Regional hyperthermia for treatment of pediatric ovarian germ cell tumors

Ruediger Wessalowski¹, Gabriele Calaminus², Eunike Velleuer¹, Oliver Milz¹, Stefan Schönberger³, Dominik T. Schneider³, Rotem Lanzman⁴, Eugen Ruckhäberle⁵, Ivo Leuschner⁶, Ulrich Göbel⁷

¹Heinrich-Heine-University, Medical Faculty, Clinic for Pediatric Oncology, Hematology and Clinical Immunology, Duesseldorf, Germany, ²University Children’s Hospital, Department of Pediatric Hematology and Oncology, Bonn, Germany, ³Pediatric Clinic, Municipal Hospital, Dortmund, Germany, ⁴Heinrich-Heine-University, Medical Faculty, Institute of Diagnostic Radiology, Duesseldorf, Germany, ⁵Heinrich-Heine-University, Medical Faculty, Department of Gynecology and Obstetrics, Duesseldorf, Germany, ⁶University of Kiel, Pediatric Pathology, Kiel, Germany, ⁷Heinrich-Heine-University, Medical Faculty, Pediatric Surveillance Unit (ESPED), Duesseldorf, Germany

Background: Girls with advanced (FIGO stage IV) or recurrent pediatric ovarian germ cell tumors after repeated and incomplete resection have an unfavorable prognosis. This also applies for patients who were treated according to the MAKEI therapy-optimization clinical trials conducted by the Society for Pediatric Oncology and Hematology (GPOH), so that in such situations additional regional hyperthermia (RHT) has been used in order to facilitate the tumor resection and to improve the prognosis. With effect from 2004, this is done within the scope of the Hyper-PEI protocol, each patient with primary treatment failure serving as its own control.

Study design: The outcomes presented here are taken from registry data base of relapsed or refractory germ cell tumors of the ovary for the purpose of a phase-II clinical investigation.

Methods: In the Hyper-PEI protocol, regional hyperthermia (41-43°C for 60 minutes, days 1+4) is carried out in parallel with PEI-chemotherapy (cisplatin 40 mg/m², days 1+4, etoposide 100 mg/m², days 1–4 and ifosfamide 1800 mg/m², days 1–4). According to response the patients received 4-6 treatment courses with time intervals of approximately 21 days. On suspicion of residual tumor the possibility of a complete surgical tumor resection (provided as 2nd-look operation) was investigated after the 3rd or 4th course.

Patients: From 20 December 1995 to 11 December 2014 a total of 22 girls/young women at 8.5-24.8 years of age (median:16.2 years) with recurrent or primary refractory ovarian germ cell tumors were treated according to the Hyper-PEI-protocol in the context of our interdisciplinary tumor board. The histological examination yielded different, mostly mixed germ cell tumors with following quantitative dominated subtypes: Yolk sac tumors (n=12), teratomas (n=6), embryonal carcinomas (n=3), and choriocarcinoma (n=1). In addition, in six tumors a malignant transformation was found.

Results: In 15/22 patients with a measurable tumor in diagnostic imaging and increased levels of tumor markers before RHT clinical treatment response was assessed: CR (n=4); PR (n=4); SD (n=6); PD (n=1). After 3-4 Hyper-PEI courses a 2nd-look operation was performed in 13/22 patients: R0 (n=9), R1 (n=3); R2 (n=1). Overall survival in this patient population with an unfavorable prognosis was 71% (95% CI 46-86). The median follow-up of surviving patients is 55 months (range 18–248).

Conclusion: A multi-modal therapy including regional hyperthermia according to the Hyper-PEI-protocol has led to long-term remission in the majority of patients with advanced refractory or recurrent ovarian germ cell tumors.

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