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Incidental tubal endometrioid adenocarcinoma – case report

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Summary

The fallopian tubes represent a highly important structure for ovarian carcinogenesis. They provide the passage of eutopic endometrium from the uterus, as well as metastatic cells from the ovaries. A direct source of tumor cells for ovarian cancer was also recently confirmed in the fallopian tubes. The authors present a case report of an incidental tubal endometrioid carcinoma with the coexistence of adenomyosis.

Key words: Fallopian tubes; Endometrioid carcinoma; Adenomyosis.

Introduction

The ovary has the largest number of tumor types in the human body. Recently, several of studies have confirmed the fallopian tubes as a site of origin for ovarian cancer [1-3]. Serous tubal intraepithelial carcinoma (STIC) arising due to oxidative stress was defined as a potential precursor of type II ovarian carcinoma. Competitively, ovarian cortical inclusion cysts (CIC) were described as an ovarian precursor for type II ovarian carcinoma. As the precursor of type I, ovarian carcinomas papillary tubal hyperplasia (PTH) and endometriosis were confirmed [4]. While PTH appears to have a tubal origin with clusters of bland epithelium and small papillae [5], endometriosis derives from the uterus. Endometriosis has the unique status of being a benign metastatic disease. Although ectopic endometrium has been known since 1927 to be the precursor of ovarian cancer, the background of malignant transformation still remains unexplained. More recently, the criteria for endometriosis associated ovarian carcinoma, including mainly endometrioid carcinoma (EC) and clear cell ovarian carcinoma (CCOC) were established. Studies comparing patients with typical epithelial ovarian cancer with endometriosis associated ovarian cancer demonstrated that the patients with the latter disease strongly differ in both biological and histological characteristics [6]. The presence of endometrial tissue in the fallopian tube can be explained either by retrograde menstruation or metaplasia of the tubal epithelium. The coexistence of uterine pathology such as adenomyosis accompanying tubal or ovarian cancer is not yet sufficiently described. This paper reports a rare case of incidental endometrioid carcinoma located in the fallopian tube of a patient with adenomyosis.

Case Report

A 47-year-old gravida 2, para 2, unemployed, smoker (five cigarettes daily) and with irregular menstrual cycles (21-28/5) was admitted to the hospital on December 11, 2013 with permanent vaginal bleeding and secondary anaemia. The family history was free of cancer. The patient had undergone strumectomy in 2006 and had substitution therapy thereafter.

From gynecological anamnesis: Cone biopsy had been performed in 1996 because of high-grade dysplasia. In 2013 curettage had been performed twice (February and October) due to vaginal bleeding with a pathological finding of dysfunctional hyperplastic endometrium. After the above procedures the patient denied any complaints. Recurrent period of vaginal bleeding occurred at the beginning of December 2013 and curettage was again performed with similar pathological result as mentioned above. Gynecological ultrasonography showed normal pelvic finding with only a two-cm myoma of posterior uterine wall and suspicion of adenomyosis. Abdominal ultrasonography excluded any other abdominal pathology. Chest X-ray appeared normal. Secondary anemia with a haemoglobin of 83 g/l indicated two transfusions before operation and the patient underwent operation on December 12, 2013 with preoperative haemoglobin of 97 g/l. All other preoperative parameters including hemograme, biochemistry, and coagulation parameters were within their reference ranges.

Surgical intervention was performed through the Pfannenstiel laparotomy. The slightly enlarged uterus with a posterior wall myoma was removed. Thereafter, due to three small ovarian cysts (5-10 mm) left adnexectomy was performed. The operation concluded after a right salpingectomy. The postoperative period for the patient was without any complications with a haemoglobin 90 g/l. The patient was discharged from the hospital on postoperative day number five. After the result of pathology, the patient was referred to the oncological institute for the next treatment.

Pathological findings

The right fallopian tube had some physiological findings. Leiomyoma (3x3 cm) was found in the uterus as well as a six-cm area of adenomyosis. The remaining results of the uterus were without any pathological findings. The left ovary showed three

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small simple cysts and normal ovarian tissue. In the left fallopian tube, endometrioid adenocarcinoma was confirmed. Incidental lesion of endometroid adenocarcinoma with three-mm diameter, grade 2 was seen in the infundibulum of the uterine tube. Tumor cells with polypoid appearance were facing the tubal lumen without invasion in the muscular layer, as well as angioinvasion. There were no cells of atypical endometriosis confirmed in the fallopian tube.

Discussion

Nowadays, in regards to ovarian carcinogenesis, the fallopian tubes represent a unique, frequently discussed structure. The conventional view of ovarian cancer development attributes a role to CIC in ovarian surface epithelium (OSE). CIC are thought to arise after invagination of the OSE and the theory is based on a number of events associated with ovulation. Rupture of the OSE during ovulation leads to recurrent trauma and repair that is associated with DNA damage which may finally result in neoplastic transformation. This theory is supported by the fact that the decrease in ovulation (parity, oral contraceptive use) is connected with a significant risk reduction of ovarian carcinogenesis [4]. On the other hand ovulation is also associated by the theory of ovarian cancer development from STIC. In 2003, Piek *et al.* hypothesized that certain types of ovarian cancer might originate from the tubal epithelium [7]. Oxidative stress supports DNA damage as a consequence of ovulation as well as DNA damage to tubal epithelium leading to the formation of STIC. These cells are then detached and implanted on ovarian and peritoneal surfaces. The ovarian microenvironment is more favourable to tumor development compared to tubal tissue. Thus, the tumor enlarges in the ovary and appears to be a primary ovarian cancer rather than a tubal cancer [4]. STIC cells were diagnosed in 4-17% of females with BRCA mutations at the time of their risk-reducing surgery. In addition, the rate of STIC in patients with serous tumors was 59%, with no STIC identified in mucinous, endometrioid, or carcinosarcoma histology [8, 9]. Based on reported data, the junction between tubal epithelium and OSE is considered to be a potential site of carcinogenesis, since the gastroesophageal or anorectal junctions are well recognized. Both theories clarify the formation of type II ovarian carcinomas. Tubo-ovarial junction seemed to play a crucial role in the presented case. Incidental carcinoma that was found in the fallopian tube had a high probability of appearing clinically as an ovarian tumor after implantation of tumor cells on the ovarian surface.

Unlike high-grade serous carcinoma, type I ovarian carcinomas develop through multiple intermediate stages and based on recent studies, PTH was described as the precursor . PTH is defined as hyperplastic tubal epithelium forming small intraluminal buds (micropapillae) that can be implanted either on ovarian or peritoneal surfaces leading to atypical proliferative serous tumors, endosalpingiosis, and non-invasive implants. Implantation of PTH is most likely facilitated during ovulation. In low-grade ovarian serous tumors up to 91% of PTH was confirmed [5].

Endometriosis as a precursor, mainly of EC and CCOC was also confirmed. Generally, 10% of all ovarian cancer patients have coexisting endometriosis. This number increases to 40% in EC patients and 50%-90% in CCOC patients [4, 6]. At the opposite end of the spectrum, the incidence of EC and CCOC in 6,398 patients with endometriosis was reported to be 0.7% [2]. Retrograde menstruation, which is one of the main theories, is assumed to be the reason for cancer development in the presently studied patient. Endometrial cells from retrograde menstruation that have attached to the tubal epithelium were the source of the tumor cells. Endometriosis induces a local imbalance in cytokine milieu as well as changes in the hormonal milieu and increases the production of growth factors, similar changes to those observed in ovarian malignancy. Microenvironment plays another important role for tumorigenesis. Old blood through abundant amount of iron induces persistent oxidative stress resulting in DNA damages [2]. The study of Yamaguchi *et al.* confirmed a higher concentration of free ions in the endometriotic cysts compared to non-endometriotic cysts. The concentration of free ions in CCOC tissue was lower than in the endometriotic cyst but higher than in the non-endometriotic cyst [10]. Most of the studies described sequential development through multiple intermediate stages. Regarding those results, atypical endometriosis represents a subsequent step, with 23% incidence in EC and 36% in CCOC. Generally, in 8% of patients with endometriosis, an atypical variant was detected. Endometriosis-associated ovarian borderline tumors are well defined tumors representing a last step before endometriosis-associated ovarian tumors. Low incidence of endometriosis in listed stages is thought to be due to imprecise detection of endometriosis [11]. No intermediate stages were seen in studied histology. Tumor cells were without atypical endometriosis or any borderline tumor cells. Thus direct progression of benign cells was confirmed.

Coexistence of other gynecological diseases suggests that there is a similar genetic background. Up to 50% of women with ovarian EC will also have simultaneous endometrial adenocarcinoma and 2% - 8% of patients with endometrial adenocarcinoma will have a synchronous ovarian carcinoma. Adenomyosis can be found in coexistence with EC. Kucera *et al.* studied 219 patients and reported malignant changes in concurrent adenomyosis in 6.8% of the patients with early-stage endometrial cancer. Two pathways of carcinogenesis are possible. Either, de novo malignant transformation of adenomyotic foci with intact eutopic endometrium, or simultaneous changes of eutopic endometrium and adenomyosis [11-13]. Culton *et al.* reported 25% of patients with endometrioid endometrial adenocarcinoma with synchronous endometrioid tumor in the ovary and synchronous endometrial and fallopian tube en-

dometrioid type cancers [14]. In the present case, there was a coexistence of adenomyosis and thus, supporting the theory of endometriosis as a primary precursor. It is well known that only an interstitial portion of the fallopian tube may have endometrioid epithelium. Thus, endometroid epithelium located in the fimbrial part originates either from eutopic endometrium or represents the result of metaplasia of tubal epithelium to endometrioid type epithelium. Metaplasia can also be a source of tumorigenesis in the presented case, although the coexistence of adenomyosis predetermines endometriosis as a primary reason of cancerogenesis. Regardless of origin, the lesions are mostly localized on the fimbrial end of the fallopian tubes. Based on reported data, bilateral salpingectomy should be an integral part of non-oncological hysterectomy.

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