RADIATION ONCOLOGY CASE

Metastases from glioblastoma disguised as a new primary malignancy

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CASE SUMMARY

A 65-year-old man with a history of glioblastoma (GBM) of the right frontotemporal lobes who was treated with radiation therapy and concurrent/ adjuvant temozolomide (TMZ) had a recurrence 3 months after standard chemoradiotherapy. He was subsequently treated with bevacizumab, lomustine, and Gamma Knife (Elekta, Stockholm, Sweden) stereotactic radiosurgery (GKSRS). Following GKSRS, he was treated with NovoCure tumor treating fields (NovoTTF; NovoCure, Portsmouth, New Hampshire). Approximately 9 months later, he developed back pain, right-sided ptosis, and sinus congestion-like symptoms. Spinal computed tomography (CT) imaging showed multilevel spinal dis-

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Because of his significant back pain, we simulated him for palliative radiation therapy to his cervical and thoracic spinal disease, as it was having the greatest impact on his quality of life. We treated his cervical disease (8 Gy \times 1) and then he requested we defer the thoracic radiation therapy to another day because of discomfort from lying on the table. The next day, the treatment conditions became unsafe secondary to the patient's inability to lie on the table and his thoracic radiation therapy was terminated. He was discharged to home with hospice and died approximately 3 weeks later.

IMAGING FINDINGS

An MRI of the head showed destructive changes in the paranasal sinuses with destruction of the left maxillary sinus and extension into the left retroantral fat, pterygopalatine fossa, and hard palate. The left lamina papyracea and left orbital roof were being invaded by a soft tissue mass in the left orbit measuring 2.6×0.9 cm, which engulfed the superior rectus, oblique, and medial rectus muscles (Figures 1 and 2).

DIAGNOSIS

The patient was diagnosed with widely metastatic glioblastoma. The initial suspicion was that he had developed a metastatic paranasal sinus primary tumor, which was disproved by his biopsy.

DISCUSSION

GBM is the most common histology of malignant primary brain tumors in adults.¹ Despite advances in surgical,

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FIGURE 1. An MRI of the brain and sinuses in T2/FLAIR sequence showing abnormal soft tissue within the superior/medial aspect of the left orbit, which appears to be contiguous with abnormal soft tissue filling the left frontal, ethmoid, and maxillary sinuses (white arrows). A small amount of mass effect is on the left medial rectus muscle.

FIGURE 2. An MRI of the brain and sinuses in spoiled gradient (SPGR) post-contrast sequence again showing the left-sided abnormal soft tissue within the left ethmoid sinus with some mass effect on the left medial rectus muscle. Also imaged is abnormal soft tissue extending into the inferior aspect of the right orbit (solid white arrow) as well as a focus of intra-cerebral disease (dashed arrow).

medical, and radiation therapies, the mortalities of GBM remain high, with a median survival ranging between 40 and 70 weeks,² although recent clinical trial data has shown promise for improving outcomes with the addition of NovoTTF.³ The majority of GBM recur locally, and distant metastasis is rare, estimated to occur in < 2% of patients.⁴ In spite of infrequent clinical presentation of distant metastases, circulating GBM cells have been detected in up to 20.6% of patients,⁵ which may lead to metastases to the lymphatics, lungs, bone, liver, and other organs.⁶

CONCLUSION

A diagnosis of GBM is a grim diagnosis from the start. When patients survive long enough to develop metastatic disease, however, the median time from detection of metastatic disease to death has been reported to be as short as 1.5 months.⁶ Although data is limited, it has been suggested that metastases to the liver have a lesser impact on survival than metastases to the lung.⁷ The treatment of choice for asymptomatic patients is systemic therapy, although when quality of life is affected by disease burden, surgical intervention or focal radiation therapy can be considered, as was the case with our patient.

REFERENCES

1. Ostrom QT, Gittleman H, Liao P, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2007–2011. *Neuro Oncol.* 2014;16: iv1-iv63.

2. Thakkar JP, Dolecek TA, Horbinski C, et al. Epidemiologic and molecular prognostic review of glioblastoma. *Cancer Epidemiol Biomarkers Prev.* 2014;23:1985-1996.

3. Stupp R, Taillibert S, Kanner A, et al. Tumor treating fields (TTFields): a novel treatment modality added to standard chemo- and radiotherapy in newly diagnosed glioblastoma—First report of the full dataset of the EF14 randomized phase III trial. *J Clin Oncol.* 33,2015(suppl; abstr 2000).

4. Khattab MH, Marciscano AE, Lo SS, et al. Antiangiogenic therapies and extracranial metastasis in glioblastoma: a case report and review of the literature. *Case Rep Oncol Med.* 2015;2015:431819.

5. Muller C, Holtschmidt J, Auer M, et al. Hematogenous dissemination of glioblastoma multiforme. *Sci Transl Med.* 2014;6(247):247ra101.

6. Lun M, Lok E, Gautam S, et al. The natural history of extracranial metastasis from glioblastoma multiforme. *J Neurooncol*. 2011;105(2):261-273.

7. Fonkem E, Lun M, Wong ET. Rare phenomenon of extracranial metastasis of glioblastoma. *J Clin Oncol.* 2011;29(34):4594-4595.