

Fallopian Tube Intraluminal Tumour Spread from Non-invasive Precursor Lesions: A Novel Metastatic Route in Early Pelvic Carcinogenesis

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**Purpose:** Pelvic serous carcinoma is usually advanced stage at diagnosis, indicating that abdominal spread occurs early in carcinogenesis. Recent discovery of a precursor sequence in the Fallopian tube, culminating in serous tubal intraepithelial carcinoma (STIC) provides an opportunity to study early disease events. This study aims to explore novel metastatic routes in STICs.

**Patients and methods:** A BRCA1 mutation carrier (patient A) that presented with a STIC and tubal intraluminal shed tumour cells upon prophylactic bilateral salpingo-oophorectomy (PBSO) instigated scrutiny of an additional 23 women who underwent a PBSO and 40 patients with pelvic serous carcinoma involving the tubes.

**Results:** Complete serial sectioning of tubes and ovaries of patient A did not reveal invasive carcinoma, but subsequent staging surgery showed disseminated abdominal disease. STIC, intraluminal tumour cells and abdominal metastases displayed an identical immunohistochemical profile (p53+/WT1+/PAX8+/PAX2-) and TP53 mutation.

In sixteen serous carcinoma patients (40%) tubal intraluminal tumour cells were found, compared to none in the PBSO group.

**Conclusion:** This is the first description of a STIC, which plausibly metastasized without the presence of invasion through intraluminal shedding of malignant surface epithelial cells in the tube and subsequently spread through the peritoneal cavity. These findings warrant a reconsideration of the malignant potential of STICs and indicate that intraluminal shedding could be a risk factor for early intraperitoneal metastasis. Though rare in the absence of invasive cancer, we show that shed intraluminal tumour cells in the Fallopian tubes from serous carcinoma cases are common and a likely route of abdominal spread.