The UK experience of a treatment strategy for pediatric metastatic medulloblastoma comprising intensive induction chemotherapy, hyperfractionated accelerated radiotherapy and response directed high dose myeloablative chemotherapy or maintenance chemotherapy (Milan strategy).


Abstract

BACKGROUND: Historically, the 5-year overall survival (OS) for metastatic medulloblastoma (MMB) was less than 40%. The strategy of post-operative induction chemotherapy (IC) followed by hyperfractionated accelerated radiotherapy (HART) and response directed high dose chemotherapy (HDC) was reported in a single center study to improve 5-year OS to 73%. We report outcomes of this strategy in UK.

METHODS: Questionnaires were sent to all 20 UK pediatric oncology primary treatment centers to collect retrospective data on delivered treatment, toxicity and survival with this strategy in children aged 3-19 years with MMB.

RESULTS: Between February 2009 and October 2011, 34 patients fulfilled the entry criteria of the original study. The median age was 7 years (range 3-15). Median interval from surgery to HART was 109 versus 85 days in the original series. The incidence of grade 3 or 4 hematological toxicities with IC and HDC was 83-100%. All 16 patients who achieved complete response by the end of the regimen remain in remission but only three of 18 patients with lesser responses are still alive (P < 0.0001). With a median follow-up of 45 months for survivors, the estimated 3-year OS is 56% (95% CI 38, 71). This result is outside the 95% CI of the original study results and encompasses the historical survival result of 40%.

CONCLUSION: Within the limits of statistical significance, we did not replicate the improved survival results reported in the original series. The reasons include differences in patient sub-groups and protocol administration. International randomized phase III studies are needed. Pediatr Blood Cancer 2015;9999:1-8 © 2015 Wiley Periodicals, Inc.

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KEYWORDS: HART; chemotherapy; induction; medulloblastoma; metastatic; myeloablative

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