IORT combined with immunotherapy in brain metastases

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Purpose/Objective

Intraoperative radiation therapy (IORT) provides a promising alternative to adjuvant external beam radiation therapy (EBRT) following surgical resection of brain metastases (BMs), by enabling timely admission to subsequent systemic treatments, which increasingly comprise novel targeted approaches such as immunotherapy. There is little evidence for ideal timing or holding of systemic treatment under irradiation. We thus sought to assess safety and efficacy of IORT in combination with immune checkpoint inhibitors (ICIs) and other targeted agents.

Material/Methods

In a multicentric approach incorporating individual patient data from six international IORT centers, all patients with BMs undergoing IORT were retrospectively assessed for combinatorial treatment with ICIs and/or targeted agents and evaluated for toxicity as per acute- and late adverse events (AEs) and cumulative rates, including wound dehiscence, radiation necrosis (RN), leptomeningeal spread, local control (LC), distant brain progression (DBP) and estimated overall survival (OS).

Results

A total of 103 lesions receiving IORT combined with immunomodulatory systemic treatment or other targeted therapies (TTs) were included. The median follow up was 13.2 (1.2-102.4) months and the median IORT dose was 25 (18-30) Gy prescribed to the applicator surface. The median lesion diameter was 34 mm. Among all AEs of grade 3 or higher (n=46), there were two grade 3 AEs (4.3%) related to IORT recorded. A 5.7% cumulative RN rate was observed. The 1-year LCR was 97.1% and the 1-year DBP-free rate 61.1%. The median estimated OS was 26 (1.2-not reached) months with a 1-year survival rate of 74.5%. Early initiation of iICIs/TTs was associated with a nonsignificant trend toward improved DBP rate and overall survival.

Conclusion

The combination of ICIs/TTs and IORT for resected BMs does not result in increased toxicity and harbors a low risk of radiation necrosis, while yielding encouraging local control outcomes. By this combinatory treatment, time gaps between surgery and systemic treatment could be shortened or avoided. The definitive role of IORT in local control after BM resection will be defined in a prospective trial.