Abstracts

Objectives There is no established screening strategy for Lynch syndrome (LS) in synchronous endometrial (EC) and ovarian cancers (OC). Most centers use mismatch repair (MMR) immunohistochemistry (IHC) on endometrium only. We aim to examine the concordance in MMR expression between tumor sites in synchronous EC/OC.

Methods Thirty women with newly diagnosed synchronous EC/OC were prospectively recruited from three cancer centers in Ontario, Canada. Tumor sites were assessed for MMR deficiency by IHC and MSI testing. All women underwent germline testing for MMR mutations.

Results Out of 30 cases, twelve cases (40%) were either MMRd or MSI-H, with 5 (17%) confirmed to have a pathogenic germline mutation: 3 MSH6, 1 MLH1 and 1 PMS2. MMR testing by IHC took place in both ovary and endometrium in 27 cases and results were discordant between two sites in 2 cases (7%). MSI testing in both sites took place in 24 cases, and results were discordant in 2 cases (8%). Out of the 5 cases with confirmed LS, performing IHC alone on endometrium would have missed the diagnosis in 1 case, and performing MSI testing alone on endometrium would have missed the diagnosis in 3 cases, which all had a MSH6 mutation. One case of LS was missed by both IHC and MSI testing.

Conclusions The incidence of LS was high in women with synchronous EC/OC (17%). Given the discordance in IHC and MSI results at the two tumor sites, consideration should be given to direct germline testing in all cases of synchronous EC/OC.

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IMPACT OF MISMATCH REPAIR PROTEIN AND PD-L1 EXPRESSION FOR THERAPEUTIC STRATIFICATION IN JAPANESE OVARIAN CLEAR CELL CARCINOMA

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Objective Ovarian clear cell carcinoma (OCCC) is a rare type of epithelial ovarian cancer that behaves comparable to a distinct entity. Novel genomic and immunological profiling-based strategies targeting OCCC remain unavailable. ARID1A, which is one of the most frequently mutated genes in OCCC, could be a druggable target as well as a regulator of mismatch repair (MMR). Most of the mutated neoantigens in MMR-deficient cancers sensitize them to immune checkpoint blockade. However, the role and frequency of MMR deficiency in OCCC are still poorly understood. We aimed to evaluate the abnormal expression frequency of MMR and PD-L1 proteins in OCCC for identifying the effective OCCC population with immune checkpoint blockade.

Methods The study cohort comprised 113 patients with OCCC treated at a single institution. Protein expression levels in ARID1A, MLH1, PMS2, MSH2, MSH6, and PD-L1 were evaluated by immunohistochemistry (IHC). We investigated the correlations between immunoreactivity for MMR/PD-L1 and clinicopathological parameters including ARID1A status.

Results MMR proteins disappeared in two cases (1.8%), specifically those who had synchronous double cancer with endometrial carcinoma and a family history of Lynch syndrome-related tumor. PD-L1 expression was diffused in 17 cases (15.0%). The diffused PD-L1 expression was significantly associated with ARID1A expression loss ($p = 0.003$), but no other correlations existed between PD-L1 expression and clinical parameter.

Conclusions Although only few Japanese OCCC cases showed MMR deficiency as evaluated by IHC, immune checkpoint signals were activated even in MMR-intact OCCC, possibly through ARID1A interaction.

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INTRA-EPITHELIAL SPREADING OF CERVICAL SQUAMOUS CELL CARCINOMA TO THE UPPER GENITAL TRACT

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Abstract 266 Table 1 Clinical characteristics of cervical squamous cell carcinoma involving the upper genital tract

Case No.	Age	Menopause	Clinical presentation	TCT	Cervix tumor size (cm)	Clinical Stage	Treatment	Post operation treatment	Follow up (months)	Prognosis	Uterine apoplexis	Pre operation condition
1	72	Y	bleeding	NA	NED	IA1	TAH+BSO	NO	48	AOD	Y	
2	53	Y	NA	HSIL	NED	IA2	TAH+BSO	R	96	AOD	N	
3	41	N	bleeding	NA	2	IB1	TAH+BSO+LN	C+R	39	AOD	N	chemotherapy
4	63	Y	NA	NA	1	IB1	TAH+BSO+LN	NA	NA	AOD	NA	NA
5	59	Y	discharge	HSIL	2.2	IB1	TAH+BSO+LN	C+R	72	AOD	N	
6	60	Y	bleeding	NA	3.5	IB1	TAH+BSO+LN	C+R	75	AOD	Y	thyroid hypo function
7	59	Y	bleeding	HSIL	1.5	IB1	TAH+BSO+LN	C+R	75	AOD	N	PTC
8	48	N	bleeding	HSIL	2.5	IIA	TAH+BSO+LN	C+R	86	AOD	N	
9	55	Y	bleeding	ASC-H	NA	IIA	TAH+BSO+LN	C+R	22	DOD	N	chemotherapy
10	52	Y	bleeding	NA	5	IIIB	TAH+BSO+LN	C+R	71	AOD	Y	immune deficiency
11	46	N	bleeding	ASC-H	4	IIIB	TAH+BSO+LN	C+R	62	AOD	N	chemotherapy
12	56	Y	bleeding	NEG	1.5	IB1	TAH+BSO+LN	C+R	1	AOD	Y	N
13	54	Y	bleeding	HSIL	1	IB1	TAH+BSO+LN	C+R	12	AOD	N	
14	58	Y	bleeding	NA	NA	IA1	TAH+BSO	C+R	20	AOD	N	
15	50	Y	NO	HSIL	NED	0	TAH+BSO	C+R	54	AOD	Y	

NA, not available; HSIL, high-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells—cannot exclude high grade squamous intraepithelial lesion; TAH, total pelvic hysterectomy; BSO, bilateral salpingo-oophorectomy; LN, lymphadenectomy; C, chemotherapy; R, radiation therapy; AOD, alive without disease; AWD, alive with disease; PTC, papillary thyroid carcinoma.

This study was designed to describe the clinicopathological characteristics of cervical squamous cell carcinoma (SCC) intra epithelial spreading to the upper genital tract.

A total of fifteen patients were enrolled, including eleven patients which were cervical SCC spreading to the endometrium, four patients whose squamous cell carcinoma intra epithelial spread along the uterine cavity to the adnexa. Clinical information and pathological data were collected. Human high risk HPV was detected by mRNA in situ hybridization.

The average age was 55.07 years old. Twelve of the fifteen patients were post menopause women. The intra epithelial spread pattern can be seen in thirteen patients. Five of the fourteen patients received a uterine apoxesis, the other pre operative condition including chemotherapy, papillary thyroid carcinoma, thyroid hypofunction, and immune deficiency. HPV was positive in all the patients' specimen, and the infection status of cervical lesions, endometrial lesions, and adnexal lesions were same. For the peculiar case twelve, the cervical CIS lesion intra epithelial spread along the mucosa of uterine cavity and fallopian tube, and invasive SCC can be identified in the uterine corpus, fallopian tubes and ovaries.

Intra epithelial spread pattern is an indolent spreading pathway of the cervical SCC, it can involve the upper uterine tract even when the cervical lesion is at a very early stage, such as CIS. The deepest invasion site may not be the primary site. The intra epithelial spread may have relationship with pre operative disposal. High risk HPV detection can help to confirm the cervical origination.

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HISTOPATHOLOGIC ULTRASTAGING OF SENTINEL LYMPH NODES IN ENDOMETRIAL CARCINOMA: A RETROSPECTIVE ANALYSIS OF THE TUEBINGEN WOMEN'S HOSPITAL 2006-2016 PATIENT COHORT

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Introduction Lymph node metastases are considered a major risk factor in endometrial carcinoma patient management and nodal assessment is an integral part of staging. While still under investigation sentinel node biopsy has been established in many centers. It has been shown that histopathologic ultrastaging leads to an increased detection of isolated tumor cells (ITC) and micrometastases (MIC). However, the clinical impact of ITC and MIC is not yet clearly defined. The aim of this study was to retrospectively perform histopathologic ultrastaging in a large series of endometrial carcinoma patients all of which have been treated at the Tuebingen University Women's Hospital.

Method Patients with sentinel node biopsy during endometrial carcinoma surgery were identified. All cases with negative sentinel nodes, were submitted to retrospective histopathologic ultrastaging (5 × 100µm intervals followed by 500µm sections

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