NEXT GENERATION LEARNING

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USCAP
Creating a Better Pathologist
EVENING SPECIALTY CONFERENCE

Gynecological Pathology
Case 1
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Dr. Bojana Djordjevic declares that she has no conflict(s) of interest to disclose.
History

• 74 year old woman
• Remote history of cervical adenocarcinoma treated with radiotherapy to the pelvis
• Now presenting with black and bloody stools
• Investigations:
  • Negative upper endoscopy
  • Failed colonoscopy but negative CT colonography
  • 6 cm left ovarian cystic mass on MRI
  • Ca-125=9 U/mL and CEA=1.4 µg/L
Findings at Laparotomy

• Left ovarian mass – benign cystic appearance
• Right ovary – unremarkable
• Appendix - shortened and firm
• No other GI tract abnormalities noted
• No peritoneal disease
Left ovary
Right ovary
Appendix
Appendix
Diagnosis

• Well differentiated adenocarcinoma of the appendix with metastases to the ovaries
• What about the fallopian tubes?
Right fallopian tube
Right fallopian tube
Right fallopian tube
Right fallopian tube

Pax8
Right fallopian tube
Case Discussion

• Case is presented to illustrate the intraepithelial pattern of fallopian tube involvement by extragenital mucinous adenocarcinoma
• Two recent retrospective case studies:

Fallopian tube metastases of non-gynaecological origin: a series of 20 cases emphasizing patterns of involvement including intra-epithelial spread

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Nongynecologic Metastases to Fallopian Tube Mucosa
A Potential Mimic of Tubal High-grade Serous Carcinoma and Benign Tubal Mucinous Metaplasia or Nonmucinous Hyperplasia

Joseph T. Rabban, MD, MPH, Poonam Vohra, MD, and Charles J. Zaloudek, MD

Extragenital Metastases to the Fallopian Tube

• Clinical context
  • Pelvic mass
  • Benign conditions – prolapse, ovarian cysts, hormonal breast cancer suppression

• Primary source
  • Colon - 15%-35%
  • Appendix – 12%-30%
  • Stomach – 9%-30%
  • Breast -15%
  • Pancreas- 5%
  • Bile duct - 5%
  • NYD upper GI/ pancreatobiliary tract- 8%

• Tumor type
  • Adenocarcinoma
    • Lymphoma
    • Neuroendocrine tumors
    • Mesothelioma
    • Urothelial carcinoma
    • GIST

Extragenital Metastases to the Fallopian Tube

- Ovarian involvement alone (without fallopian tube) is more common
- Fallopian tube involvement alone (without ovary) is relatively rare

*All presented with peritoneal carcinomatosis

Extragenital Metastases to the Fallopian Tube

• Gross appearance
  • 35% of fallopian tubes with metastases appear normal
  • Compared to only 14% of ovaries

• Grossing protocol considerations
  • 46% of cases identified over a 4 year period with a grossing protocol that required complete submission of fallopian tubes
  • Rest of the cases identified over a 19 year period
Extragenital Metastases to the Fallopian Tube

• Topography
  - Fimbria and/or non-fimbriated portions

• Microanatomy
  - Serosa (60-76%)
  - Lumen (17-55%)
  - Wall (54-70%)
  - Lymphovascular space (38-45%)
  - Mucosa (29-40%)
    - Mucosal involvement may be the only pattern in a minority of cases (8%)
    - Mucosal tumors favored the fimbriae (79%)

Extragenital Metastases to the Fallopian Tube

• Microscopic features
  • High or low grade cytology

Extragenital Metastases to the Fallopian Tube

• Microscopic features
  • Mucosal involvement
    • Single layer or stratified (ie. micropillae, cribriform, solid)
Extragenital Metastases to the Fallopian Tube

• Microscopic features
  • Mucosal involvement
    • Block-like replacement or comingling (Paget-like) with the native mucosa
    • Mucinous differentiation is common – intraluminal mucin or signet ring cells
Extragenital Metastases to the Fallopian Tube

• Microscopic features
  • Dissecting stromal mucin, particularly in association with appendiceal primaries
Extragenital Metastases to the Fallopian Tube

- Potential mechanisms of metastatic tumor spread to the fallopian tube
  - Direct extension
  - Lymphovascular spread
  - Transperitoneal/transtubal spread

Fallopian tube involvement by extragenital metastases ...

...may be more common than we thought but is under-recognized because:

1. FTs are not collected from the majority of patients with extragenital malignancies (ie. without an associated pelvic mass)
2. In cases of a pelvic mass, in toto submission of FTs has become a recent standard
3. Intramucosal involvement might be easy to miss unless one remembers to look for it (esp. if ovary is involved)

...is rare, particularly when:

1. FT is the only site
2. There is intramucosal involvement only
Why is this phenomenon relevant to every day practice?

• Prophylactic bilateral salpingectomy and oophorectomy in the high risk *BRCA1/2* mutation carrier population - a successful ovarian cancer risk reduction strategy

• Salpingectomy and salpingectomy with hysterectomy – also recently shown to reduce ovarian cancer risk in an unselected population

Finch et al. JAMA. 2006.
Rebbeck et al. NEJM. 2002.
Why is this phenomenon relevant to every day practice?

• United States and Canadian societies of gynecologic oncology now recommend that salpingectomies accompany hysterectomies for benign indications

• Ovaries (with normal appearance on intraoperative visualization) will be left in the patient

• The fallopian tubes become the only organ in which diagnosis of early extragenital metastases may be made
  • Pathologist awareness of subtle patterns of involvement (ie. mucosal) is important
  • Careful gross examination, impact on grossing protocol

Why is this phenomenon relevant to every day practice?

AUDIENCE POLL

• What is the section submission protocol for fallopian tubes at your institution in cases of hysterectomy for benign indications (fibroids, adenomyosis, uterine prolapse)?
  • Entire fallopian tube in toto
  • Fimbriated end in toto
  • Representative sections
Differential Diagnoses - “mucosal only” lesions

• Metaplastic changes in fallopian tube epithelium
  • Secretory
  • Transitional
  • Endometrioid
  • Mucinous
  • Eosinophilic
  • Pregnancy-related

Differential Diagnoses - “mucosal only” lesions

• Mucinous metaplasia
  • Patient with ruptured diverticulum and peritonitis. Normal appendix.
  • Inflammation
  • Variety of metaplasia types – Panneth cell, goblet, pyloric

Case contributed by Dr. Z Eslami
Differential Diagnoses - “mucosal only” lesions

• Mucinous metaplasia
  • Patient with ruptured diverticulum and peritonitis. Normal appendix.
  • Immunophenotype “in transition” – Mullerian markers are lost and intestinal markers are acquired to a different extent across different epithelial regions.

• NOT a perfect IHC mirror image

• Consider the pattern of expression and the overall histological appearance.
Differential Diagnoses - “mucosal only” lesions

- Pre-neoplastic and neoplastic fallopian tube lesions
  - Secretory cell outgrowths
  - Secretory tubal intraepithelial lesions
  - Serous tubal carcinoma in situ

Quick et al. Mod Path. 2011.
Differential Diagnoses - “mucosal only” lesions

• Pre-neoplastic and neoplastic fallopian tube lesions
• Immunohistochemistry pitfalls
  • Beware of the elevated Ki-67 index and aberrant p53 expression in high grade lesions that resemble serous carcinoma
    • Pax 8, Wt-1 and estrogen receptor to confirm fallopian tube origin
      • When Pax 8 is positive but Wt-1 and/or estrogen receptor are not....

• Fallopian tube mucosal involvement by uterine serous carcinoma
  • Typically Wt-1 negative, estrogen receptor staining variable

Singh et al. Histopathol. 2015.
Fallopian tube

Wt-1
Endometrium
Summary

• Prophylactic salpingectomies in low risk patients are on the rise

• When ovaries are not present in the specimen, fallopian tubes may be the only organ in which diagnosis of extragenital disease may be made (or strongly suspected)
  • Trigger further patient evaluation

• Extragenital metastases to the fallopian tube may not be grossly visible in many cases - impact on grossing protocols

• Patterns of fallopian tube involvement
  • “Mucosal only” pattern may be difficult to recognize
    • Remember the differential diagnoses
    • Beware of pitfalls with use of immunohistochemistry
Thank you