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Radiology Finding of Endometriosis Malignant Transformation into Ovarian Clear Cell Carcinoma: A Rare Case

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ABSTRACT

Introduction: One of the risk factors for ovarian cancer is endometriosis. The most prevalent type of ovarian cancer linked to endometriosis is ovarian clear cell carcinoma. The CT scan examination helps identify the type of treatment for each mass lesion and distinguishes endometriomas from other lesions.

Case Presentation: MSCT was done on a 42 years old female with abdominal pain and distention over a year; showed a cystic mass (16HU) with solid component (36HU) partly unclear borders, irregular edges, with dimensions \pm 14.3 x 16.8 x 16.3 cm in the pelvic and abdominal cavity, impression originates from the adnexas, when administered contrast shows an increased enhancement in contrast (83HU), also found free fluid density(17HU) in abdominal cavity, suggestive malignant ovarian mass. A pathology anatomy examination was done and confirmed clear cell carcinoma of the left ovary, endometriotic cyst in the right ovary, and external endometriosis in the omentum

Conclusion: Endometriosis rarely develops into clear ovarian cell carcinoma; the preoperative characterization of an ovarian cyst and the CT appearance of ruptured endometriotic cysts are comparatively distinct from those of burst functional cysts.

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INTRODUCTION

About 10% of women of reproductive age have endometriosis, a chronic inflammatory disease marked by endometrial-like tissue outside of the uterus. It is a difficult diagnosis to make because it is linked to infertility, abdomino-pelvic pain, and other nongynecologic symptoms [1]. Though it primarily invades the parietal peritoneum and pelvic organs, ectopic endometrial tissue can invade any portion of the body. Malignant tumors and endometriosis share similarities in terms of proliferation, infiltration, and metastasis. Endometriosis is a common condition affecting fertile women, with a 0.7% to 2.5% chance of malignant transformation [2].

Visual inspection by laparoscopy, ideally with histological confirmation, has been the gold standard for diagnosing endometriosis. The lack of an effective noninvasive diagnostic for endometriosis causes a considerable delay in diagnosis. Surgical treatment techniques may be guided by imaging that establishes the presence of an endometriosis cyst or deep infiltrating endometriosis [3]. By evaluating benign complex cystic adnexal masses using CT scanning, it was possible to distinguish endometriomas from other lesions and possibly determine the best course of treatment for each mass lesion based on the hyperdense portion and the presence or absence of cul-de-sac obliteration [4].

Even though endometriosis is benign, it is linked to a higher risk of several diseases, such as ovarian cancer linked to endometriosis (EAOC). Though rare, ovarian cancer is more likely in women who have endometriosis, especially in cases of endometroid and clear-cell carcinomas [5]. While some studies have shown that malignant transformation through atypical endometriosis, which is defined as glands with atypical

cytology or architecture, occurs clinically in 0.7 to 1.6% of patients in an 8-year follow-up, others have shown that ovarian carcinoma is present in 5 to 10% of cases of endometriosis [6]. Specifically, numerous investigations verify that endometrioid tumors and clear cell carcinoma are the epithelial ovarian cancer histotypes most strongly associated with endometriosis [7].

A rare subtype of epithelial ovarian cancer with distinct clinicopathological characteristics is ovarian clear cell carcinoma [8]. Compared to women with the most prevalent high-grade serous histology, women with clear cell carcinomas are typically younger and have been detected at an earlier stage. Given that endometriosis is found in over 50% of patients with clear cell carcinoma, it can be regarded as a precursor to the tumor and a major risk factor for the development of ovarian clear cell carcinoma [9]. For preoperative staging and postoperative restaging, a CT scan is still the recommended approach, and radiologists play a critical role in recognizing this kind of tumor [10].

CASE PRESENTATION

A 42-year-old female came to Dr. Soetomo General Hospital with complaints about abdominal pain and distention over a year. A physical examination found ascites and bilateral lower abdominal mass. An abdominal ultrasound examination was done and we found the suspected bilateral ovarian mass. Result from Cancer Antigen (Ca-125) was high (119.0 U/mL).

Abdominal MSCT axial, sagital, and coronal view showed a cystic mass (16 HU) with a solid component (36 HU) with partly unclear borders, irregular edges, with dimensions +/- 14.3x 16.8 x 16.3 cm in the pelvic cavity to the abdominal impression originates from the

adnexa, which when administering contrast shows an increased enhancement in contrast (83 HU). There is a density of free fluid (17 HU) in the abdominal cavity to the pelvic cavity accompanied by pressure from the bowel system towards the central abdomen. The conclusion of MSCT was cystic mass with solid components in the pelvic and abdominal cavity with detail of the expansion suggestive malignant ovarian mass with ascites.

During the operation, it found left ovarian mass (approximately $14.5 \times 13 \times 9$ cm) and a right ovarian mass (approximately $6.5 \times 5 \times 2$ cm) with cystic mix solid were seen which showed grade II-III adhesions between the tumor mass and the sigmoid, rectum, and anterior abdominal wall. The cyst wall ruptured and a brownish cyst fluid of 1300 cc was released. Also were found 50 cc abdominal serohaemorrhagic free fluid. Bilateral salphingo-oophorectomy and frozen section were performed with frozen section results is malignant, clear cell carcinoma (Fig. 2).

Pathological anatomy examination from the left ovarian mass showed tissue composed of papillary, partly tubulocystic, consisting of a proliferation of anaplastic epithelial cells, with round nuclei, pleomorphic, hyperchromatic, partly eccentrically located, the cytoplasm is broad and clear. The distribution of hyaline globules is visible. The tumor grows invasively between the hyalinized stroma and penetrates the capsule. From right ovarian mass showed ovarian tissue with multiple corpus albicans. The distribution of hemosiderophages is visible. There were no visible signs of malignancy. The final results for pathological examinations are clear cell carcinoma (left ovarian mass) and endometriotic cyst (right ovarian mass).

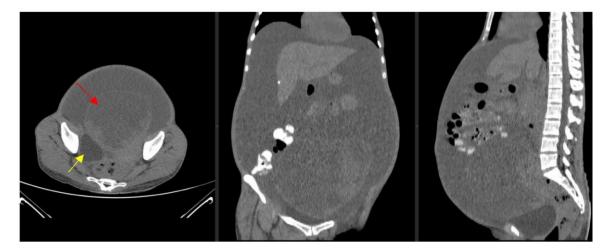


Fig 1. This figure show dextra ovarian mass (+/- 6,5 x 5 x 2 cm) which is endometriotic cyst (YELLOW ARROW), and also sinistra ovarian mass (+/- 14,5 x 13 x 9 cm) which is clear cell carcinoma (RED ARROW)

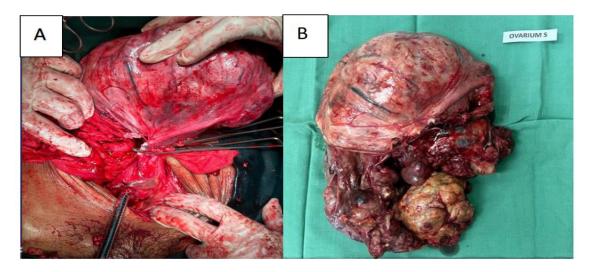




Fig. 2 A and B: Gross appearance of left ovarian mass with size $+/-14.5 \times 13 \times 9 \text{ cm}$; C: Gross appearance of right ovarian mass with size $+/-6.5 \times 5 \times 2 \text{ cm}$; and D: Ascites fluid from abdominal cavity to pelvic cavity +/-50 ml

DISCUSSION

The ectopic implantation of endometrial glands and stroma—functional tissue lining the uterus—outside of the uterine cavity is the hallmark of endometriosis, a chronic, estrogen-dependent disorder [11]. A higher risk of ovarian, endometrial, and breast cancer is linked to endometriosis. Predictive risk factors include growing older, being postmenopausal, having greater levels of CA 125, having a larger endometrioma, and having a chronic illness [12]. Endometriosis has been linked to microenvironmental variables necessary for malignant transformation, including oxidative stress, immune cell dysfunction, inflammation, steroid hormones, and stem cells; however, the precise carcinogenic process is yet unknown [13]. Breast cancer, endometrioid ovarian cancer, and endometrioid adenocarcinoma of the

endometrium may be linked to hyperestrogenism caused by overactivity of the aromatase enzyme. On the other hand, clear cell tumors show very little expression of estrogen receptors, are unaffected by estrogens, and may be associated with oxidative stress brought on by free iron from endometriomas. Malignancies linked to endometriosis have mutations in several genes, including p53, PTEN, ARID1A, KRAS, and CTNNB1 (Catenin-beta-1) [14].

The two most common histological subtypes of malignant endometriosis are clear-cell carcinoma and endometrioid carcinoma [15]. It has been established that endometriosis is more common in women with epithelial ovarian cancer than in the general population, particularly in endometrioid and clear cell types. Common genetic changes, including mutations in the bcl, p53, and PTEN genes, have been observed in both

neighboring endometriotic lesions and ovarian malignancies. These findings raise the possibility of a malignant genetic transition spectrum. Moreover, endometriosis has been linked to a persistent inflammatory condition that releases cytokines. These cytokines work in a complicated system where they can induce or suppress their own synthesis. They can also lead to uncontrolled mitotic division, development, and differentiation, migration, or apoptosis, which are processes that are comparable to those of cancer [16].

A hyperdense focus found inside an ovarian cyst on CT images is predictive of endometrioma and should assist in differentiating it from other pelvic masses [17]. When a woman's CT scan shows bilateral or multilocular ovarian cysts with thick walls and loculated ascites that are limited to the pelvic cavity with pelvic fat infiltrations, the diagnosis of a ruptured endometriotic cyst should be indicated [18].

Since it was originally recorded in 1954, ascites induced by endometriosis have been documented in about 60 cases, making it a unique condition. Furthermore, there aren't many reports of this kind of case in Caribbean literature. Surgical methods for treating ascites often do not maintain fertility. This is because, in women with increased serum cancer antigen (CA-125), ascites have been linked to gynecological cancers [19].

The presence of ovarian malignancy in the presence of pelvic endometriosis, unilateral or contralateral ovarian endometriosis, or histological evidence of the transition from benign to malignant endometriosis defines the diagnosis of endometriosis associated with ovarian carcinoma [10]. There were cystic tumors with solid areas in clear cell carcinoma. The majority of lesions were well-defined, oval, and unilocular. On a simple scan, the cystic or necrotic portion's CT value varied from 12 to 28 HU. The cystic masses' spherical, few solid protrusions had distinctly uneven enhancements following contrast [20].

CONCLUSION

It is uncommon for endometriosis to transform into ovarian clear cell carcinoma; nevertheless, it can occasionally coexist with pelvic or solitary ovarian endometriosis. When a big cystic mass with a solid component is discovered on a CT scan along with ascites, the differential diagnosis may be endometrial cyst and malignant ovarian mass.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

REFERENCES

- Quesada, J. et al. (2023) 'Endometriosis: A Multimodal Imaging Review', European Journal of Radiology, 158, p. 110610. doi:10.1016/j.ejrad.2022.110610.
- Mikhaleva LM, Davydov AI, Patsap OI, et al. Malignant transformation and associated biomarkers of ovarian endometriosis: a narrative review. *Adv Ther*. 2020;37(6):2580–2603. doi:10.1007/s12325-020-01363-5
- 3. Hsu AL, Khachikyan I, Stratton P. Invasive and noninvasive methods for the diagnosis of endometriosis. Clin Obstet Gynecol. 2010 Jun;53(2):413-9. doi: 10.1097/GRF.0b013e3181db7ce8. PMID: 20436318; PMCID: PMC2880548.
- Baek, I. K., Kim, H. S., Jeon, D. S., Park, Y. S., Kim, H. J., & Rhee, H. S. (1997). CT findings of endometrioma: Differential points from other benign complex cystic adnexal masses. *Journal of the Korean Radiological Society*, 37(4), 725. https://doi.org/10.3348/jkrs.1997.37.4.725
- Steinbuch SC, Lüß A-M, Eltrop S, Götte M, Kiesel L. Endometriosis-Associated Ovarian Cancer: From Molecular Pathologies to Clinical Relevance. International Journal of Molecular Sciences. 2024; 25(8):4306.
 - https://doi.org/10.3390/ijms25084306
- Matsumoto T, Yamazaki M, Takahashi H, et al. Distinct β-catenin and PIK3CA mutation profiles in endometriosis-associated ovarian endometrioid and clear cell carcinomas. Am J Clin Pathol. 2015:144:452–452.
- 7. Sambasivan S. Epithelial ovarian cancer: Review article. Cancer Treat. Res. Commun. 2022;33:100629. doi: 10.1016/j.ctarc.2022.100629
- 8. Stewart J, Cunningham N, Banerjee S.New therapies for clear cell ovarian carcinoma. International Journal of Gynecologic Cancer 2023;33:385-393.
- Gadducci A, Multinu F, Cosio S, Carinelli S, Ghioni M, Aletti GD. Clear cell carcinoma of the ovary: Epidemiology, pathological and biological features, treatment options and clinical outcomes. Gynecol Oncol. 2021 Sep;162(3):741-750. doi: 10.1016/j.ygyno.2021.06.033. Epub 2021 Jul 8. PMID: 34247767.
- Rodrigues S, Braga M, Félix A, Cunha TM. Clear cell carcinoma of the ovary: Clues for radiologists to perform a correct diagnosis. Curr Probl Diagn

- Radiol. 2024 Mar-Apr;53(2):271-279. doi: 10.1067/j.cpradiol.2023.10.003. Epub 2023 Oct 21. PMID: 37925237.
- 11. Tsamantioti ES, Mahdy H. Endometriosis. [Updated 2023 Jan 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK5677 77/
- 12. Dahiya, A., Sebastian, A., Thomas, A., George, R., Thomas, V., & Peedicayil, A. (2021). Endometriosis and malignancy: The intriguing relationship. *International Journal of Gynecology & Mamp; Obstetrics*, 155(1), 72–78. https://doi.org/10.1002/ijgo.13585
- Sun Y, Liu G. Endometriosis-associated Ovarian Clear Cell Carcinoma: A Special Entity? J Cancer. 2021 Sep 23;12(22):6773-6786. doi: 10.7150/jca.61107. PMID: 34659566; PMCID: PMC8518018.
- 14. Mogensen JB, Kjær SK, Mellemkjær L, Jensen A. Endometriosis and risks for ovarian, endometrial and breast cancers: a nationwide cohort study. Gynecol Oncol. 2016;143(1):87-92.
- 15. Bahall, V., De Barry, L. & Rampersad, A. Clear cell carcinoma arising from abdominal wall endometriosis—a report on two cases and literature review. *World J Surg Onc* **20**, 86 (2022). https://doi.org/10.1186/s12957-022-02553-x

- Nezhat, F., Datta, M. S., Hanson, V., Pejovic, T., Nezhat, C., & Nezhat, C. (2008). The relationship of endometriosis and Ovarian Malignancy: A Review. Fertility and Sterility, 90(5), 1559–1570. https://doi.org/10.1016/j.fertnstert.2008.08.007
- 17. Buy JN, Ghossain MA, Mark AS, Deligne L, Hugol D, Truc JB, Poitout P, Vadrot D. Focal hyperdense areas in endometriomas: a characteristic finding on CT. AJR Am J Roentgenol. 1992 Oct;159(4):769-71. doi: 10.2214/ajr.159.4.1326887. PMID: 1326887.
- 18. Lee YR. CT Imaging Findings of Ruptured Ovarian Endometriotic Cysts: Emphasis on the Differential Diagnosis with Ruptured Ovarian Functional Cysts. Korean J Radiol. 2011 Jan-Feb;12(1):59-65.
 - https://doi.org/10.3348/kjr.2011.12.1.59
- Bahall V, De Barry L, Harry SS, Bobb M. Gross Ascites Secondary to Endometriosis: A Rare Presentation in Pre-Menopausal Women. Cureus. 2021 Aug 10;13(8):e17048. doi: 10.7759/cureus.17048. PMID: 34522526; PMCID: PMC8427934.
- 20. Li X, Ye Z. Clear cell carcinoma of the ovary: multi-slice computed tomography findings. World J Surg Oncol. 2015 Apr 1;13:133. doi: 10.1186/s12957-015-0546-1. PMID: 25889109; PMCID: PMC4395879