Abstract

The authors sought to determine the incidence, time course, and risk factors for overall adverse radiation effect (ARE) and symptomatic ARE after stereotactic radiosurgery (SRS) for brain metastases. METHODS All cases of brain metastases treated from 1998 through 2009 with Gamma Knife SRS at UCSF were considered. Cases with less than 3 months of follow-up imaging, a gap of more than 8 months in imaging during the 1st year, or inadequate imaging availability were excluded. Brain scans and pathology reports were reviewed to ensure consistent scoring of dates of ARE, treatment failure, or both; in case of uncertainty, the cause of lesion worsening was scored as indeterminate. Cumulative incidence of ARE and failure were estimated with the Kaplan-Meier method with censoring at last imaging. Univariate and multivariate Cox proportional hazards analyses were performed. RESULTS Among 435 patients and 2200 brain metastases evaluable, the median patient survival time was 17.4 months and the median lesion imaging follow-up was 9.9 months. Calculated on the basis of 2200 evaluable lesions, the rates of treatment failure, ARE, concurrent failure and ARE, and lesion worsening with indeterminate cause were 9.2%, 5.4%, 1.4%, and 4.1%, respectively. Among 118 cases of ARE, approximately 60% were symptomatic and 85% occurred 3-18 months after SRS (median 7.2 months). For 99 ARE cases managed without surgery or bevacizumab, the probabilities of improvement observed on imaging were 40%, 57%, and 76% at 6, 12, and 18 months after onset of ARE. The most important risk factors for ARE included prior SRS to the same lesion (with 20% 1-year risk of symptomatic ARE vs 3%, 4%, and 8% for no prior treatment, prior whole brain radiotherapy [WBRT], or concurrent WBRT) and any of these volume parameters: target, prescription isodose, 12-Gy, or 10-Gy volume. Excluding lesions treated with repeat SRS, the 1-year probabilities of ARE were < 1%, 1%, 3%, 10%, and 14% for maximum diameter 0.3-0.6 cm, 0.7-1.0 cm, 1.1-1.5 cm, 1.6-2.0 cm, and 2.1-5.1 cm, respectively. The 1-year probabilities of symptomatic ARE leveled off at 13%-14% for brain metastases maximum diameter > 2.1 cm, target volume > 1.2 cm³, prescription isodose volume > 1.8 cm³, 12-Gy volume > 3.3 cm³, and 10-Gy volume > 4.3 cm³, excluding lesions treated with repeat SRS. On both univariate and multivariate analysis, capecitabine, but not other systemic therapy within 1 month of SRS, appeared to increase ARE risk. For the multivariate analysis considering only metastases with target volume > 1.0 cm³, risk factors for ARE included prior SRS, kidney primary tumor, connective tissue disorder, and capecitabine. CONCLUSIONS Although incidence of ARE after SRS was low overall, risk increased rapidly with size and volume, leveling off at a 1-year cumulative incidence of 13%-14%. This study describes the time course of ARE and provides risk estimates by various lesion characteristics and treatment parameters to aid in decision-making and patient counseling.
Adverse radiation effect after stereotactic radiosurgery for brain metastasis; hazard ratio; picture archiving and communication system; SRS = stereotactic radiosurgery; UCSF = University of California, San Francisco; WBRT = whole-brain radiation therapy; brain metastasis; brain/radiation effects; dose-response relationship; necrosis; oncology; radiation; radiation injuries; radiosurgery/adverse effects; stereotactic radiosurgery

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