Case Report

Co-Existing Ovarian Mucinous Cystadenocarcinoma with Mature Cystic Teratoma: A Rare Case Report†

Komsun Suwannarurk MD*,
Yudthadej Thaweekul MD*, Karicha Mairaing MD*,
Yenrudee Poomtavorn MD*, Wichet Piyawong MD**,
Wanwisa Himakhun MD***, Kornkarn Bhamarapravatana PhD****

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** Gynecological Oncology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*
*** Department of Radiology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*
**** Department of Pathology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*
***** Department of Preclinical Science, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*

Background: *Mature cystic teratoma is the most common benign germ cell ovarian tumor. Malignant transformation is uncommon. The pathology is mostly composed of squamous cell carcinoma. Mucinous cystadenocarcinoma should be differentiated between malignant transformation and the coincidental occurrence.*
Case Report: *A case of an early stage mucinous ovarian cancer co-existing with mature cystic teratoma at the same ovarian side was reported. A 57-year-old woman presented with incidental palpable pelvic mass for two weeks. Right ovary consisted of multiloculated cyst and mature cystic teratoma. The patient underwent an exploratory laparotomy for a large ovarian cyst evaluation. Mucinous ovarian cancer was diagnosed as FIGO stage IC3 after operation. Histopathology report showed mucinous cystadenocarcinoma and mature cystic teratoma of the right ovary. There was no additional abdominal abnormality. Immunohistochemistry staining supported the diagnosis of metastatic adenocarcinoma of colon or intestinal type of mucinous ovarian cancer. Further investigation for locating other primary cancer site was then performed. The result was negative. The intestinal-type mucinous ovarian cancer co-existing with mature cystic teratoma of the right ovary was the final histopathological reading. The patient was then started on carboplatin/paclitaxel combination chemotherapy for 6 cycles after surgery. The patient showed complete remission at the end of the chemotherapy treatment.*
Conclusion: *This was a rare case of mucinous ovarian cancer co-existing with mature cystic teratoma. Clinical acumen, immunochemistry staining and metastatic survey investigation played important roles for the final diagnosis.*

Keywords: *Ovarian cancer, Mucinous, Dermoid*

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Mature cystic teratoma (MCT) or dermoid cyst is the most common benign germ cell ovarian tumor. It could occur at any age with a peak incidence in the first two decades of life. Most MCT cases were asymptomatic and usually incidentally found during routine pelvic examinations[1]. Malignant transformation is uncommon. The pathology is mostly composed of squamous cell carcinoma. It is known that the lining epithelial of mucinous ovarian tumors contained intracytoplasmic mucin; however, it resembled those of endocervix, gastric pylorus or intestine[1]. Mucinous cystadenocarcinoma should be identified as metastatic cancer or malignant transformation. However, it was difficult to do based on histology alone[2,3]. The co-existing of mucinous tumor and MCT was a rare situation. The diagnosis should be able to distinguish the metastatic cancer from intestine and malignant transformation.

Correspondence to:
Suwannarurk K, Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani 12120, Thailand.
Phone: +66-2-9269343, Fax: +66-2-9269685
E-mail: k_suwannarurk@yahoo.com

Case Report

A 57-year-old woman (para 0-0-0-0) came to the gynecology clinic, Thammasat University Hospital. Her chief complaint was asymptomatic incidental palpable pelvic mass for two weeks. She was a healthy-

looking, menopaused 10 years, non-smoking and esthetic female. There was no underlying disease or past medical history. Her younger twin sister had died from advanced ovarian cancer 10 years earlier. She never underwent pelvic examination. Her mother suffered and died from colonic cancer. The pedigree of this case was represented in Fig. 1. She was single and had no sexual experience.

Pre-operative investigation was conducted on the patient. Chest x-ray, hemoglobin level, blood chemistry and liver enzyme profiles were all normal. Huge pelvic cystic mass above the umbilicus was detected from abdominal and pelvic examination. A cervical cytology investigation during preoperative visit showed negative result for intraepithelial lesion or malignancy (NILM).

The patient then underwent the abdomen-pelvis computerized tomography (CT) scan. CT scan reported a well-defined lobulated contour solid and cystic mass at pelvic cavity upward to umbilical region. The upper mass portion consisted of multiloculated cyst with solid component. The lower mass portion contained mainly multiple fat and calcific components. The measurements were 8.9x9.6x14.9 cm in antero-posterior, transverse and coronal dimension (Fig. 2). This huge pelvic mass showed the displacement effects to bowel loops, uterus and superior aspect of urinary bladder. Imaging result showed no additional abdominal abnormality.

The patient decided to proceed to the surgical stage after receiving thorough counseling about her disease. Exploratory laparotomy was performed via a midline incision. The operation composed of total hysterectomy, bilateral adnexectomy, infracolicomentectomy, peritoneal biopsy and pelvic lymphadenectomy. A peritoneal cytology examination was requested. The result was positive for malignancy cells. Intra-operative gross examination of the uterus showed smooth uterine serosa. The right ovarian tumor consisted of two portions of solid-cystic masses (Fig. 3). The upper mass portion was measured at 10x8x6 cm. It showed multilobulated cyst with mucin content measuring 0.5-5 cm in diameter. The lower mass portion was measured at 11x5x6 cm. It consisted of multilobulated cyst containing sebum, hair, fat nodule and bone. No metastatic lesions were detected in the rest of the abdominal cavity. Bilateral pelvic lymph node dissection and infracolicomentectomy were then performed. Paraaortic lymph node sampling was not performed during this operation due to difficulty of case and initially pelvic lymph node metastasis was

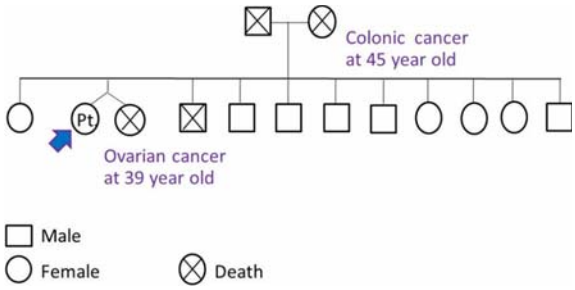

Fig. 1 Pedigree of this patient.

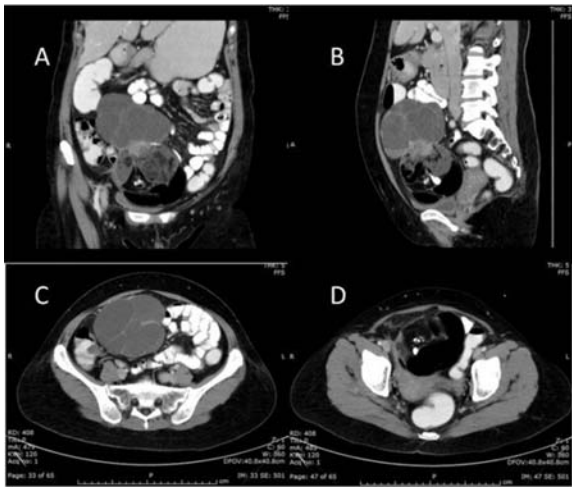

Fig. 2 Abdominal CT scan of this patient demonstrated a well-defined lobulated contour solid and cystic mass with containing multiple fat and calcific components at pelvic cavity upward to umbilical region. Cystic portion (upper portion) showed multiple enhancing septation and solid nodules. Lower portion of mass showed solid cystic, fat and calcification components. A) Coronal plane. B) Axial plane of lower pelvis. C) Cross section plane of mass at upper portion. D) Cross section plane of mass at lower portion.

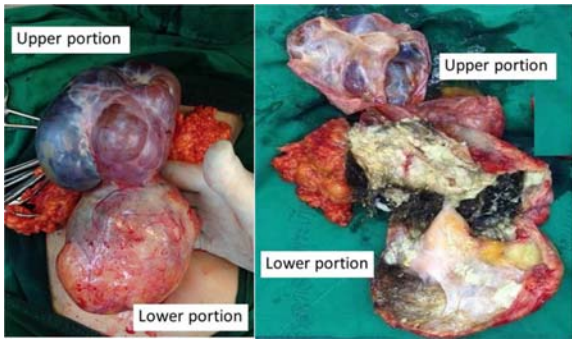

Fig. 3 The right ovarian cyst composed of two portion; upper and lower.

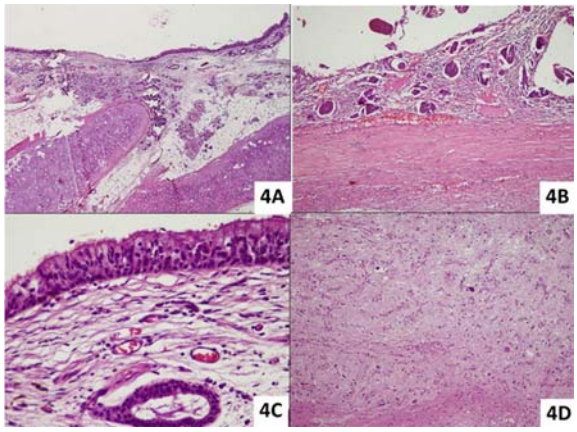

Fig. 4 Mature cystic teratoma component; consisting of mature derivative of ectoderm, mesoderm and endoderm: A) Differentiation of cartilage and skin appendages (H&E: 40x). B) Differentiation of hair follicles (H&E: 100x). C) Differentiation of respiratory epithelial lining (H&E: 100x). D) Differentiation of brain and neuronal tissue (H&E: 40x).

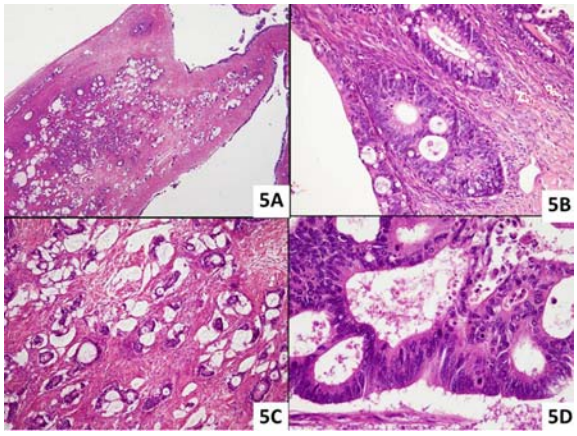

Fig. 5 Mucinous carcinoma component: A) Mucinous carcinoma, infiltrative invasion (H&E 40x). B) Mucinous carcinoma, continuum of architecture and cytology atypia from benign to boderline mucinous tumor (H&E 40x). C) Mucinous carcinoma, frankly carcinomatous area of infiltrative invasion (H&E 100x). D) Mucinous carcinoma, complex gland with cytological atypia and increased mitotic activity (H&E 400x).

not grossly suspicious. Pathological results of both were negative. Final histopathological reports were mucinous adenocarcinoma and mature cystic teratoma in upper and lower portion, respectively (Fig. 4-6).

The mucinous adenocarcinoma of the right ovary was further investigated to identify the exact primary site. The additional immunohistochemistry staining was performed. The mucinous cancer showed positive staining for CDX-2 (homeobox genes encoding nuclear homeodomain transcriptional factors essential to intestinal organogenesis) and cytokeratin 20 (CK20). The cytokeratin 7 (CK 7) and estrogen receptor (ER) staining reported negative.

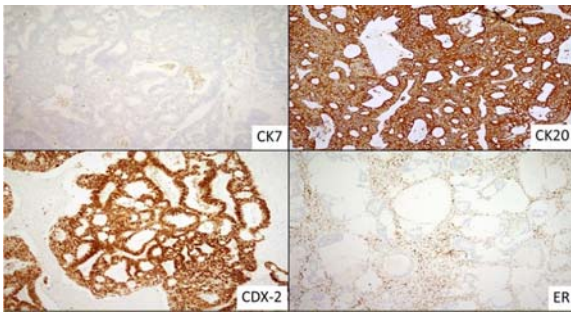

Fig. 6 Immunohistochemistry staining revealed CK7 negative, CK20 positive, CDX-2 negative and ER (estrogen receptor) negative.

Further investigation for locating other primary cancer site was then performed. Gastroscopy was not performed due to strongly evidence of metastatic gastrointestinal cancer from immunostaining. The CT colonography and mammography were performed after gastrointestinal cancer surgeon consultation. Both studies reported negative finding.

Finally, her diagnosis was mucinous ovarian cancer FIGO stage IC3 (peritoneal cytology positive for malignancy) co-existing with MCT. However, optimal surgical removal (no residual tumor or lesser than 1 cm in diameter) was achieved. The patient was counseled with diagnosis, staging, treatment and further management. After thoroughly counseling, she received six cycles of combined chemotherapy consisting of carboplatin (area under the curve 5) and paclitaxel (175 mg/m^2) every 4 weeks.

After six courses of combination chemotherapy (carboplatin/paclitaxel), the complete remission (CR) was achieved according to RECIST criteria[4]. Further investigation for locating any persistent or recurrent cancer site was performed. The result yielded no evidence of cancer. Tumor marker pattern of CA125, CA199 and HE4 were in normal range as presented in Fig. 7. She was requested to do her follow-up at gynecological oncology clinic.

Discussion

Mucinous cystadenocarcinoma of the ovary

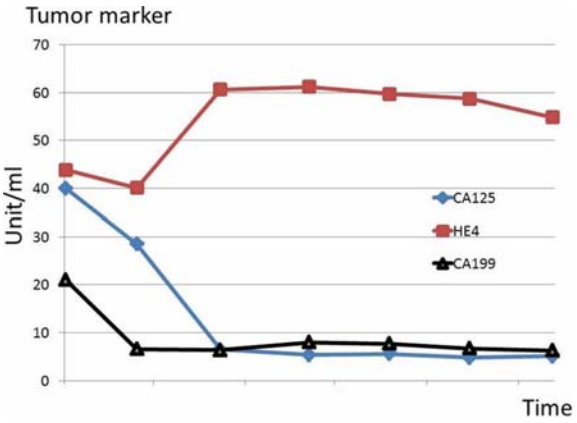

Fig. 7 Tumor marker (composed of CA125, CA199 and HE4) after surgery and during chemotherapy.

had the lining epithelium with mucin-secreting. It resembled to those of endocervix, gastric pylorus or intestine[2]. In this case, the epithelial line was intestinal subtype. It could not distinguish between metastatic carcinoma for gastrointestinal tract based on histology alone[2,3].

When the mucinous cancer was found with mature cystic teratoma in the same site ovary, there were three of natural progressions. First, the mucinous cancer was metastasized from other primary cancer especially from intestinal cancer. The second, the mucinous cancer was the malignant transformation arising in mature cystic teratoma.

Malignant transformation was squamous cell carcinoma that took around 0.5-2% from previous literature[5]. Eighty percent of malignant transformation was squamous cell carcinoma[7]. Only 0.5% of MCT was mucinous cystadenocarcinoma[8]. The prognosis of cases with malignant transformation was very poor[9,10]. The third, the mucinous cystadenocarcinoma occurred with incidental MCT. In the last situation, the prognosis of disease did not differ from mucinous cancer that occurred alone.

This case needed the further investigation to distinguish between primary or metastatic cancer. Immunohistochemistry staining in this case was performed. The immunohistochemistry staining in this case showed CK7-/CK20+ profile. This profile was the most common profile in lower intestinal tract tumors, uncommon in upper gastrointestinal tract tumors and rarely seen in primary ovarian tumors[11]. However, 64% of mucinous ovarian cancer had high-level expression of CDX2[12]. Mucinous cancer that originated from stomach, colon and breast had positive for ER staining at percentage of 0, 0 and 80, respectively[13]. Compared to serial histopathological and imaging investigation, the diagnosis was co-existing mucinous cystadenocarcinoma of the ovary.

The further treatment was standard combined chemotherapy. Currently, women diagnosed with early and advanced epithelial ovarian cancer underwent cytoreductive surgery followed by adjuvant platinum (carboplatin) and taxane-based (paclitaxel) chemotherapy. This regimen was widely accepted according to GOG-111 protocol[10].

From history, the patient's mother died from colonic cancer and her twin younger sister had died from advanced ovarian cancer. Now she developed ovarian cancer. Hereditary non-polyposiscolon cancer Lynch syndrome (HNPCC), which included multiple adenocarcinomas, involves a combination of colon cancer and endometrial or ovarian cancer and other malignancies of the gastrointestinal and genitourinary systems[14] was one of the major concerns. The patient had three younger sisters from her pedigree. The remained younger sisters may have benefit from genetic counseling. A full pedigree analysis of this family should be performed by a geneticist to more accurately determine the risk. Verification of the histological diagnosis of the family members' ovarian cancer should be done. The decision about the management could be best done after careful counseling and appropriate investigation.

Conclusion

This was a rare case of mucinous ovarian cancer co-existing with mature cystic teratoma. Clinical acumen, immunochemistry staining and metastatic survey investigation played important roles for final diagnosis. The accurate taking of history might have helped the other members of the cancer survivor's family. The investigation for the remaining members of cancer survivor's family should be performed with the aim of decreasing the ovarian cancer risk.

What is already known on this topic?

Mature cystic teratoma (MCT) or Dermoid cyst is the most common benign germ cell ovarian tumor. Malignant transformation is uncommon. The pathology is mostly composed of squamous cell carcinoma. It is known that the lining epithelial of mucinous ovarian tumors contained intracytoplasmicmucin; however, it resembled those of endocervix, gastric pylorus or intestine. Mucinous cystadenocarcinoma should be identified as metastatic cancer or malignant

transformation. However, it was difficult to do this based on histology alone. The co-existence of mucinous tumors and MCT was a rare situation.

What this study adds?

Clinical acumen, immunochemistry staining and metastatic survey investigation played important roles for final diagnosis. The accurate taking of history might have helped the other members of the cancer survivor's family. The investigation for the remaining members of the cancer survivor's family should be performed with the aim of decreasing the risk of ovarian cancer.

Potential conflicts of interest

None.

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มะเร็งรังไข่ชนิดมิวซินัส ซิสตะดีโนมา ที่พบร่วมกับถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่: รายงานผู้ป่วยหายาก

คมสันติ์ สุวรรณฤกษ์, ยุทธเดช ทวีกุล, กริชา ไม้เรียง, เย็นฤดี ภูมิถาวร, วิเชษฐ์ ปียะวงศ์, วันวิสาข์ หิมะคุณ, กรณ์กาญจน์ ภมรประวัติธนะ

ภูมิหลัง: *ถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่เป็นเนื้องอกชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่ที่พบบ่อย การกลายเป็นมะเร็งพบได้ไม่บ่อย พยาธิวิทยาส่วนใหญ่เป็นมะเร็งชนิดสแควมัสเซลล์มะเร็งรังไข่ชนิดมิวซินัส ซิสตะดีโนมา ต้องวินิจฉัยแยกโรคระหว่างการกลายเป็นมะเร็งหรือเป็นภาวะเกิดขึ้นร่วมกัน*

รายงานผู้ป่วย: *รายงานผู้ป่วยมะเร็งรังไข่ชนิดมิวซินัส ซิสตะดีโนมา ที่พบร่วมกับถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่ผู้ป่วยหญิงอายุ 57 ปีมาพบแพทย์ด้วยอาการคลำก้อนที่ท้องน้อยโดยบังเอิญมา 2 สัปดาห์ รังไข่ข้างขวาประกอบด้วยถุงน้ำหลายถุงและถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่ผู้ป่วยได้รับการผ่าตัดสำรวจช่องท้องและกำหนดระยะโรคเนื่องจากมีถุงน้ำรังไข่ขนาดใหญ่ ได้รับการวินิจฉัยมะเร็งรังไข่ชนิดมิวซินัส ซิสตะดีโนมาระยะหนึ่งซีสาม ภายหลังการผ่าตัด ผลทางพยาธิวิทยาเป็นชนิดมิวซินัส ซิสตะดีโนมาและถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่ของรังไข่ข้างขวาไม่พบความผิดปกติอื่นในช่องท้อง การย้อมทางอิมมูโนฮิสโตเคม สนับสนุนการวินิจฉัยมะเร็งลำไส้ใหญ่ชนิดแพร่กระจายหรือมะเร็งรังไข่ชนิดมิวซินัส การสืบค้นเพื่อวินิจฉัยโรคเพิ่มเติมเพื่อหาต้นกำเนิดของมะเร็ง ไม่พบว่ามาจากที่ใดมะเร็งรังไข่ชนิดมิวซินัส ซิสตะดีโนมา ที่พบร่วมกับถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่เป็นการวินิจฉัยขั้นสุดท้าย ผู้ป่วยได้รับยาเคมีบำบัดชนิดคาร์โบพลาตินและพาคลิแทคเซลจำนวน 6 รอบภายหลังผ่าตัดทุก 4 สัปดาห์ภายหลังผ่าตัด ผู้ป่วยได้รับการวินิจฉัยว่าไม่พบมะเร็งภายหลังครบการรักษาด้วยยาเคมีบำบัด*

สรุป: *เป็นรายงานผู้ป่วยมะเร็งรังไข่ชนิดมิวซินัส ซิสตะดีโนมาที่พบร่วมกับถุงน้ำรังไข่ชนิดกลุ่มเซลล์เจริญเติบโตเต็มที่ ความแม่นยำทางคลินิก การย้อมทางอิมมูโนฮิสโตเคม และการตรวจหาการแพร่กระจายของมะเร็งมีบทบาทสำคัญต่อการวินิจฉัยขั้นสุดท้าย*