ISP-6-11 A Case Report of Combined Large Cell Neuroendocrine Carcinoma and Endometrioid Carcinoma of the Endometrium：Shared Gene Mutation Signature between the Two Histologic Components

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[Case report] A 61-year-old Japanese woman was diagnosed with FIGO Stage IB endometrial cancer with combined with Grade1 EC and LCNEC. The metastasis of lymph nodes in right bronchopulmonary area, mediastinum and brain were also found. Finally, she developed pleuritis and epicarditis carcinomatosa and died of cancer 51 months after the surgery. [Background] Gene alterations in uterine NE-carcinomas are still not understood. We examined gene alterations in the mutation-hotsopts of selected 50 cancer-associated genes. [Results] The EC and LCNEC components shared identical alterations in PTEN, PIK3CA and FGFR3. PTEN alteration was almost homozygous R130G missense single-base substitution (SBS). PIK 3CA was heterozygous for a missense SBS resulted in R88Q. Only the EC contained another missense heterozygous SBS on FGFR3 resulted in A374T. Both the EC and LCNEC components had heterozygous SBS on CTNNB1, but the EC contained G34R whereas the LCNEC contained T41A. In addition, both components had unique mutations each other, but with low allele frequency estimated less than 5%. The EC contained a H83Y mutation on CDKN2A and a T41A mutation on CTNNB1. On the other hand, the LCNEC had a R140W mutation on IDH2. [Conclusions] The gene mutation signature strongly supported the idea that the two components derived from a common precursor lesion or the LCNEC was originated from the pre-existing EC.

ISP-6-12 Endometrial Metastasis from Primary Rectal Carcinoma

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[Introduction] Metastases to the uterine endometrium from an extra genital site are a rare event. As in primary endometrial carcinoma, abnormal uterine bleeding is the most common symptom of such metastases. The misdiagnosis of another original cancer as a primary endometrial carcinoma should be avoided. Here we report a case of endometrial metastasis from a primary rectal carcinoma. [Case] A 63-year-old Japanese woman was admitted to our hospital with postmenopausal abnormal uterine bleeding. Endometrial cytology revealed an adenocarcinoma. Endometrial sampling showed multiple fragments of proliferative endometrial tissue mixed with irregular glands lined by atypical cells with elongated, hyperchromatic nuclei and solid sheets of neoplastic cells. The neoplastic glands were positive for CDX2 and CK20 and negative for CK7. The tumor was histologically diagnosed as metastatic endometrial carcinoma originating in the rectum. The endometrial metastasis was treated solely by tumor removal. [Discussion] Although rare, extra genital sites should be considered as possible primary sites of metastatic endometrial carcinoma. In addition to the clinical history, a thorough histological examination including immunohistological staining is necessary to diagnose metastatic carcinoma.

ISP-7-1 MicroRNA let-7c contributes to acquired resistance to paclitaxel in endometrial serous carcinoma

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[Objective] Endometrial serous carcinoma (ESC) is a rare phenotype of endometrial carcinoma known for the poorest prognosis in gynecological cancers. One of the reasons of miserable clinical course of ESC is acquired chemo-resistance, because there are few choices of chemo-agent. Thus, the objective of this study is to investigate mechanisms of paclitaxel resistance from the aspect of microRNA (miRNA). [Methods] ESC cell line USPC1 and paclitaxel (PTX) resistant cell line (USPC 1/PTX-R) derived in our laboratory were used. Expression of let-7c was examined by qRT-PCR in drug resistant cells and compared with their parental cell. Alteration of drug-resistance was analyzed after let-7c precursor transfection. Moreover we searched for the possible target of let-7c including HMGA2, Bcl-xl and other candidate. [Results] The expression of let-7c was decreased in USPC1/PTX-R. After let-7c precursor transfection to USPC1/PTX-R, the decreased resistance for PTX was observed compared with negative control. [Conclusion] Let-7c contributes to acquired resistance to PTX in ESC.