Triple synchronous ovarian carcinomas: an unlikely association of serous carcinoma with large cell neuroendocrine carcinoma and granulosa cell tumour

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CLINICAL PRESENTATION

History of Present Illness: A 55-year-old woman presents to the emergency department with abdominal pain, early satiety and an unintentional weight loss of 32 kilograms over the previous year.

Past Medical History: Long standing rheumatoid arthritis with chronic deformities, neuropathy, hypertension, and migraine headaches

Medications: Multiple medications for rheumatoid arthritis but had been unresponsive to a number of treatments. There have been issues of patient medication noncompliance.

Social History: No alcohol, tobacco, or drug use

Family History: Three maternal aunts with breast carcinoma and one maternal aunt with breast and ovarian carcinoma; all diagnosed in their fifties

Physical Exam: Mild tenderness to palpation of the right and left upper quadrants as well as mild distention. Atrophic vaginal mucosa and palpable, mobile bilateral adnexal masses

Imaging Findings:

Abdominal and pelvic CT revealed a 7.4 cm left adnexal mass and mild periaortic adenopathy.
A transvaginal ultrasound showed a 7.8 cm solid mass of the left adnexa with a complex cyst inferior to the mass as well as a multi-cystic right ovary and free fluid in the right upper quadrant

Laboratory Findings:

Elevated CA-125
• Serum CA-125: 1377 U/mL (normal = 46 U/mL))

Operative Findings:

Exploratory laparotomy revealed significant disease in the pelvis with both ovaries filling the pelvis and densely adherent to the sigmoid colon.
The patient underwent total hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and tumour debulking with excision of multiple mesenteric, peritoneal and colon serosal nodules. Debulking was suboptimal due to significant lymphadenopathy associated with the small bowel and colon mesentery such that almost the entire root of the mesentery was involved.

Pathologic Findings

- Both ovaries completely replaced by tumour (Figure 1A, 1B)
- Each ovary involved by two types of tumours (Figure 2A, 2B)
- High-grade serous carcinoma* was present in both ovaries
Poorly differentiated with papillary architecture
Markedly pleomorphic nuclei and frequent mitoses
- High-grade large cell neuroendocrine carcinoma (LCNEC)** was identified in the left ovary as the second tumour
Large neuroendocrine cells forming solid nests
Brisk mitosis and prominent nucleoli
- Granulosa cell tumour*** was identified in the right ovary as the second tumour
Small, bland, cuboidal cells in nests
- High-grade serous carcinoma and LCNEC both metastasized and were seen metastatic to the uterus, cervix, omentum, peritoneum and small and large bowel mesentery

Final Pathologic Diagnosis:

Triple synchronous ovarian carcinomas consisting of high-grade serous carcinoma, high-grade large cell neuroendocrine carcinoma (LCNEC) and granulosa cell tumour

GROSS AND MICROSCOPIC FINDINGS

1A: A 10.5 cm solid left ovarian mass composed of high-grade serous carcinoma* and LCNEC**

1B: A 9.5 cm solid right ovarian mass composed of serous carcinoma* and granulosa cell tumour***

2A. Left ovary with high-grade serous carcinoma* adjacent to high-grade LCNEC** (H&E, 10x)

2B. Right ovary with high-grade serous carcinoma* adjacent to granulosa cell tumour*** (H&E, 10x)

Follow-up

- Despite her family history, the patient declined genetic testing
- Received chemotherapy with 6 cycles of etoposide and cisplatin
- CA-125 normalized after chemotherapy
- Post-treatment CT showed no evidence of disease
- One year post-surgery, the patient is doing well, and has no evidence of disease

DISCUSSION AND CONCLUSION

- To the best of our knowledge, this case is the first report of triple synchronous ovarian carcinomas in the same patient, composed of serous carcinoma, LCNEC and granulosa cell tumour ¹⁻⁷
- LCNEC of the ovary is considered to be highly aggressive and its presence in an otherwise usual type epithelial tumour is likely to have a negative prognostic impact ^{2-4,7}
- Follow-up of our patient may shed light on the natural course of this unusual combination of aggressive carcinomas, given the patient's choice not to pursue further maintenance treatment.

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