

3. Kasper, B., P. Strobel, and P. Hohenberger, Desmoid tumors: clinical features and treatment options for advanced disease. *Oncologist*, 2011. 16(5): p. 682–93.

Prevalence of benign findings in female genital tract in women with endometrial cancer.

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INTRODUCTION

Endometrial cancer is the most common gynecological malignancy in developed countries [1]. Therefore, we investigated incidence of benign findings in genital tract of these patients.

AIM

The aim of this study was to analyze prevalence of benign pathological changes in uterus and ovaries in women with endometrial cancer.

METHODS

The study is a retrospective analysis based on anonymous data from The University Hospital in Kraków. Endometrial cancer (EC) patients encountered between 2009 and 2019 were identified from pathology records. We determined the presence of benign pathological changes in uterus body (adenomyosis and leiomyomata), cervix (cervicitis, metaplasia, dysplasia, ovula Nabothi) and ovaries (endometriosis). 524 patients were included in the analysis.

RESULTS

Median age of patients was 61 with interquartile range 14. The most common condition coexisting with EC were leiomyomata – 318 cases (60,69%). The coincidence of adenomyosis or endometriosis with EC was confirmed in 86 (16,41%) and 80 (15,27%) cases respectively.

Concerning cervix pathologies: cervicitis was diagnosed in 67 (12,62%), cervical intraepithelial neoplasia (CIN) in 33 (6,30%) and metaplasia in 29 (5,53%) cases subsequently. Cancerous infiltration of the cervix was confirmed in 71 cases (13,55%) - mostly diagnosed as stage II according to FIGO classification: 47 cases (66,20%), but also present in 24 (33,80%) stage III cases. The vast majority of patients 329 (62,79%) had the cervix free of abnormalities.

CONCLUSION

The analysis showed that the incidences of leiomyomata and adenomyosis among women with endometrial cancer are slightly lower compared to white women general population [2,3]. On the contrary, the incidence of endometriosis in the study group was comparable to general population as well as CIN [4,5]. Further investigations are needed to clarify the influence of the benign changes in female genital tract on clinical and pathological features of the endometrial cancer.

References:

1. Banas T, Juszczyk G, Pitynski K, Nieweglowska D, Ludwin A, Czerw A. Incidence and mortality rates in breast, corpus uteri, and ovarian cancers in Poland (1980–2013): an analysis of population-based data in relation socio-economic changes. *OncoTargets and Therapy*. 2016, 9:4121-4127.

2. Stewart EA, Cookson C, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. *BJOG*. 2017; 124: 1501–1512.

3. Vercellini P, Viganò P, Somigliana E, Daguati R, Abbiati A, Fedele L. Adenomyosis: epidemiological factors. *Best Pract Res Clin Obstet Gynaecol*. 2006; 20: 465–477.

4. Basta A, Brucka A, Górski J, Kotarski J, Kulig B, Oszukowski P, Poreba R, Radowicki S, Radwan J, Sikora J, Skret A, Skrzypczak J, Szyłło K, Polish Gynecologic Society Experts Group. The statement of Polish Society's Experts Group concerning diagnostics and methods of endometriosis treatment. *Ginekol Pol*. 2012; 83: 871–876.

5. Macdonald M, Crossley J, Ellis K, Dudding N, Lyon R, Smith JHF, Tidy JA, Palmer JE. Prevalence of high-grade cervical intraepithelial neoplasia in women with persistent high-risk HPV genotypes and negative cytology. *Cytopathology* 2018; 29: 133–142.

A role of radiotherapy for adrenal gland metastases – a single institution experience.

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INTRODUCTION

Adrenal glands are often the metastatic site of various cancers. Radiotherapy (RT) techniques such as stereotactic body radiation therapy (SBRT) and motion-management methods could be new promising modalities in this indication.

AIM

The aim of the study was to assess the effectiveness of RT in the management of patients with adrenal metastases.

METHODS

The study group was a retrospective cohort of patients who received RT for adrenal metastases in our institute between 2013–2019. The following parameters were analyzed: indication for RT, pathology of primary tumor, radiotherapy technique, total dose (TD), equivalent 2-Gy dose (EQD2), dose per fraction (FD), early and late tolerance, local response (LR), progression free survival (PFS). Toxicity was assessed using Common Terminology Criteria for Adverse Events v4.0.

RESULTS

Totally n=40 patients were found. Two patients were irradiated sequentially to both glands with at least two months interval, thus n=42 RTs were analyzed. The indications for RT were: oligometastases (n=12), oligoprogression (n=27), palliative (n=3). The most common diagnoses were: melanoma (n=21) and lung cancer (n=12). The following RT techniques were used: 3D-conformal (n=8), IMRT/VMAT (n=10), SBRT (n=24). In n=27 patients motion-management were used. FD varied from 2 to 12 Gy, and TD from 20 to 50 Gy. EQD2 varied from 23 to 116 Gy. Acute grade 2 toxicities were observed in two patients. No significant late toxicity was observed.

RT allowed to obtain complete response in two patients, partial response in 15 patients, stable disease in 14 patients and progressive disease in three patients. In eight patients, data regarding LR were not available. In-field progression at any time occurred in nine patients. PFS was 6 months (2–8).

CONCLUSION

Modern RT allowed for high LR with good treatment tolerance in patients with adrenal gland metastases.

FOXO3-REST Axis: a Therapeutic Target for Medulloblastoma?

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INTRODUCTION

Medulloblastoma has poor outcome due also to adverse events caused by the treatment [1]. An improved anti-tumor strategy is needed to enhance patient survival rate. REST is a transcription factor overexpressed in medulloblastoma cells and it's associated with the formation of this brain tumor and the low survival rate, suggesting an oncogenic role [2][3].

AIM

Resveratrol is able to reduce REST expression and the transcription factor FOXO3 could be an intermediate, since FOXO binding sites are present in REST promoter and its activity can be modulated through acetylation status modification [4][5]. Based on this, the aims of this study were to confirm the resveratrol-induced REST reduction, understand the engagement of FOXO3 in this mechanism and verify if resveratrol can also modulate FOXO3 expression.

METHODS

DAOY cells were transfected with siRNA against FOXO3 for 48 hours to study the modulation of REST expression. Moreover, DAOY cells were treated with resveratrol, at three concentrations (100 micromolar, 200 micromolar and 400 micromolar) and at three timepoints (24 h, 48 h and 72 h), to evaluate the expression of both transcription factors.

RESULTS

Transfected cells demonstrated a significant decrease of FOXO3 protein levels. On the other hand, these cells demonstrated a substantial increase of REST expression. Furthermore, resveratrol-treated cells demonstrated a significant decrease of REST and FOXO3 protein levels in a dose-dependent manner, in two timepoints. In turn, these cells demonstrated a noteworthy decreased of REST mRNA levels in a dose-dependent manner, in all timepoints.

CONCLUSION

According to this study, resveratrol was able to significantly decrease FOXO3 and REST protein levels. It's important to study the role of resveratrol in FOXO3 transcription, to confirm that both transcription factors are downregulated at mRNA level. Future perspectives will also include studies to evaluate that FOXO3 could bind REST promoter and the consequent effect on its expression, and the role of REST in FOXO3 expression.

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References:

1. Ribi, K., Rely, C., Landolt, M., Alber, F., Boltshauser, E., & Grozzer, M. (2006). Outcome of Medulloblastoma in Children: Long-Term Complications and Quality of Life. *Neuropediatrics*, 36, 357–365. <https://doi.org/10.1055/s-2005-872880>
2. Lawinger, P., Venugopal, R., Guo, Z. S., Immaneni, A., Senguita, D., Lu, W., . . . Majumder, S. (2000). The neuronal repressor REST/NRSF is an essential regulator in medulloblastoma cells. *Nature Medicine*, 6(7), 826–831. <https://doi.org/10.1038/77565>
3. Taylor, P., Fangusaro, J., Rajaram, V., Goldman, S., Irene, B., Macdonald, T., . . . Gopalakrishnan, V. (2012). REST is a Novel Prognostic Factor and Therapeutic Target for Medulloblastoma. *Molecular Cancer Therapeutics*, 11(8), 1713–1723. <https://doi.org/10.1158/1535-7163.MCT-11-0990>

4. Brunet, A., Sweeney, L. B., Sturgill, J. F., Chua, K. F., Greer, P. L., Lin, Y., . . . Greenberg, M. E. (2004). Stress-Dependent Regulation of FOXO Transcription Factors by the SIRT1 Deacetylase. *Science*, 303(5666), 2011 LP – 2015. <https://doi.org/10.1126/science.1094637>

5. Guida, N., Laudati, G., Anzilotti, S., Secondo, A., Montuori, P., Renzo, G., . . . Formisano, L. (2015). Resveratrol Via Sirtuin-1 Downregulates RE1-Silencing Transcription Factor (REST) Expression Preventing PCB-95-Induced Neuronal Cell Death. *Toxicology and Applied Pharmacology*, 288. <https://doi.org/10.1016/j.taap.2015.08.010>

Volatile exometabolome profiling of human renal cell carcinoma cell lines for biomarker discovery

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INTRODUCTION

Renal Cell Carcinoma (RCC) constitutes approximately 90–95% of all kidney neoplasms and is the second most lethal urological cancer. Current diagnostic techniques rely on imaging techniques and an invasive procedure (biopsy) is always required for histopathologic confirmation of malignancy. For these reasons, the identification of accurate biomarkers to develop faster, less invasive and more sophisticated diagnostic techniques is of utmost importance. Metabolomics has been widely applied in cancer biomarker discovery arising from the fact that cancer cells are metabolically reprogrammed to control the energy required by the rapid growth and development of the tumor, producing a specific “metabolic signature”.

AIM

To evaluate the potential of volatile organic compounds (VOCs) and volatile carbonyl compounds (VCCs) to discriminate the exometabolome of RCC from non-tumoral cell lines, and two different histological subtypes (clear cell and papillary RCC) in both metastatic and non-metastatic stages.

METHODS

Headspace-solid phase microextraction/gas chromatography-mass spectrometry (HS-SPME/GC-MS)-based metabolomics was applied for the volatile profiling of culture medium of five different tumoral cell lines, namely three clear cell (769-P, 786-O and Caki-1) and two papillary RCC (Caki-2 and ACHN), and one non-tumoral cell line (HK-2).

RESULTS

Multivariate and univariate analysis unveiled a panel of metabolites responsible for the discrimination between each RCC cell line vs. non-tumoral cells, metastatic vs. non-metastatic and clear cell vs. papillary RCC cell lines, mostly belonging to alcohols, aldehydes, alkanes and ketones classes. Some metabolites were found similarly altered for all RCC cell lines compared