Synchronous Endometrial Malignant Mixed Mullerian Tumor and Ovarian High-Grade Serous Carcinoma: A Case Report and Review of Literature

Felix E. Menkiti1  Ifeoma F. Ezejiofor2  Michael E. Chiemeka2  Chukwudi R. Osakwe3

1Department of Anatomic Pathology and Forensic Medicine, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria
2Department of Anatomic Pathology and Forensic Medicine, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria
3Department of Obstetrics and Gynaecology, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra state, Nigeria

Address for correspondence Felix E. Menkiti, FMCPath, Department of Anatomic Pathology and Forensic Medicine, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria (e-mail: menkiti_f@yahoo.com).

Abstract
Keywords
- endometrial malignant mixed Mullerian tumor
- serous ovarian carcinoma
- synchronous cancers

Synchronous cancers account for 0.7 to 1.8% of all gynecologic malignancies. Although synchronous endometrial and ovarian cancers are well reported in the literature, they are largely synchronous endometrioid cancers; no reported case of synchronous endometrial malignant mixed Mullerian tumor (MMMT) and ovarian serous carcinoma is seen. We therefore report a case of synchronous endometrial MMMT and ovarian serous carcinoma in a 60-year-old Nigerian female.

Introduction
Gynecological cancers account for 7.2% of cancers worldwide, with 1.6 and 2.1% occurring in the ovary and uterine corpus, respectively.1 Synchronous cancers account for 0.7 to 1.8% of all gynecologic malignancies, approximately 50% of which are accounted for by synchronous endometrial and ovarian cancers (SEOCs).2,3 SEOCs have been reported to account for approximately 3 to 10% and 3 to 5% of ovarian cancers and endometrial cancers, respectively.4,5 Matsuo et al in a retrospective study reported a changing trend in the pattern of SEOCs: a decreasing synchronous ovarian cancer among endometrial cancers and increasing synchronous endometrial cancer among ovarian cancer, and the peak age of incidence being late 40s.6 Although SEOC is well reported in literature, none has reported synchronous endometrial malignant mixed Mullerian tumor (MMMT) and ovarian high-grade serous carcinoma. However, there were reported cases of synchronous ovarian carcinoma in cases of MMMT of one ovary, broad ligament and mesentry7–10; and synchronous primary ovarian and uterine MMMT.11 We therefore report a case of MMMT of the endometrium occurring simultaneously with ovarian high-grade serous carcinoma in a 60-year-old Nigerian female.

Case Report
A 60-year-old postmenopausal female presented with a history of 5 months’ recurrent vaginal bleeding and 1 month constipation with associated lower abdominal pain but no abdominal swelling. There was no family history of breast, ovarian, or colonic tumor. Physical examination of the abdomen revealed a bulky uterus with empty pouch of Douglas. Abdominopelvic sonogram revealed an endometrial mass with possible peritoneal seedlings, while chest radiogram was normal. Other investigations done, including serum electrolyte urea and creatinine, liver function test, full blood count, urinalysis, retroviral screening, hepatitis B virus surface antigen, and electrocardiography were all normal. Exploratory laparotomy was done, with subtotal hysterectomy and right salpingo-oophorectomy (and the sample sent to histopathology department for analysis), but constipation persisted necessitating further evaluation for possible primary or secondary colorectal tumor.

Asian J Oncol 2019;5:89–92

DOI https://doi.org/10.1055/s-0039-3401368
ISSN 2454-6798.

©2019 Spring Hope Cancer Foundation & Young Oncologist Group of Asia
Following evaluation, no lesion was noted in the breast and colorectum. Patient was discharged home 4 weeks later following good postoperation condition. Chemoirradiation was planned for the patient. About 8 weeks postsurgery, the constipation resolved and she had improved clinically. Patient could not receive the chemotherapy due to financial constraint and was subsequently lost to follow-up.

The collected surgical sample and peritoneal fluid were received in the histopathology department. The specimen consisted of subtotal hysterectomy and right salpingo-oophorectomy tissues, with ragged friable mass filling the endometrial cavity; the fallopian tube was unremarkable while the ovary which measured 7.0 cm × 4.5 cm × 3.0 cm has a smooth surface and a nodular cut surface (Fig. 1). On histologic examination, the endometrium revealed a malignant mixed epithelial and mesenchymal neoplasm with high nuclear grade and frequent mitosis invading but not extending beyond the myometrium; features consistent with MMMT (Figs. 2 and 3). The histologic sections of the right ovary showed invasive simple and complex arborizing papillae and glands lined by cells having high-grade nuclear features and moderate cytoplasm, with brisk mitosis and necrosis, consistent with high-grade serous carcinoma of the right ovary (Fig. 4). The peritoneal aspirate cytology was negative for the tumor cells.

**Discussion**

SEOC is the simultaneous occurrence of both endometrial and ovarian cancers at the time of diagnosis. Although a rare instance, SEOC is the most frequent of the synchronous female genital tract cancers, which accounts for 0.7 to 1.8% of all gynecologic malignancies. SEOCs occur in younger women than those with either of primary ovarian or primary endometrial malignancies. A population-based retrospective analysis of SEOCs by Matsuo et al showed that among the endometrial cancer cohorts, synchronous primary endometrioid endometrial and ovarian tumors accounted for majority of the cases; while synchronous primary nonendometrioid ovarian and endometrial tumors accounted for only 16% of the cases, 21.8% accounted for the high-grade (grades 2 and 3) tumors. In their study, grade 3 synchronous primary nonendometrioid ovarian and endometrial carcinomas to which group the index case belongs, accounted for only 5% of the SEOCs.

The study by Kobayashi et al showed that majority of SEOCs are sporadic cancers. However, several studies have been invested to unraveling the pathogenesis of SEOCs, which established a clonal relationship via gene sequencing. Several mutated genes have been found, some of which have syndromic association. Irving et al showed association between β-catenin mutations and SEOCs. A review by Dogan et al found microsatellite instability and subsequent mutations in mismatch repair genes compatible with hereditary nonpolyposis colorectal cancer (HNPCC) present in 40% of women with SEOC and suggested a strong link between SEOC and HNPCC in young women.
Synchronous Endometrial MMMT and Ovarian High-Grade Serous Carcinoma

Menkiti et al.

Endometrial MMMT and ovarian cancer is an uncommon carcinoma that poses a diagnostic challenge. The index patient had laparotomy with total hysterectomy and unilateral salpingo-oophorectomy, and was subsequently worked up for chemotherapy and radiotherapy. Although several studies have reported a better prognosis for SEOCs compared with single occurring and metachronous tumors, the more informative population-based study by Matsuo et al, over a period of four decades, showed that survival of SEOC largely depends on the histologies of the two cancer sites. An international multicenter, case–control study also revealed that the prognosis of SEOCs is same with singly occurring endometrial or ovarian carcinoma when matched for age, FIGO stage, histology, and Eastern Cooperative Oncology Group performance status.

Conclusion
SEOCs are rare group of tumors commonly presenting as synchronous primary endometrioid carcinomas of the ovary and endometrium. Synchronous nonendometrioid endometrial and ovarian cancer is even rarer, with no reported case of synchronous endometrial MMMT and ovarian serous carcinoma seen after extensive literature search. We have reported a rare case of synchronous endometrial MMMT and ovarian serous carcinoma.

Conflict of Interest
None declared.

References
7 Günakan E, Tohma YA, Haberal AN, Ayhan A. Bilateral synchronous ovarian tumours: an uncommon case and review of the literature. Przegl Menopauz 2018;17(2):97–100

Asian Journal of Oncology Vol. 5 No. 2/2019