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Incidental Serous Tubal Intraepithelial Carcinoma Detected by a Surgery for Ectopic Pregnancy

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Abstract

Serous tubal intraepithelial carcinoma is a putative precursor of high-grade serous carcinoma, which is the most common histological type of ovarian or pelvic peritoneal cancer. Serous tubal intraepithelial carcinoma is commonly found in patients with breast cancer susceptibility gene mutations who undergo risk-reducing salpingo-oophorectomy. Incidental serous tubal intraepithelial carcinoma found by a non-prophylactic surgery is rare. A 33-year-old woman referred to our hospital for a diagnosis of ectopic pregnancy. She underwent a laparoscopic right salpingectomy. Pathologically, ectopic pregnancy in the ampulla of the right fallopian tube was confirmed and serous tubal intraepithelial carcinoma was observed in the fallopian tube. Subsequently, she underwent a laparoscopic hysterectomy, bilateral oophorectomy, and left salpingectomy as additional treatment. She has experienced no recurrence thus far for 37 months since the surgery.

Keywords

Serous Tubal Intraepithelial Carcinoma, Ectopic Pregnancy, Laparoscopic Surgery

1. Introduction

Serous tubal intraepithelial carcinoma (STIC) is a putative precursor of high-grade serous carcinoma (HGSC), which is the most common histological type of ovarian or pelvic peritoneal cancer. STIC is commonly found in patients with breast cancer susceptibility gene (BRCA) mutations who undergo risk-reducing salpingo-oophorectomy (RRSO). Incidental STIC found by a non-prophylactic surgery is rare. Here, we present a case of STIC incidentally found by a surgery

for an ectopic pregnancy.

2. Case Presentation

A 33-year-old woman, gravida 7 para 2 (5 artificial abortions and 2 vaginal labors), presented to a hospital complaining of irregular genital bleeding and lower abdominal pain, with a positive gestational test. She was suspected of having an ectopic pregnancy. She referred to our hospital for a diagnosis and surgery. She was in 5 weeks and 5 days of gestation, based on the date of her last menstrual period. She had no family history of cancer. Upon the first clinical examination, genital bleeding and lower abdominal tenderness with peritoneal irritation were present. Transvaginal sonography revealed a moderate to large intra-abdominal hemorrhage in the Douglas' pouch and a cystic region that appeared to be the gestational sac in the right fallopian tube. The results of biochemical blood examination were almost within normal limits, except for a lower hemoglobin concentration and elevated β human chorionic gonadotropin (1209.4 mIU/mL). Accordingly, she was diagnosed of having a right fallopian tube rupture due to ectopic pregnancy, and a laparoscopic right salpingectomy was performed. There were no significant intraoperative findings, except for the ectopic pregnancy. She was pathologically diagnosed with ectopic pregnancy at the ampulla of the right fallopian tube and STIC. We suggested either follow-up or additional treatment to the patient. She and her husband decided to undergo a total laparoscopic hysterectomy and bilateral salpingo-oophorectomy. During the surgery, cytology results of the peritoneal washings were negative for malignancy. There was no residual tumor pathologically in the uterus or adnexa. She has been followed up for recurrence by examining level of serum CA125 and using computed tomography. She received estrogen replacement therapy using estradiol transdermal gel (1 mg/day). At the time of this report, she has no evidence of disease 37 months after the surgery.

3. Pathological Findings

A rupture of the ampulla of the right fallopian tube was observed. Villi were present in the fallopian tube. In addition, epithelial tube thickness was partially increased. There was increased epithelial cell stratification, enlarged nuclei and nuclear rounding, and hyperchromasia (**Figure 1(a)**). Immunohistochemical staining was highly positive for MIB1 and p53 (**Figure 1(b)** and **Figure 1(c)**, respectively). The patient was diagnosed with ectopic pregnancy and STIC in the right fallopian tube.

4. Discussion

To our knowledge, there is no previous report of STIC discovered along with ectopic pregnancy. STIC may be precursor lesions of HGSC of the ovary or fallopian tube. RRSO in carriers of BRCA mutations or women with high risk of heredity breast and ovarian carcinoma (HBOC) is a choice to prevent ovarian

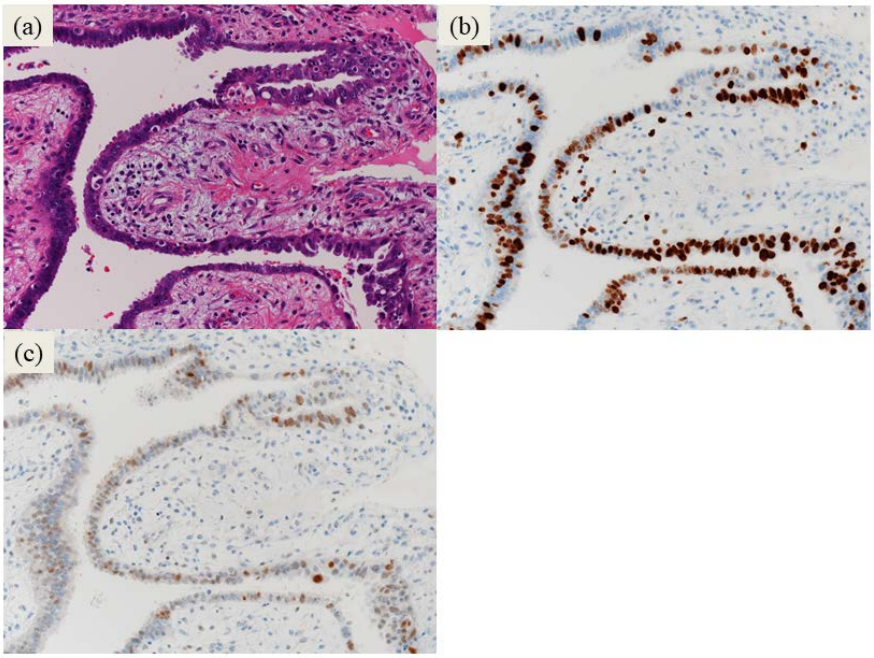

Figure 1. Microscopic findings of serous tubal intraepithelial carcinoma (STIC) in the fallopian tubal epithelium. (a) Hematoxylin and eosin staining. The STIC lesion stained (b) highly positive for MIB-1, and (c) p53.

and tubal cancers [1] [2]. Incidence of STIC was reported to be 0.6% - 6.0% in patients with BRCA1 or BRCA2 mutations who undergo RRSO and 1.0% - 1.6% in patients with strong family history [3]-[8]. Upon reviewing literature, STIC was detected in 27 of 952 cases (2.8%) of patients with BRCA mutations and 5 of 389 cases (1.3%) of patients with a family history of ovarian or breast cancer [3]-[8]. Among the patients with BRCA mutations or strong family histories who have undergone RRSO, the mean age at diagnosis of STIC was 53.0 - 54.3 years (range 39 - 77) [3] [4]. In our case, although she was not examined BRCA mutation status, she did not have a family history of ovarian or breast cancer. She was accidentally diagnosed as STIC at 33 years old.

There are no common criteria for absolute diagnosis of STIC. Currently, most STICs have been diagnosed using a combination of morphology and immunohistochemical analysis for p53 and Ki-67. Morphologic features of STIC include at least 1 mitotic figure, epithelial stratification (more than 2 cell layers), apoptotic bodies, nuclear enlargement and/or nuclear rounding, marked pleomorphism, abnormal chromatin and nuclear molding [9]. TP53 mutation is assumed when positive immunohistochemical staining for p53 is noted for more than 75% of cells or completely negative. Using a Ki-67 labeling index threshold of 10% to differentiate between STIC and normal fallopian tube epithelium, the sensitivity and specificity were 100% and 96.4%, respectively [10]. MIB-1 and Ki-67 labeling were used to diagnose this case. We diagnosed this case as STIC by the pathological findings of the morphology, TP53 mutation, and high Ki-67 labeling index.

There have been few reports of incidental STIC in patients unknown to carry BRCA mutations. In women with low risk of HBOC, the incidence of STIC was 4 in 522 cases (0.77%) [11]. Upon reviewing the literature, the median age at the time of diagnosis of incidental STIC by a surgery for benign disease was 61 years (range, 39 - 86 years), and only one of 44 cases was diagnosed among patients younger than 40 years old, while 5 of 44 cases were diagnosed in patients younger than 50 years old [11] [12] [13] [14]. The surgeries used to treat those patients included 35 bilateral salpingo-oophorectomies, 5 unilateral salpingo-oophorectomies, and 5 salpingectomies, with one case of both unilateral salpingo-oophorectomy and contralateral salpingectomy. Unilateral or bilateral adnexa persisted without additional treatment in only 4 of 44 cases [11] [12] [13] [14]. The conditions that were comorbid with STIC included 10 case of endometriosis, 5 ovarian serous borderline tumors, 4 ovarian serous benign tumors, 4 endometrioid endometrial cancers, 3 leiomyomas, 2 mature cystic teratomas, 2 endometrial hyperplasia, 2 non-gynecological cancers, 1 ovarian mucinous benign tumor, and 1 ovarian fibroma [11] [12] [13] [14]. Additional surgeries were performed in 6 patients with pure STIC at primary diagnosis, and 3 of those tumors were upstaged to HGSC [11] [12] [13] [14]. Wethington *et al.* reported that among cases of isolated STIC after RRSO, the benefit of surgical staging is minimal, and short-term (range, 16 - 44 months) clinical outcomes are favorable [4]. However, in our case, the patient underwent only a right salpingectomy. Very few cases of STIC treated without oophorectomy have been reported. It is still unclear whether an additional surgery is necessary in such cases. We provided the patient with enough available information, and she decided to undergo a total laparoscopic hysterectomy, left salpingectomy and bilateral oophorectomy. Fortunately, there was no residual tumor. However, she was in her 30s, and estrogen replacement therapy was needed.

In conclusion, this is the first report of STIC diagnosed in a patient with an ectopic pregnancy in her early 30s. STIC might cause dysfunction of the ciliated epithelium in the fallopian tube. Therefore, the fallopian tube of patients with ectopic pregnancy should be closely observed, even for patients with no family history of ovarian or breast cancer.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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