Longitudinal diffusion MRI in PCNSL treated with methotrexate, rituximab, and temozolomide (MRT).

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Abstract Text:

Background: High-dose methotrexate (HD-MTX) is the backbone of therapy for PCNSL but induction chemotherapy can also include temozolomide and rituximab (MRT). We evaluated baseline tumor ADC values and change in ADC values as markers of response. Methods: After receiving IRB consent, we retrospectively evaluated PCNSL patients treated at our hospital with MRT. Patients were treated in 28-day induction cycles: HD-MTX (8g/m² - dose adjusted based on creatinine clearance) on days 1 and 15; rituximab (375 mg/m²) weekly for 6 doses; and temozolomide (150-200 mg/m²) on days 7-11 of each cycle for a goal of 12 cycles. HD-MTX was continued every 2 weeks until complete response (CR). Brain MRI was done after every other MTX treatment to assess response. Volume of contrast enhancing tumor and median tumor ADC values at baseline, 1 month, and 2 months after treatment began was measured. Results: From August 2003 to September 2013, 42 patients received MRT as first-line therapy at the time of initial diagnosis and 10 received MRT as salvage therapy at first or second recurrence. The median age of all patients was 63 (range 49-84). With first-line MRT therapy, there were 34 CRs (median cycles to CR = 4), 5 PRs, 2 PD’s, and 1 nonevaluable for response. With salvage MRT therapy, there were 6 CRs (median cycles to CR = 4), and 4 PR’s. After a median follow-up of 23.5 months in the first-line group and 51.6 months in the relapse group, 14 patients have progressed and 6 died (1 from an unrelated heart attack). After analysis of 22 imaging datasets, 18/22 patients saw a reduction of >70% in enhancing volume from baseline to month 2 of treatment. Shorter time to CR was associated with lower baseline median tumor ADC (p=0.035). There was no statistically significant association in baseline or change in ADC and PFS or OS. Conclusions: MRT resulted in a promising early response rate. Lower baseline tumor ADC was associated with shorter time to CR so may be a helpful biomarker. Lower ADC may reflect hypercellular, rapidly proliferating tumor that is more sensitive to chemotherapy. The lack of association with tumor ADC and survival was likely because of the few progression/death events in our dataset and longer term follow-up is needed with more imaging time points.
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