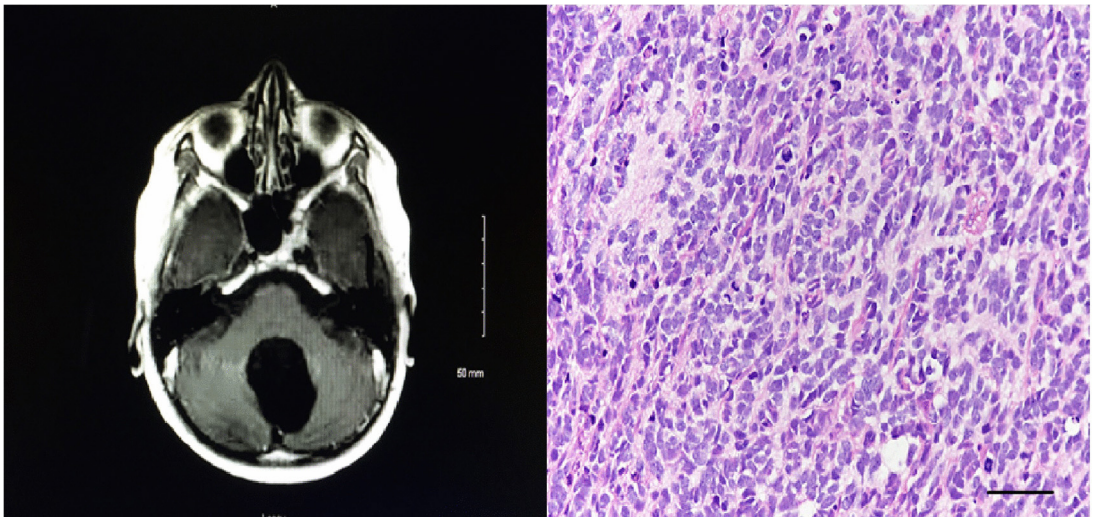

Fig. 2 – Postoperative T1 with contrast MRI after gross tumor resection (Panel A, left); histopathology of resected brain tumor, indicating medulloblastoma (Panel B, right).