FERTILITY SPEARING SURGERY IN CHILDREN WITH OVARIAN MASSES

Introduction/Background Ovarian masses (whether benign or malignant) are rare in children. They count 2.6 cases per 100,000 girls per year and 50% of them are malignant. Because of the young age of the patient the decision for radicality of the surgery is usually difficult.

Methodology We present retrospective analysis of children and adolescent girls with adnexal mass operatively treated from 2013 to 2022 in University Medical center Ljubljana, where we operated all of ovarian malignant tumors in children in Slovenia. Clinical presentation, intraoperative procedures, histopathologic findings and postoperative follow up were collected from medical records and analyzed.

Results In period of 10 years 69 young patients with ovarian mass were operated, 15 of them were malignant, 54 had benign histology. Median age of the patients with malignant tumors was 14.2 years, with benign tumors was 16.1 years. In the malignant group there were 6 borderline tumors, 2 immature teratomas, 3 disgerminomas (2 of them siblings with Swayer syndrom), 2 yolk sac tumors, 1 sclerosating stromal tumor and 1 Sertoli Leydig cell tumor. Benign masses were devided into 19 mature teratomas, 6 paraovarian cysts, 12 cystadenomas (6 serous, 6 mucinous), 3 cistadenofibromas (2 serous, 1 mucinous), 1 endometrioma, 1 ovarian fibroma and 14 functional cysts. 28 from the patients with benign masses had torsion. All the patients had fertility spearing surgery. Four patients with malignant histolgy had adjuvant chemotherapy (2 disgerminomas and 2 yolk sac tumors), one patient with yolk sac tumor had early relapse and second line chemotherapy. Until now all of the patients are in remission.

Conclusion Fertility spearing operation in children with ovarian mass is feasible and could be the treatment of choice, as it preserves reproductive potential.

Disclosures Authors have no disclosures.

GERMLINE AND SOMATIC GENETIC PROFILES OF EPITHELIAL OVARIAN CARCINOMA PATIENTS SENSITIVE AND RESISTANT TO PLATINUM DERIVATIVES ESTIMATED BY TARGETED DNA SEQUENCING

Introduction/Background About 80% of patients with epithelial ovarian cancer (EOC) relapse in the first 2 years from diagnosis. Data on treatments after the second line are poor and based on small retrospective studies. Despite benefits after the third line are unclear, some patients are heavily treated with increased toxicities and hospitalization. Aim of the study is to investigate survival outcomes of EOC patients treated with ≥ three chemotherapy lines and to identify predictive factors of response to treatments, in order to adequately select patients who could benefit from subsequent chemotherapy lines.

Methodology Recurrent EOC patients received ≥ three lines of chemotherapy at Mauriziano Hospital of Turin between 2016 and 2022 were retrospectively analyzed. Progression-free survival (PFS) and overall survival (OS) were assessed according to chemotherapy lines. Prognostic factors associated with chemotherapy responses were investigated.

Results 68 patients and 180 lines of treatment were evaluated. OS progressively decreased with subsequent chemotherapy lines from 17 to 8 months, while PFS was not resistance. This study aimed to provide target DNA sequencing of 144 genes with potential involvement in resistance of EOC in surgically resected patients. Results were associated with clinical data and survival and validated using data from the whole exome sequencing (WES) and databases.

Methodology Target DNA sequencing of 144 gene panel in 48 pairs of EOC tumor and blood samples. The examined preselected 144 target gene panel was composed of the most important oncodriver genes in EOC, interacting genes as well as genes associated with the risk of EOC and resistance development. Comparison with WES of the next 50 blood and tumor tissue sample pairs, evaluation of platinum resistance status, and complete follow up. Validation of crucial variants using TCGA and GENIE datasets.

Results Germline genetic profile revealed as the most mutated genes RAD51B (20%), BRCA1/2 (14/9%) a DNH14 (11%). Analysis of somatic variants revealed as the most mutated genes TP53 (98%), CSMD1/2/3 (19/21/35%), and CFTR (23%). Mutation exclusivity was found for germline variants in RAD51B (p=0.002), BRCA1 (0.015) and DNH14 (0.036) and somatic variants in TP53. High TP53 mutation rate in patients with high grade serous ovarian carcinoma was confirmed by WES and TCGA and/or GENIE datasets analysis. In contrast to WES, TP53 splicing mutations were covered to a higher extent by targeted sequencing.

Conclusion Taken together, we assessed specific germline and somatic profiles of EOC patients using targeted DNA sequencing with potential to be associated with sensitivity to therapy especially in TP53 gene regions.

Disclosures This study was supported by running projects of the Czech Health Research Council grant no. NU20-09-00174 and Cooperatio program no. 207035, ‘Maternal and Childhood Care’ by 3rd Faculty Medicine, Charles University.
significantly reduced after third recurrence (p = 0.558). Patients who received more lines of chemotherapy had better OS (p = 0.018). In the multivariate analysis adjusted for clinicopathologic factors, platinum-sensitivity > 12 months and the administration of ≥ three lines of treatment were independent prognostic factors for OS (p < 0.0001 and p = 0.002, respectively), while ECOG and rechallenge with platinum for PFS (p = 0.02 and p = 0.0009, respectively). In the multivariate analysis according to single line of therapy, platinum-sensitivity (p = 0.013), platinum rechallenge (p = 0.016) and maintenance treatment (p = 0.005) resulted associated with better PFS at the second recurrence and maintenance therapy preserved its prognostic value up to fourth line (p = 0.015).

Conclusion Platinum-sensitivity and receiving ≥ three lines of treatment are independent prognostic factors for OS. Platinum-sensitivity, platinum rechallenge and maintenance therapy are associated with improved PFS in third line; maintenance therapy remains an independent prognostic factor even in subsequent treatments.

Disclosures The authors declare that there are no conflicts of interest.

#646 GENE EXPRESSION OF MEMBRANE TRANSPORTERS: IMPORTANCE FOR PROGNOSIS AND PROGRESSION OF OVARIAN CARCINOMA

1,2Martin Hruda*, 3Katerina Elsonová, 5Beatrice Mohelníková Duchonová, 6Ela Cerovská, 3,4Marie Ehrlichová, 3Ivan Gut, 1,2Lukáš Skapa, 3,6Radka Václavíková. 1University Hospital Královské Vinohrady, Prague, Czech Republic; 2Third Faculty of Medicine, Charles University, Prague, Czech Republic; 3Toxicogenomics Unit, National Institute of Public Health, Prague, Czech Republic; 4Biomedical Center, Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic; 5Pálacký University and University Hospital Olomouc, Olomouc, Czech Republic; 6Faculty of Science, Charles University, Prague, Czech Republic; 7University Hospital Motol, Prague, Czech Republic; 8Faculty of Medicine and University Hospital in Pilsen, Pilsen, Czech Republic; 9Department of the Molecular Biology of Cancer, Institute of Experimental Medicine, Academy of Science, Prague, Czech Republic

Abstracts

Introduction/Background Membrane transporter proteins (for example ABC, SLC and ATPases) take part in oncogenesis and the formation of chemoresistance, however the interpretation of their importance in ovarian cancer prognosis is still limited.

Methodology Gene expression profiling was performed on 39 ABC and 12 SLC transporters and 3 ATPases in epithelial ovarian cancer (EOC) tissues and the results were assessed with respect to prognosis and clinical presentation of EOC patients. In a cohort of tissues with primary EOC (n = 57) and control tissues (n = 14) we assessed relative expression of genes and compared it with the clinical and survival information. The data was verified on a separate cohort (n = 60).

Results 6 ABC genes and the SLC22A18 gene were considerably over-expressed in the cancer tissues in comparison with control tissues and the expression of 12 ABC genes, 5 SLC genes, ATP7A, ATP1B1 was reduced. The expression of ABCA12, ABCC3, ABCG6, ABCD3, ABCG1, SLC22A5 genes was greater in HGSC in comparison with other types. Expression of ABCA2 was considerably related to tumour grade in both cohorts. Particularly, the expression levels of ABCA9, ABCA10, ABCC9 and SLCL16A14 were considerably related to PFS in both pilot and verification groups. ABCG2 level was related to PFS in the grouped patient cohort.

Conclusion The genes ABCA2, ABCA9, ABCA10, ABCG2 and SLCL16A14 represent new potential markers of epithelial ovarian cancer progression and collectively with the discovered association between the expression of ABCA12, ABCC3, ABCC6, ABCD3, ABCG1, SLC22A5 and HGSC they should be investigated more extensively in future studies.

Disclosures This study was supported by running projects of the Czech Health Research Council grant no. NU22-08-00186 and Cooperatio program no. 207035, ‘Maternal and Childhood Care’ by 3rd Faculty Medicine, Charles University.

#676 PROGNOSTIC VALUE OF IMMUNE INFILTRATE IN HIGH-GRADE SEROUS OVARIAN CARCINOMA ACCORDING TO PLATINUM-SENSITIVITY/RESISTANCE STATUS

1Marie Gabrielle Courtès*, 2Isabelle Treilleux, 3José Sandoval, 4Laura Salabert, 5Pierre Meeus, 6Nicolas Chopin, 7Camille Chakiba, 8Nathalie Bendriss-Vermare, 9Isabelle Ray-Coquard, 10Sabrina Croce, 11Sana Intidhar Labidi Galy, 12Olivier Tredan. 1HUG, Geneva, Switzerland; 2Centre Léon Bérard, Lyon, France; 3Institut Bergonié, Bordeaux, France; 4INSERM, Bordeaux, France

Abstracts

Introduction/Background Although the prognostic value of immune infiltrate has been extensively explored in HGSOC, very few studies explored it according to platinum-sensitivity/resistance status, an important factor for stratifying subsequent therapy.

Methodology Here, we questioned the prognostic value of 5 immune cell subsets (CD3+ and CD8+ T cells, FoxP3+ regulatory T cells, CD68+ and CD163+ tumor-associated macrophages) identified by immunohistochemistry in high-grade serous ovarian carcinoma using a clinically annotated tissue-microarray of 134 tumor samples.

Results We found that high intra-epithelial CD3+ T cell in tumor core was significantly associated with prolonged OS in all patients (HR=0.53; 95% CI [0.3–0.88]; p = 0.03), and those who had platinum-sensitive disease (HR=0.51; 95% CI [0.27–0.94]; p = 0.03). Similarly, a high density of CD68+ TAMs in tumor core was significantly associated with better OS in all patients (HR=0.49; 95% CI [0.27–0.91]; p = 0.02), and those who had platinum-sensitive disease (HR=0.46; 95% CI [0.24–0.89]; p = 0.02). Unexpectedly, there was a trend toward better survival in platinum-resistant patients who had stromal accumulation of FoxP3+ Treg (HR=0.27; 95% CI [0.06–1.15]; p = 0.08).

Conclusion A deeper spatial and phenotypical characterization of tumor immune microenvironment in HGSOC according to platinum-sensitivity/resistance status is warranted for tailoring precision immunotherapy in this deadly disease.

Disclosures Together, our findings suggest that the prognostic value of immune infiltrate in HGSOC differs according to platinum-sensitivity/resistance status.