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Incidental Serous Tubal Intraepithelial Carcinoma: A Case Report

Prachi Arun, Nikita Prasad *, Anu Sahjlan, Anjum Bhukal, Manika Yadav, Aditi Baghla

Department of Pathology, Maharaja Agrasen Medical College, Agroha, India

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ABSTRACT

High-grade pelvic serous carcinoma (HGSC) is the most common type of pelvic cancer among females. Serous tubal intraepithelial carcinoma (STIC) is an established precursor of HGSC, albeit rare and underdiagnosed. Its incidence ranges from <0.01% to 3% in BRCA carriers or those with a strong family history of breast or ovarian cancer. A 32-year-old P2L2 female underwent bilateral tubectomy for family planning, with no known family history of cancer. Histopathological examination of the fallopian tube revealed unilateral STIC. Incidental STIC mandates prolonged follow-up. Diagnosing tubal precursor lesions (such as SCOUT, STIL, STIC) to HGSC is crucial in identifying at-risk patients. The SEE-FIM protocol, along with a low immunohistochemistry threshold, is recommended. Due to its rarity and challenging diagnostic criteria, a high degree of suspicion on the part of pathologists and adequate follow-up are essential to reduce morbidity and mortality.

1. Introduction

Ovarian malignancies afflict approximately 2,00,000 women worldwide every year. It is the seventh leading cause of cancer-related deaths among women.^[1] Among these, high-grade serous carcinoma (HGSC) is the most common type of pelvic cancer in females and is responsible for most epithelial ovarian cancer-related deaths.^[2] Unfortunately, the majority are detected at an advanced stage, with a dismal prognosis. Research has altered our understanding of HGSC pathogenesis, which was previously thought to originate from the ovarian surface epithelium. The fallopian tube has now emerged as the site of origin of primary pelvic serous carcinomas (PPSC) detected in the fallopian tube, ovary, or peritoneum.^[3] A plethora of histologically identifiable "precursor" lesions in the fallopian tube have materialised, and include Secretory Cell Outgrowths (SCOUTs), p53 signature, Serous Tubal Intermediate Lesions (STILs), and Serous Tubal Intraepithelial Carcinoma (STIC).^[4] STIC is the earliest morphologically recognizable form of pelvic high-grade serous carcinoma, and arises in the distal fimbriated end of the fallopian tube. STIC is a rare pathological diagnosis in women undergoing salpingectomy for benign indications (<0.01%). A secretory cell lesion, characterized by cellular depolarization, an increased nuclear-to-cytoplasmic ratio, hyperchromasia, nuclear molding, prominent nucleoli, and mitotic figures, is present. Abnormal

immunohistochemical (IHC) staining of p53 and Ki-67 supports its diagnosis.^[5] In this report, we present a case of an isolated unilateral STIC incidentally found during benign gynaecologic surgery, along with a brief literature review.

2. Case Presentation

A 32-year-old P2L2 female presented to the Gynaecology OPD for family planning options. The patient had no significant medical or familial history of cancer. Pre-operative ultrasonography was unremarkable. A bilateral tubectomy specimen was sent to the histopathology lab. We received two tubal bits measuring 1.0 cm and 0.7 cm in length, respectively. On cut surfaces, both showed patent lumina. No other finding was discernible grossly. Microscopic sections from one tubal bit showed tumor cells partly replacing the mucosa. (Fig. 1) These cells exhibit a high N: C ratio, a high degree of pleomorphism, hyperchromasia, prominent nucleoli, and occasional mitotic activity. (Fig. 2) A complete lack of stromal invasion is noted. On IHC, these tumor cells are positive for p53 and Ki-67. (Fig. 3) A final histopathological diagnosis of Serous Tubal Intraepithelial Carcinoma (STIC) was given. However, the other tubal segment showed no pathological abnormality. In view of the above histomorphological findings and insignificant family history, close follow-up is advised.

* Corresponding author. Nikita Prasad

E-mail address: nikita_prasad92@yahoo.in

Department of Pathology, Maharaja Agrasen Medical College, Agroha, India

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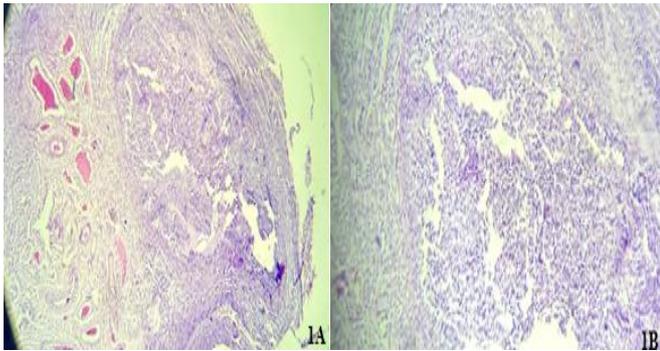
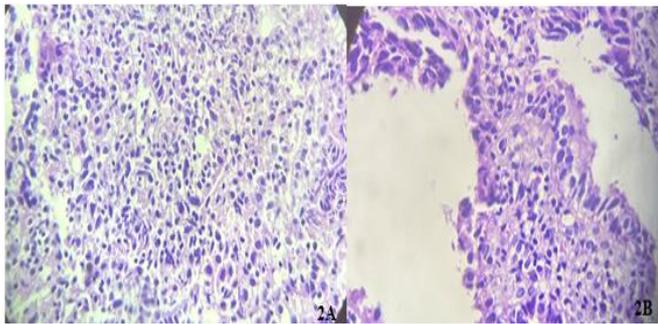


Fig. 1. Microsections of the distal fimbriated end of the fallopian tube. At low magnification, the area of STIC demonstrates increased epithelial thickness and nuclear stratification compared to areas of normal tubal epithelium. 1A : (H and E, 40X) 1B: (H and E, 100X).



Figs. 2 A and B. Evident nuclear atypia, including hyperchromatism, prominent nucleoli, loss of polarity, and increased mitotic figures. (H and E, 400X).

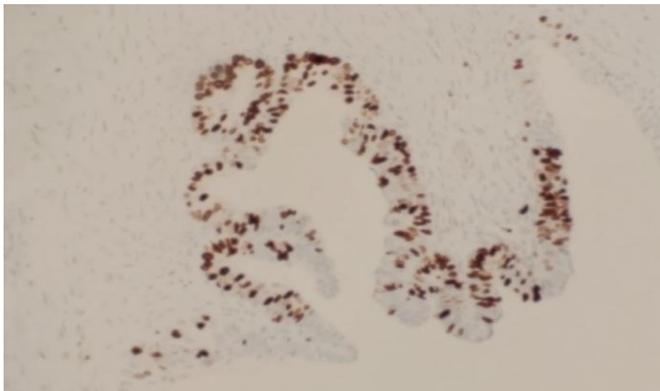


Fig. 3. Tumor cells showing strong and diffuse nuclear TP53 staining. (400X).

Consensus-based criteria to diagnose STIC

Processing and macroscopy

Each fallopian tube (regardless of indication for salpingectomy) should have the fimbriated end fully embedded according to the Sectioning and Extensively Examining the Fimbriated End (SEE-FIM) protocol. The proximal portion is serially cross-sectioned at 2.0-3.0 mm intervals, and the distal fimbriated end is longitudinally sliced into four sections.

Microscopy

STIC exhibits an abrupt transition from normal background tubal epithelium. Examination of the fallopian tube should start at low power. Cytological atypia (which is identical to high-grade serous ovarian cancer, HGSC) is mandatory for the diagnosis of STIC. Distinctive cytologic changes for diagnosis include a high nuclear-to-cytoplasmic ratio along with nuclear pleomorphism, enlargement, and hyperchromasia.

IHC

P53 and Ki67 staining are only required in cases of abnormal morphology. An aberrant p53 staining is mandatory to diagnose an STIC. Missense mutations result in strong, diffuse staining for p53, while null mutations show complete loss of staining. The wild-type p53 pattern (no mutation) exhibits weak, patchy nuclear staining.

3. Discussion

A whole spectrum of precursor lesions to extrauterine HGSC has been described in the fallopian tube, including the nearly normal-appearing p53 signatures, SCOUTs, serous tubal epithelial proliferations or lesions of uncertain significance (STEP-US), STILs, and STIC. STICs are established precursors to HGSC due to their shared somatic TP53 mutations and relative telomere shortening.^[6] Incidence of isolated STIC varies from <0.1% in the general population up to 3% in risk-reducing salpingo-oophorectomy females with increased risk for developing HGSC. STICs are detected in 50–60% of patients with sporadic pelvic HGSC.^[7] SCOUT comprises discrete linear segments of 30 or more secretory cells without an intervening ciliated cell. P53 signature is characterised by a linear stretch of at least 12 positive nuclei in a morphologically normal epithelium.^[4] The terms STILs, tubal intraepithelial lesions in transition (TILT), or STEP-US are used to describe a spectrum of intermediate atypical epithelial changes that resemble STIC, but fall short of this diagnosis. These are best reported as a descriptive finding, with a comment that the lesion is insufficient for a diagnosis of STIC.^[8] STIC is traditionally diagnosed with a combination of unequivocal histology with IHC for abnormal p53 ("all or none") and high Ki-67 index.^[3]

However, these morphological interpretations are subjective with low interobserver agreement. An international Delphi study has suggested consensus-based recommendations for the diagnosis of STIC, subdivided into five domains: processing and macroscopy; microscopy; immunohistochemistry; interpretation and reporting; and miscellaneous.^[9] A novel study recognizes two distinct morphological subtypes of all precursor lesions, FLAT (flat surface in >90% lesions) and BLAD (budding, loosely adherent, or detached in >10% area), which may be utilised for risk stratification.^[10] Early detection is fundamental in reducing overall mortality. The Society of Gynecologic Oncology and the American College of Obstetricians and Gynecologists suggest opportunistic salpingectomy for women undergoing hysterectomy for benign indications to reduce the risk of HGSC.^[11] In cases of incidental STIC detection, there is currently no consensus regarding management. After considering the risk-benefit ratio, close surveillance and follow-ups at 6-month intervals, including gynecologic examinations, CA-125 testing, and ultrasound examinations, may be recommended.^[5] Recent research suggests STIC to be regarded as a lesion with uncertain malignant potential. 50% of all carcinomas identified in risk-reducing salpingo-oophorectomy specimens are in the form of STIC.^[8] According to Stewart et al, STIC identified in patients with negative genetic testing are also at risk of subsequent HGSC.^[12] However, no genetic testing was done in our case. Further research is needed to identify additional risk factors beyond those associated with BRCA. STIC is a rare and difficult

histopathological diagnosis with a similarly controversial clinical management. Nevertheless, an emphasis on opportunistic salpingectomy, the SEE-FIM protocol, diagnostic criteria using IHC, and close follow-up is recommended.

4. Conclusion

The most fatal subtype of epithelial ovarian cancers is HGSC. As 80% of ovarian cancers occur in women with no known family history, the risk of tubo-ovarian cancers should be considered in all gynecological surgeries. Incidental STIC detection mandates adequate prolonged follow-up. Guidelines suggest opportunistic salpingectomy, but treatment recommendations remain inconclusive. Future preventive measures may include removal of the entire tube with all hysterectomies, as well as fimbriectomy (and not simple tubal ligation) for sterilization. Diagnosing tubal precursor lesions (such as SCOUTs, STILs, STICs) to HGSC is crucial to identify at-risk patients. Thorough sampling of fallopian tubes (SEE-FIM protocol) along with a low threshold for IHC is recommended. However, pathologic diagnosis remains challenging due to its rarity and the difficulty in interpretation.

Conflict of Interest

The authors declared that there is no conflict of interest.

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