

A Case Report of Combination Treatment for Brain Meningioma: A Different Approach

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Abstract

Meningiomas are among the most common primary tumors of the central nervous system. We describe the case of an 82-year-old woman with meningioma, the epicenter of which was above the sella, causing her terrible headaches and severely compromised visual acuity. Although the patient was eligible for stereotactic radiosurgical treatment (SRS), she was treated with conventional 3D conformal radiotherapy (3DCRT), at her will. We discuss alternative and innovative approaches regarding non-chemotherapy drugs, with concurrent radiation treatment.

Categories: Internal Medicine, Radiation Oncology, Neurosurgery

Keywords: Stereotactic Radiosurgery, meningioma, arachidonic acid, eicosanoids, apoptosis, abscopal effect

Introduction

Most meningiomas are benign tumors and only a small fraction is atypical or even malignant. Histological type does not correlate always to prognosis since the location of the tumor and the compression phenomena can cause serious morbidity or mortality. Patients bearing tumors sized under 3.5 cm, especially when they are adjacent to sensitive brain structures, are candidates for stereotactic radiosurgery (SRS). The current practice is the simultaneous use of corticosteroids in order to reduce peritumoral edema concerning brain tumors during radiation treatment.

Case Presentation

An 82-year-old woman with severe headaches and progressive visual loss for one year's duration was diagnosed with meningioma (Figures 1-3), encompassing the optic chiasm and compressing the pituitary gland, with a maximal diameter of 3.2 cm. Due to its location, the tumor was considered inoperable, and although she was eligible for SRS, 3D conformal radiation treatment was scheduled.

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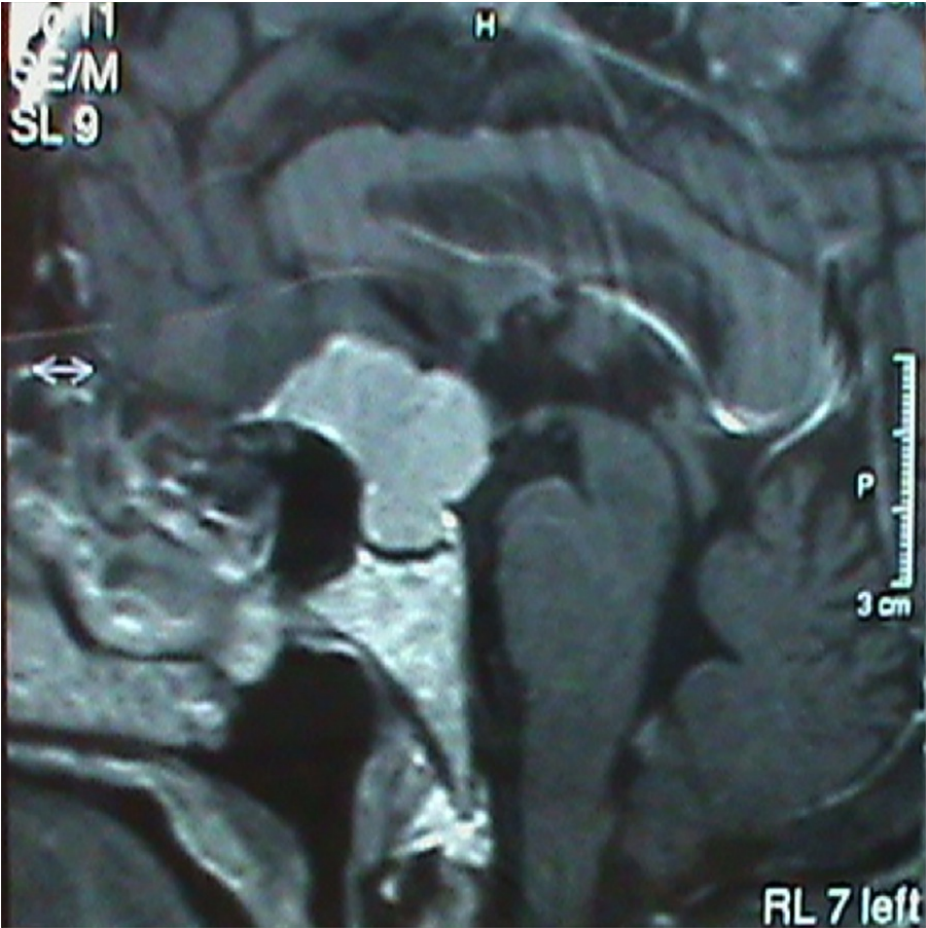


FIGURE 1: Sagittal T1, prior RT

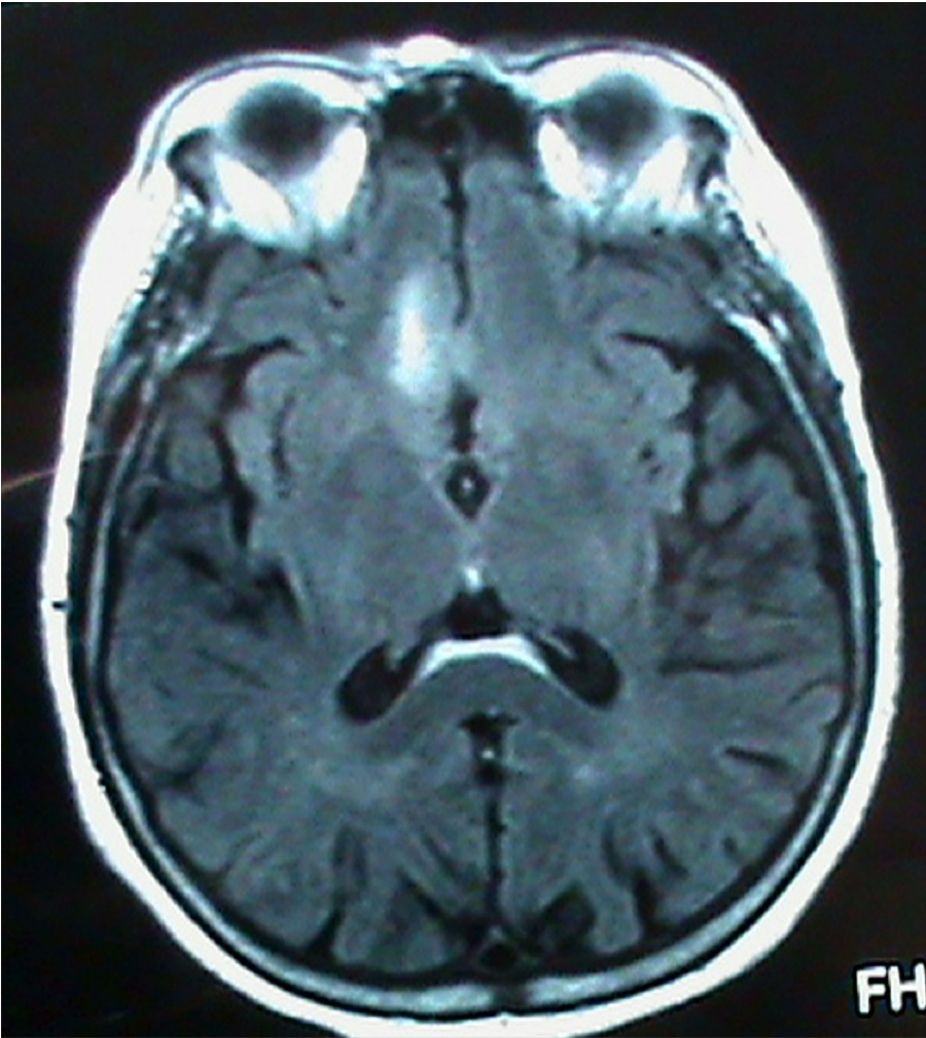


FIGURE 2: Axial T1 Flair, showing edema, prior RT

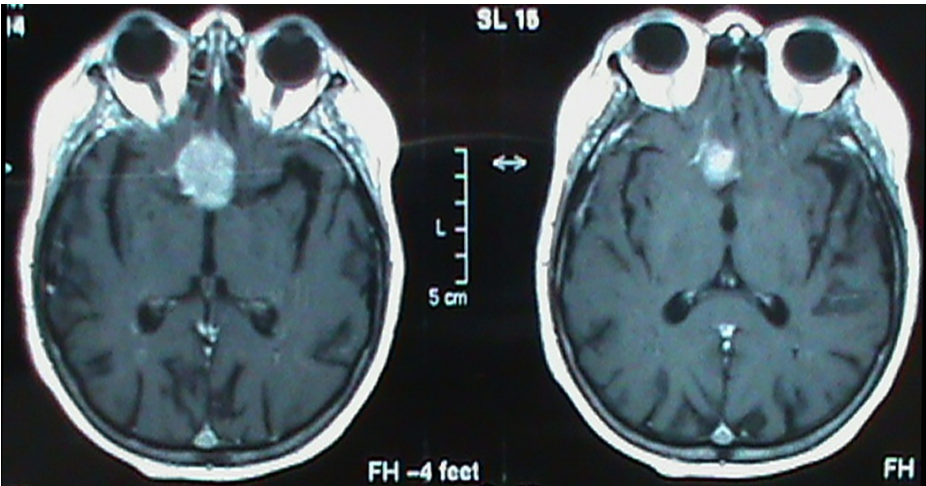


FIGURE 3: Axial T1, prior RT

Due to the patient’s past medical history (mild arthritis), she had been treated with prednisolone 7.5 mg qd for two years. Since her meningioma diagnosis, three months ago, her steroid medication was increased to 16 mg of methylprednisolone qd a.m., which she continued to take until the initiation of her radiation

treatment. Due to the protracted steroid treatment, she acquired cushingoid characteristics which worsened with the steroid dose increment.

Radiation therapy started in March 2011. The patient received 54 Gy in 2 Gy fractions five days a week. Beginning the day of her irradiation treatment, she also began taking acetazolamide 250 mg qd, valproic acid 500 mg bid, and cimetidine 400 mg bid. Prednisolone 5 mg qd was also prescribed due to the assumption that her hypothalamus-pituitary-adrenal axis was suppressed.

Ten days after the initiation of her RT treatment, the patient mentioned that her headaches completely disappeared and her vision improved. Upon completion of her treatment, the patient noted improvement in her visual acuity and her cushingoid features were significantly less prominent.

We ordered a new brain MRI 10 days after the completion of the patient's 3DCRT, which revealed negligible edema (Figures 4-6) in accord to the patient's subjective improvement. We scheduled a new MRI imaging of the brain in three months period, in order to evaluate the tumor size and characteristics. Since the patient had experienced no adverse effects whatsoever clinically and biochemically, she was advised to continue the same drug regimen until her next imaging study.

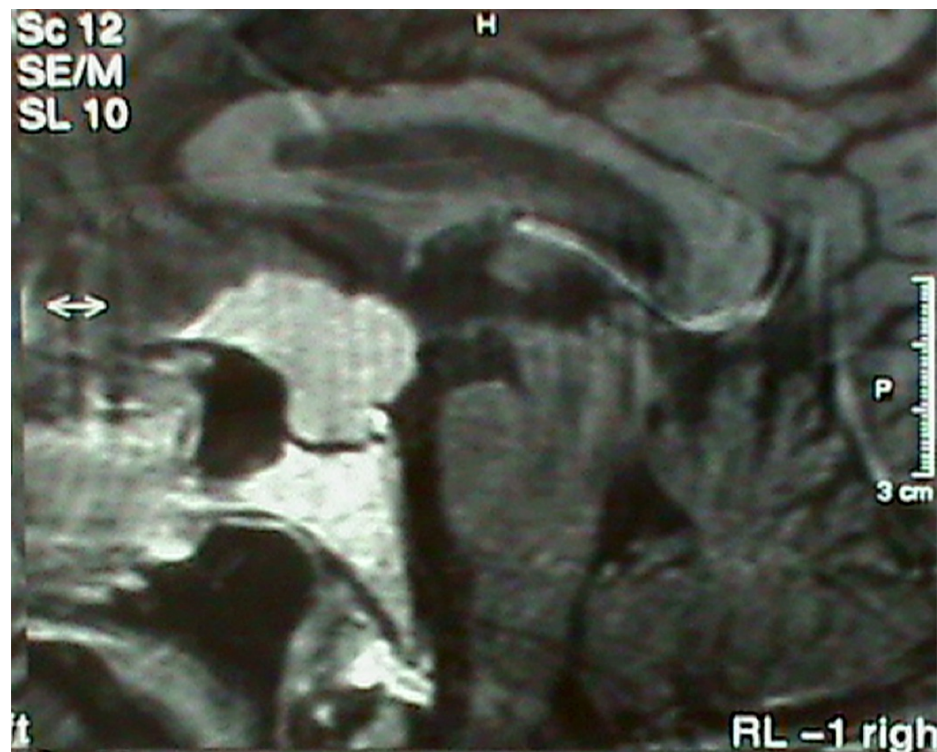


FIGURE 4: Sagittal T1, 10 days after RT

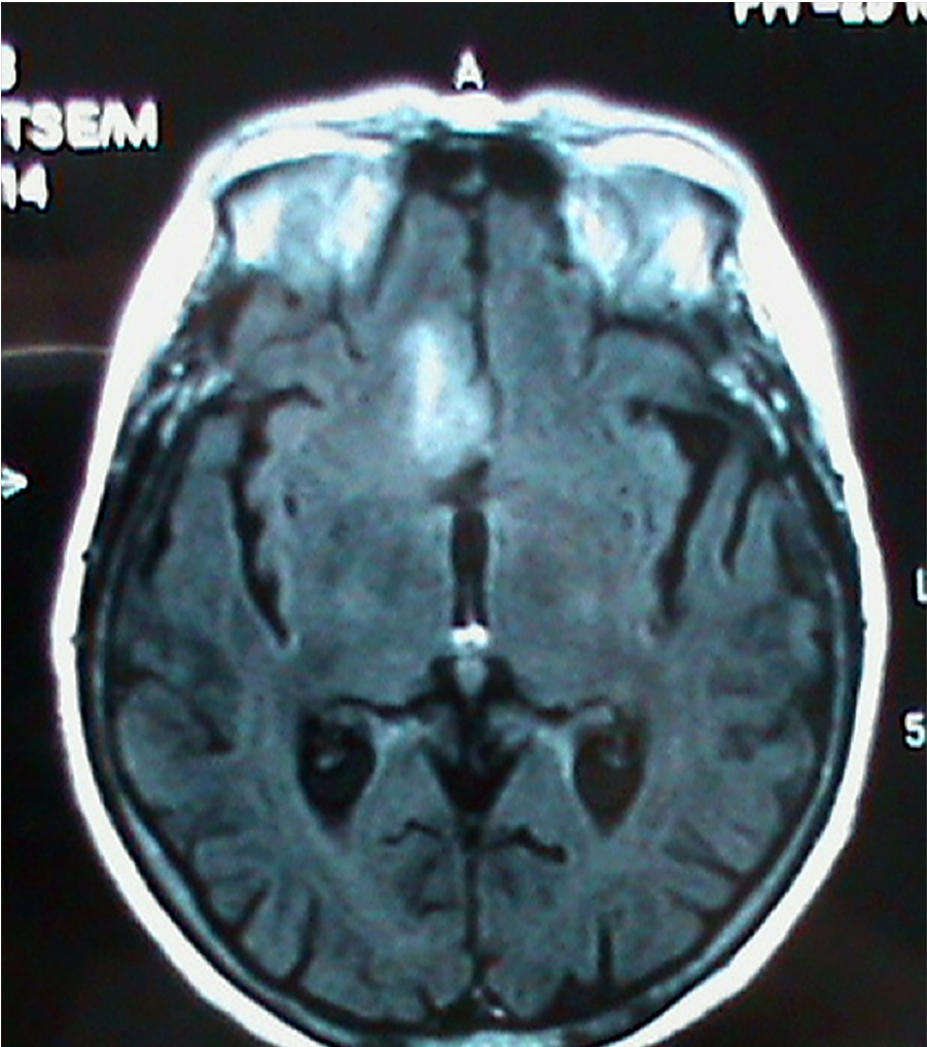


FIGURE 5: Axial T1 Flair, showing edema, 10 days after RT

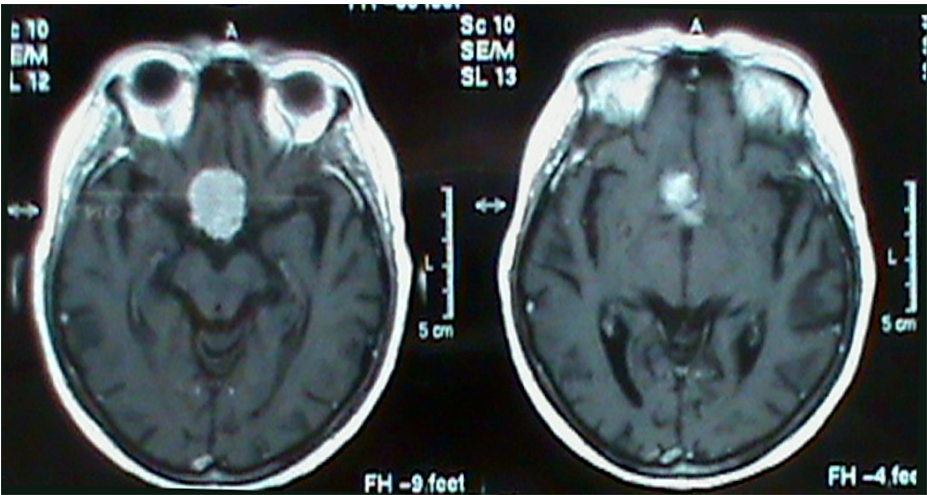


FIGURE 6: Axial T1, 10 days after RT

Discussion

Prescribing steroids in order to minimize peritumoral edema, especially during radiation treatment of brain

tumors located near sensitive structures, has been a common practice. Although their efficacy is well-established, they produce multiple side-effects and have a profound negative influence on cytokine release and immune cell function. The immune system, as a whole, plays an integral role in destroying cancer cells and perhaps is the key element of the radiation treatment abscopal effect and an important factor in the bystander effect [1].

Recently, alternative steroid sparing agents have been utilized in order to reduce brain tumor edema, such as boswellic acids which act as 5-lipoxygenase (5-LOX) inhibitors, with quite satisfying results [2]. The blockage of arachidonic acid (ARA) cascade could minimize radiation treatment adverse reactions through reduction of pro-inflammatory eicosanoids and could possibly also enhance therapeutic results. Upregulation of intracellular unesterified ARA could accentuate both pathways of apoptosis, extrinsic and intrinsic [3-9].

There are three arachidonic acid depleting enzyme classes: cyclooxygenases (COX-1 and COX-2), lipoxygenases (5-LOX, 12-LOX, and 15-LOX), and cytochrome P450 (CYP450). Inhibition of each one of them raises intracellular ARA levels, although combined inhibition could provide the most profound results [10]. Corticosteroids prevent the release of ARA from cancer cells via inhibition of cytosolic phospholipase A2 (cPLA2), an action which results in less available pro-inflammatory mediators, but also in less intracellular ARA. There is evidence that in some cases corticosteroids are counter-productive when they are used in combination treatments [11-12].

Cimetidine is a competent CYP450 inhibitor, and valproic acid downregulates both COX2 isoenzyme and long-chain acyl-CoA synthetase [13-14], thus boosting intracellular ARA levels. An addition to its effect on ARA cascade is the ability to inhibit histone deacetylase (HDAC) [15-17]; studies regarding its therapeutic potential in cancer are either completed or underway.

Acetazolamide, an inhibitor of all carbonic anhydrase (CA) isoenzymes and aquaporin-4 [18], could contribute as an add-on treatment for edema alleviation. Interestingly enough, CA inhibitors demonstrate anti-cancer activity [19-20], because tumors rely on carbonic anhydrases (especially isoenzymes IX, XII, IV) in order to survive the acidic environment they create and sustain. Another aspect of the indiscriminate CA inhibition is the effect on the mitochondrial CA Va and CA Vb, which could result in less lipogenesis [21] of the cancer cells due to the diminished action of pyruvate carboxylase. De novo lipogenesis protects cancer cells from free radicals, minimizing membrane polyunsaturated fatty acids (PUFAS) [22]. Blocking CA activity could enhance known therapeutic modalities.

Conclusions

Non-toxic treatments utilizing a multi-angled approach can enhance local radiotherapy effects, leaving healthy tissues largely unharmed. It is also conceivable that the propagation of apoptotic and necrotic death of cancer cells can, even without immunoparetic interventions, promote unanticipated benefits, such as the abscopal effect.

Additional Information

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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