Brain metastases treated with radiosurgery alone: An alternative to whole brain radiotherapy?

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Background

The incidence of brain metastases as a result of systemic cancer is 20-40%. Many cases are identified in asymptomatic patients by screening neuroimaging. Whole brain radiotherapy (WBRT) extends survival in these patients by 3-5 months, but is associated with morbidity including alopecia, fatigue, long-term cognitive problems, and it may delay delivery of other treatments for extracranial cancer. Stereotactic radiosurgery (SRS) in combination with WBRT has become an important approach to treat patients with a few small brain metastases. However, some have questioned the added value of WBRT after SRS. SRS is a minimally invasive alternative to surgical resection. The authors present a retrospective study of their experience with SRS alone to treat brain metastases.

Patients and Methods

- Study duration: 1987-2001
- 172 out of 1003 patients with brain metastases treated with SRS alone without fractionated WBRT (remainder had SRS plus WBRT or SRS for progression after resection)
- Inclusion criteria: maximum tumor diameter 3.5cm, no major neurologic deficit due to mass effect, no medically refractory seizures

Radiosurgical Technique:

- used gamma knife
- stereotactic frame used with stereotactic MRI for treatment planning
- maximum dose varied from 20 to 40 Gy (median dose = 36 Gy)
- marginal dose from 11 to 22 Gy (median dose 20 Gy)
- isodose line for tumor margin varied from 30-80%.
- 50% isodose line used in 140 pts (81.4%)
- tumor volume 0.1-24.9cm 3 (median 2.8 cm 3)

Follow-up:

- Imaging scheduled at 2,5,8, and 12 months in first year and 3-4 month intervals thereafter

Results

- 132 pts died, 32 remained alive at publication of study
- median survival 8 months
- 1 year survival rate 36%
- 2 year survival 25%

- Significant predictors for survival (by multivariate testing):
- - Primary tumor status (p=0.003) (patients with no evidence of disease or stable disease vs pts with synchronous or progressive dz)
  - Malignant melanoma (p=0.005)
  - Age (p=0.008) (pts < 60 yr survived longer than >= 60 yr)
  - KPS score (p=0.01) (KPS >=90 survived longer than < 90)

Tumor control:

- Only 121 patients (out of 172) evaluable with follow up imaging
- 16% had local recurrence
- 15 patients had local recurrence only
- 41 patients had remote recurrence only
- 5 patients had both local and remote recurrences

Local tumor control:

- Tumor volume alone was significant in both univariate and multivariate analysis (p=0.02 and 0.026)
- For brain mets < 4.0 cm 3, local control was 84% vs 49% at 1 year for > 4.0 cm 3

Remote tumor control:

- No predictive factor significant for remote tumor control

Complications:

- Developed in <10% pts (11/172 pts had complication)
- 16 patients (13.2%) had peritumoral edema
- 5 patients (4.1%) had later intratumoral hemorrhage
- actuarial rate for persistent complications was 5.6%

Cause of Death:

- Only obtained in 116 patients
- main cause of death was extracranial disease in about 80%
- 11.2% died as a result of brain mets
- 79.3% died as a result of progression of extracranial disease
- 5.2% died as a result of combination of brain mets and extracranial disease
- 4.3% died of other diseases

Author’s Conclusions

- primary tumor status and KPS score had stronger correlation with survival
- 1 year survival rate until death from brain mets was 77% compared with 36% overall survival rate (which suggests that main limitaion on survival was extracranial disease and not brain metastases)
- tumor volume alone affected local tumor control
- For patients with recurrences after radiosurgery, WBRT or radiosurgery are usually effective as salvage therapy
- Patients < 60 yrs with good control of primary tumor and high KPS are good candidates for radiosurgery alone

Their recommended present management:

- Surgical resection followed by WBRT or SRS when average tumor diameter >3cm

- WBRT with radiosurgical boost for smaller tumors when >2 metastases
- Radiosurgery alone when 1 or 2 metastases <3cm in maximum diameter

Discussion

According to most reports, patient survival after radiosurgery alone was not different from that in patients who had combined SRS and WBRT (because patients died from progression of extracranial disease rather than brain metastases). These results are confirmed in this study. Initial avoidance of WBRT may lead to improved patient quality of life. However, information on quality of life is not available in this study. These results are not a product of a randomized study, and therefore there may be a selection bias for patients who had better prognostic factors and it may not be appropriate to compare their median survival to historical standards. In addition, 30% of patients were lost to follow up. This subgroup may have had less favorable outcomes and the intracranial control rate may not be as good as reported. In addition, most intracranial recurrences were remote recurrences (38% were remote tumor recurrence whereas 17% were local recurrence). These recurrences were not in the radiation field, and they probably would have been decreased with WBRT.

In conclusion, this article demonstrates that SRS may be a reasonable alternative to surgical resection. Patients treated using SRS may have improved quality of life when contrasted with patients treated using WBRT. A reasonable future study would be SRS vs SRS + WBRT with improved quality of life as primary outcome goal. However, at the current time, WBRT remains a part of standard of care treatment in patients with brain metastases.