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High-dose chemotherapy and autologous stem-cell transplantation in children with Ewing's Sarcoma/PNET

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Abstract

The five-year event-free survival (EFS) for patients with localized pediatric Ewing's sarcoma/PNET is 70–80%, but in high-risk groups (metastatic disease, unfavorable localization, or large initial tumor mass) it is only 20–30%. Some research data shows evidence that high-dose chemotherapy (HDCT) with autologous hematopoietic stem-cell transplantation (auto-HSCT) can be a promising option for this group.

Patients and methods: From 2003 to December 2009 we treated 23 pediatric patients with histologically proven high-risk Ewing's sarcoma/PNET. The male-female ratio was 2.8:1, and the median age at diagnosis 12.6 years. All patients received 6 courses of polychemotherapy (ifosfamide, vincristine, doxorubicin, and etoposide), surgical treatment, or local irradiation (48–56 Gy). 8 patients then received maintenance chemotherapy, and for 15 patients this was substituted with HDCT with auto-HSCT. Conditioning regimens were busulfan 16 mg/kg and melphalan 140 mg/m² (n=13), and melphalan 140–200 mg/m² (n=2). The stem-cell sources were bone marrow (n=7), peripheral blood stem cells (n=3), and both (n=5). The mean CD34+ cell dose was 3.15 x 10⁶/kg.

Results: In the maintenance therapy group (n=8) 7 patients relapsed (5 patients with metastatic relapse died, 2 patients with local relapse are alive after salvage therapy), and 1 patient died of sepsis.

In the HDCT group (n=15) 12 of the patients are alive (6–41 months after HDCT), and 8 of them remain in remission. All children transplanted during partial remission or disease progression later relapsed. Only 2 patients who achieved complete remission at the end of induction chemotherapy developed late relapses.

The toxicity of HDCT regimens was moderate: grade II–III mucositis (n=15), febrile neutropenia (n=12), and toxic hepatitis (n=3).

Conclusions: HDCT with auto-SCT significantly lowers the relapse rate in pediatric patients with high-risk Ewing's sarcoma/PNET, who achieved CR after induction chemotherapy.

Keywords: Ewing sarcoma, PNET, autologous transplantation, high-dose chemotherapy, maintenance therapy

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