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Brain-sparing total meningeal radiation for a patient with widespread progressive meningiomas using helical intensity modulated radiation

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Abstract

Multiple meningioma is a rare but difficult clinical entity. We describe the case of a patient with widespread progressive meningiomas who could not safely have surgery or radiosurgery. We have previously treated these patients with whole brain radiation, despite the risks of neuropsychological side effects. In this case, we treated with a novel use of helical intensity modulated radiation therapy: brain-sparing total meningeal radiation. The brain-sparing technique allowed us to treat the patient's meninges with higher doses than would have been possible with whole brain radiation and with the goal of achieving long-term disease control.

Keywords

Multiple meningiomas; Helical intensity modulated radiation therapy; Tomotherapy; Conformal radiotherapy

1. Introduction

Multiple meningioma is a diagnosis that refers to the sequential or simultaneous diagnosis of two or more distinct meningiomas, not necessarily of the same pathologic subtype [1]. It is an infrequent diagnosis, representing approximately 4% of cases of all meningiomas [2,3]. The standard of care for symptomatic or progressive meningiomas is surgical resection even in the setting of multiple meningiomas. However, eventually the problem may become so widespread that it is no longer possible to control with surgery or radiation localized to individual growing lesions. In such cases, we have previously used whole brain radiation, despite the risks of neuropsychological side effects.

In this report, we present a patient with widespread progressive meningiomas who was treated with a novel use of helical intensity modulated radiation therapy (IMRT): brain-sparing total meningeal radiation.

2. Case report

This is a 51-year-old male who originally presented with left-sided upper and lower extremity weakness 8 years ago. Initial work-up MRI showed a large right parasagittal meningioma which was subsequently gross totally resected. Pathologic review revealed the diagnosis of typical (grade 1) meningioma. Over the next few years, his left-sided weakness improved though he did not attain his pre-diagnosis baseline strength. At the same time, he developed periodic Jacksonian seizures involving the left lower extremity. He was followed with serial brain MRIs which eventually demonstrated recurrent disease within the initial resection cavity. He had a repeat gross total resection 4 years ago. This time, he had a difficult postoperative course with multiple complications resulting in a lengthy hospital stay. Subsequent MRIs over the next 3 years revealed a second recurrence within the surgical cavity as well as nine other areas of abnormal thickening along the right and left parasagittal meninges, left frontal convexity, left parietal convexity, falx cerebri, and left tentorial leaflet, all of which were suggestive of meningioma. Because the patient had relatively stable symptoms, he deferred treatment until 8 months ago. Prior to our evaluation, the patient was seen by an outside neurosurgeon and radiation oncologist who recommended whole brain radiation for his widespread meningeal disease. Out of concern for the cognitive side effects of whole brain radiation, the patient sought our opinion on the possible role of stereotactic radiosurgery (SRS). At the time of our consultation, the patient had at least 10 meningiomas all of which appeared to have progressed compared to his previous MRI 6 months earlier (See Figs. 1 and 2).

The patient is ethnically Chinese but he was born and raised in Vietnam. He had no family history of meningiomas, though he did report several brothers and sisters with multiple subcutaneous nodules in the skin of their backs and extremities. These lesions apparently developed in adult hood. The patient did not have any subcutaneous nodules. The patient did not have juvenile cataracts. Genetic analysis for NF2 had not been done. As far as the patient was aware, no family members have been diagnosed with NF1 or NF2. The patient had no prior history of radiation treatment. His physical examination revealed diminished strength in his left upper (4/5) and left lower (3/5) extremities. His cranial nerve examination and his sensation to light touch were normal.

Owing to the number and size of his lesions and the fact that all of his meninges appeared predisposed to forming meningiomas, we advised against SRS and initially recommended whole brain radiation. The patient expressed significant reluctance towards having this treatment. Therefore, we developed a radiation treatment plan using helical IMRT that conformed dose to the patient's meninges and meningiomas (See Fig. 3). The patient was treated once with daily fractions of 1.8 Gray (Gy). He was initially prescribed a total dose of 45 Gy, but because of the excellent normal brain-sparing achieved by the helical IMRT plan and the limited toxicity experienced by the patient during treatment, he was ultimately treated with a total dose of 50.4 Gy. While radiation exposure to normal brain parenchyma could not be completely eliminated, our treatment limited the whole brain dose to a total of 26 Gy.

During the treatment, the patient experienced mild skin erythema along the scalp. He did not have any worsening of his left-sided lower extremity weakness, nor increased frequency of his Jacksonian seizures. He did not require any steroids during or immediately after treatment. The patient was seen in follow-up 6 and 14 months after treatment. At the 14-month follow-up visit, the patient noted subjective improvement in his left lower extremity coordination and strength. The frequency of his periodic left lower extremity seizures was unchanged at approximately one per month. He also noted decreased visual acuity bilaterally since the end of his treatment most noticeable with reading, which may be indicative of early radiation-induced cataract formation. Follow-up brain MRIs at 6 and 14 months showed no change in the size of his 10 meningiomas and no new lesions.

3. Discussion

Our patient had clinical characteristics typical of patients with multiple meningiomas. Antinheimo et al. performed a population-based study of multiple meningiomas in Helsinki, Finland. The authors found an incidence of approximately one in one million. The median age was 61 years. Of the meningiomas that had pathologic evaluation, 96% were histologic grade I. An estimated 24% of cases were associated with NF2 [3]. Our patient differs from many of the cases of multiple meningiomas reported in the literature in that he had 10 lesions at the time of our treatment. A majority of patients in the published reports had 2–4 lesions [4,5].

The standard of care for symptomatic or growing meningiomas is surgical resection. Numerous reports have described the successful treatment of multiple meningiomas using surgical resection alone [4,5]. SRS is a more recent option for multiple meningioma patients in cases where surgery is inappropriate. Surgery and SRS have also been combined in the same patient with multiple meningiomas [6].

Patients with widespread meningiomas cannot be effectively treated by either surgery or SRS as recurrence in the untreated areas may be a relentless problem. There is no standard of care for patients with widespread meningiomas, but we have previously treated these patients with whole brain radiation to a total dose of 45 Gy in 1.8 Gy fractions. Dose response studies of meningiomas suggest that the desired dose of radiation for local control of grade 1 meningiomas is greater than 52 Gy in 1.8–2.0 Gy fractions [7]. For solitary grade 1 meningiomas, our standard is to treat the lesion with 54 Gy in 1.8 Gy fractions. However, such high total doses cannot be used in whole brain treatments without unacceptable rates of radiation toxicity [8]. Therefore, the patients with widespread meningiomas who have been treated with whole brain radiation have necessarily been treated with suboptimal doses.

The use of helical IMRT allowed us to treat our patient's entire meninges with higher doses than would have been safely possible with whole brain radiation. Conformal treatment of a complex structure like the meninges was possible using the relatively new technique of helical IMRT. Fig. 4 shows the distribution of dose achieved by helical IMRT planning in comparison to a conventional 3D radiation plan that uses two opposed lateral fields. Figs. 5 and 6 show the dose volume histograms for the helical IMRT plan and conventional 3D

whole brain plan, respectively. With the conventional 3D whole brain plan, no normal brain is spared from the total prescribed dose to the meninges.

IMRT refers to a radiation planning method that uses software algorithms to optimize treatment beam shapes and beam angles. The planning process for IMRT differs from conventional radiation planning in several important ways. In conventional treatment planning, the treatment team places a standard set of beams initially and then adjusts angles and shapes using a trial-and-error approach. In IMRT planning, the team identifies the target and critical structures to be avoided and determines dose criteria for each. Optimization software then applies a specified number of beams and iteratively adjusts beam shapes and angles until a dose distribution is produced which most closely resembles the pre-determined criteria. IMRT optimization software can produce a plan with conformality that is far beyond the practical limitations of the conventional trial-and-error methods of even the most experienced treatment teams. Helical IMRT adds another level of sophistication as it allows for the continuous delivery over 360° beam angles. Non-helical IMRT treatments require repositioning of the arm of a linear accelerator which can take a significant time. Thus, the number of beam angles of non-helical IMRT plan is limited by the practical concern of minimizing patient treatment time.

To our knowledge, this is the first reported case of brain-sparing total meningeal radiation. While follow-up has only been 14 months, this treatment appears to have stopped or slowed further growth of his tumors that had been rapidly progressing prior to the treatment. Moreover, the acute and late side effects of treatment have been minimal.

Our patient declined whole brain radiation out of concern for the known risks of acute and late radiation toxicities. During whole brain treatment and in the first 3–4 weeks after treatment, the most common neurologic side effects are headache and fatigue. The acute side effects of radiation therapy are thought to be related to transient disruption of the blood brain barrier and consequent edema [9]. It is unclear whether our brain-sparing technique decreased the patient's overall risk of blood brain barrier disruption and acute sequelae. While the integral dose to the whole brain was less with the brain-sparing technique, the portions of the peripheral brain did receive a higher dose because we prescribed a higher dose than we would have with whole brain treatment. Possible long-term sequelae of treatment include chronic fatigue, cognitive slowing, decreased short-term memory, word-finding problems, and rarely, focal motor/sensory deficits [10]. The late effects of radiation are due to a combination of parenchymal and endothelial cell death. Of parenchymal brain cells, oligodendroglial cells are thought to be most radiation-sensitive, which may explain why the late effect of radiation necrosis is more commonly seen in white matter than grey matter [11]. Our brain-sparing technique preferentially spared white matter (see Fig. 4), and for this reason may have decreased this patient's overall risk of late radiation toxicity compared to whole brain radiation.

In conclusion, this is the first report of brain-sparing total meningeal radiation for a patient with widespread meningeal disease. The treatment was accomplished using helical IMRT, a new radiation planning and treatment technique. This brain-sparing technique allowed us to

treat his meninges with higher doses than would have been possible with whole brain radiation and with the goal of achieving long-term disease control.

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Fig. 1.

An axial slice of the patient's pre-treatment T1 sequence MRI. The slice shows evidence of four of the patient's 10 meningiomas.

Fig. 2.

A coronal slice of the patient's pre-treatment T1 sequence MRI. The slice shows evidence of extensive skull deformity secondary to multiple craniotomies and multiple areas of meningeal thickening.

Fig. 3.

The panel shows the dose distribution on his planning CT scan of his helical IMRT plan in the axial, sagittal and coronal dimensions. The areas of brain within the shaded region received at least 50.4 Gy.

Fig. 4.

The CT images in row A show the isodose curves for the helical IMRT plan. The innermost curve in the row A images (red in web version) represents the 66% isodose line. Brain within this curve would receive less than 66% of the total prescribed dose (in web: there are two green curves, one within the skull and the other outside of it. The green curves represent the 95% isodose lines. Tissue between these two green lines receives at least 95% of the prescribed dose). The CT images in row B show the isodose curves for a conventional 3D whole brain plan that uses two opposed lateral fields. The innermost curve (in the row B images in red in web version) represents the 103% isodose line. Brain within this curve receives 103% of the total prescribed dose (in web: the outermost line (in green) represents the 95% isodose curve. Tissue within this line receives at least 95% of the prescribed dose). None of the brain in the conventional 3D whole brain plan receives less than 66% of the total prescribed dose.

Fig. 5.

The dose–volume histogram for the helical IMRT plan shows relative sparing of normal brain compared to the target structure, the meninges. Note that this dose–volume histogram was produced for the patient's original prescription of 45 Gy. The patient ultimately received a total dose of 50.4 Gy, but the relative relationship between normal brain and meninges as represented by this histogram would be preserved.

Fig. 6.

The dose–volume histogram for a conventional 3D whole brain plan shows no sparing of normal brain compared to the target structure, the meninges. Note that this dose–volume histogram was produced for the patient's original prescription of 45 Gy. The patient ultimately received a total dose of 50.4 Gy, but the relative relationship between normal brain and meninges as represented by this histogram would be preserved.