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## Hyperfractionated Accelerated Radiotherapy in the Milan Strategy for Metastatic Medulloblastoma

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**Purpose:** With a view to improving the prognosis for patients with metastatic medulloblastoma, we tested the efficacy and toxicity of a hyperfractionated accelerated radiotherapy (HART) regimen delivered after intensive sequential chemotherapy.

**Patients and Methods:** Between 1998 and 2007, 33 consecutive patients received postoperative methotrexate (8 g/m<sup>2</sup>), etoposide (2.4 g/m<sup>2</sup>), cyclophosphamide (4 g/m<sup>2</sup>), and carboplatin (0.8 g/m<sup>2</sup>) in a 2-month schedule, then HART with a maximal dose to the neuraxis of 39 Gy (1.3 Gy/fraction, 2 fractions/d) and a posterior fossa boost up to 60 Gy (1.5 Gy/fraction, 2 fractions/d). Patients with persistent disseminated disease before HART were consolidated with two myeloablative courses and circulating progenitor cell rescue.

**Results:** Patients were classified as having M1 (n = 9), M2 (n = 6), M3 (n = 17), and M4 (n = 1) disease. Seven patients younger than 10 years old who achieved complete response after chemotherapy received a lower dose to the neuraxis (31.2 Gy). Twenty-two of the 32 assessable patients responded to chemotherapy; disease was stable in five patients and progressed in five patients. One septic death occurred before radiotherapy. Eight patients experienced relapse after a median of 12 months. Fourteen of the 33 patients underwent consolidation therapy after HART. With a median 82-month survivor follow-up, the 5-year event-free, progression-free, and overall survival rates were 70%, 72%, and 73%, respectively. No severe clinical complications of HART have emerged so far.

**Conclusion:** HART after intensive postoperative chemotherapy, followed by myeloablative chemotherapy in selected cases, proved feasible in children with metastatic medulloblastoma. The results of our treatment compare favorably with other series treated using conventional therapies.

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