A BRCA-Negative Patient With Incidental Serous Tubal Intraepithelial Carcinoma

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ABSTRACT

Introduction: The incidence of STIC is increasing because of standardization of fallopian tube fimbria examination. We report a case of incidental STIC in a patient being treated for cervical dysplasia. A case report is presented with a review of the literature.

Case Description: This is a 46-year-old BRCA− patient who had repeated cervical intraepithelial neoplasia (CIN) type III and underwent robot-assisted total laparoscopic hysterectomy and bilateral salpingectomy, after a subsequent incidental finding of STIC. Laparoscopic surgical staging was completed and 18-month surveillance had been achieved at this writing.

Discussion: Incidental STIC in patients without genetic susceptibility to hereditary breast and ovarian cancer (HBOC) syndrome has been reported. Patients found to have an incidental STIC lesion should be considered for completion of surgical staging and surveillance and should be referred for BRCA1 or -2 mutation testing. A good outcome is likely.

Key Words: Risk reducing salpingectomy, Serous tubal intraepithelial carcinoma.

INTRODUCTION

Serous tubal intraepithelial carcinoma (STIC) is a precursor lesion of the fallopian tube that can lead to extraterine high-grade serous carcinoma.1 STIC is now present in 0.6 to 7% of fallopian tubes in bilateral salpingo-oophorectomy when performed as a risk-reducing procedure in women who are BRCA1 or -2 germline mutational carriers.2 STIC may also present incidentally in BRCA− patients in whom there is not a high threshold of clinical suspicion, given the lack of risk factors, with a reported incidence of 0.1% in women more than 50 years of age.3 We hereby present a case of an incidental finding of STIC in a patient who underwent a robot-assisted total laparoscopic hysterectomy and bilateral salpingectomy related to recurrent cervical intraepithelial neoplasia (CIN) type III on cone biopsy of the cervix with positive margins. Informed consent was obtained from the patient for reporting this case. The Institutional Review Board ruled that approval was not required.

CASE REPORT

A 46-year-old gravida 0 female patient presented with recurrent CIN III on a cone biopsy of the cervix, with positive margins. She had undergone multiple prior cone procedures and had a short cervix. The review of systems was unremarkable. She had a medical history of an unspecified platelet dysfunction with a few postoperative...
bleeding episodes after minor surgeries. She had no history suggestive of familial cancer. The case was reviewed at our multidisciplinary conference (MDC) and she was counseled about her options for treatment, including surveillance versus hysterectomy. She opted for a robot-assisted ovary-sparing total laparoscopic hysterectomy—bilateral salpingectomy. Salpingectomy was recommended as an elective prophylactic measure against fallopian tube and ovarian cancer. After the available evidence guidelines and recommendations were presented to her, she opted for the procedure.

The pathology report showed high-grade dysplasia of the cervix without carcinoma. The left fallopian tube showed focal STIC (Figures 1 and 2). The atypical cells showed overexpression of p53 (Figure 3) and increased labeling of Ki-67 (Figure 4). The right fallopian tube was unremarkable. The case was presented again at MDC, consultation obtained, and the available relevant literature reviewed. The patient was counseled again and agreed with the recommendation to undergo a laparoscopic bilateral oophorectomy, omentectomy, multiple biopsies, and washings. Preoperative workup included a CA125 tumor marker value, which was normal; and a computed tomographic (CT) scan of the chest abdomen and pelvis, which showed no evidence of metastatic disease. Genetic testing was ordered and returned negative results for hereditary breast and ovarian cancer syndrome (HBOC). All biopsies were negative for carcinoma or precursors. The patient received platelet transfusion before each surgery per hematology consultant recommendations, and both surgeries were uncomplicated.

Surveillance was instigated in the form of a review of systems, physical examination, and CA125 testing every 6 months. The patient remained without evidence of recurrent disease 18 months after diagnosis.

**DISCUSSION**

The incidental discovery of STIC or small tubal HGSC has been reported in patients who undergo salpingectomy for mostly benign reasons.\(^3\) This finding was established after complete systemic examination of fallopian tubes, including those from women with low risk of cancer—namely, those not suspected to have HBOC syndromes. As the number of elective bilateral salpingo-oophorectomy (BSO) or opportunistic salpingectomy without oophorectomy rises, intuitively there will be an expected rise in the incidence of STIC and small tubal HGSC, as more laboratories now routinely perform an extensive examination of the fallopian tube fimbria. Although STIC is generally reported in association with BRCA1 and -2 mutations, studies have documented an association of STIC with serous ovarian cancer, irrespective of BRCA1 or -2 mutation.\(^5\) Morphologic diagnosis of STIC requires 2 or more diagnostic features in 10 or more consecutive secretory cells in fallopian tube tissue. The diagnostic criteria for STIC have evolved and now include identifying p53 expression and proliferative indices, such as Ki-67.\(^6\)

In a recent case series, the outcomes of incidental fallopian tube HGSCs and STICs in women at low risk of hereditary breast and ovarian cancer were reviewed.\(^6\) Pa-
patients with known *BRCA* mutations, a hereditary cancer syndrome, or a positive personal or family history were excluded from the study. The term “incidental” was defined as identification of STIC or HGSC after removal of ovaries or fallopian tubes or both for reasons unrelated to HGSC, and HGSC was suspected neither clinically nor upon macroscopic examination of surgically obtained specimens. Patients either had STIC without invasive malignancies, STIC with invasive HGSC, or STIC with non-HGSC invasive malignancies. Patients in the case series initially presented with a variety of symptoms; however, no patient presented with abnormal cervical pathology, as was the case with our patient. Seven of the 18 patients with STIC had completion staging surgery (defined as total abdominal hysterectomy, omentectomy, and peritoneal washings), 3 were found to have HGSC. In addition, only 2 of the 9 patients with STIC who did not have invasive malignancies reported a completion staging surgery performed without additional disease identified. The case series concluded that completion staging surgery in informed patients, weighing the risks of a second surgical procedure, is a reasonable option for patients without *BRCA* who have been diagnosed with incidental STIC or HGSC. Although the case series was limited by the lack of information regarding the *BRCA* status of 15 of the 18 patients, the study findings retain clinical significance. The only other study in the literature reporting on outcome of STIC in *BRCA* mutation carriers concluded that the prognosis is favorable and the yield of surgical staging is low. Whereas peritoneal washings were the most common site of disease spread (15%), when lymph nodes were sampled (in 24% of their cohort), they were all negative.²

The role of *BRCA* screening is highly relevant, especially in patients in whom *BRCA* status is unknown. Knowing *BRCA* status clarifies the risk stratification of the patient, which results in earlier and more complete surgical interventions in high-risk versus low-risk patients. In addition, identification of *BRCA* carriers offers the option of further surveillance, risk-reducing surgery (ie, mastectomy), and identification of the need to test family members.

The natural history and most appropriate management of STIC lesions for both high- and low-risk patients, remains unknown, in part because of the rarity of such presentations, the heterogeneity of reported management, and the lack of long-term follow-up of patients with an incidental diagnosis of STIC. We appreciate, on the basis of the literature, that the short-term clinical outcome of isolated STIC in high-risk patients is favorable. Gynecologic oncologists should use the Pelvic–Ovarian Cancer Interception (POINT) Project (http://www.bwhpathology.org/POINT/point_purpose.aspx) to help build up the data collection and the science on this topic.

It remains to be clarified what the optimal extent of surgical staging is in isolated STIC cases such as ours. No benefit to lymph node dissection has heretofore been suggested. The role and efficacy of adjuvant chemotherapy and surveillance in this setting also remains unknown. We performed completion staging surgery consisting of laparoscopic bilateral oophorectomy, omentectomy, pelvic washings, and peritoneal biopsies immediately after the diagnosis of STIC. Our case highlights the management considerations that follow the diagnosis of incidental

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Figure 3. The atypical cells showed strong diffuse staining for expression of the tumor suppressor p53.

Figure 4. Increased labeling of Ki-67 indicates an increased proliferation index. No invasive component was seen.
STIC, and, with continued surveillance, we anticipate a favorable outcome.

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