

eISSN : 2579-8324

pISSN : 2579-8323

Address for Correspondence:Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127**Website:**<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>**CASE REPORT****Ovarian Clear Cell Carcinoma Which Detected in Ascitic Fluid Smear**Muthia Kamelia¹, Aswiyanti Asri¹, Syamel Muhammad²

Affiliation authors: 1. Anatomical Pathology Department, Faculty of Medicine, Andalas University, Dr. M. Djamil Central General Hospital Padang, West Sumatera, Indonesia; 2. Sub Division of Gynecological Oncology, Obstetrics and Gynecology Department, Faculty of Medicine, Andalas University, Dr. M. Djamil Central General Hospital Padang, West Sumatera, Indonesia

Correspondence to: Muthia Kamelia, email: muthiakamelia@gmail.com, Hp: 085355646803

Abstract

Objective: To report the case of ovarian clear cell carcinoma with involvement of both ovaries and metastatic to ascitic fluid and the label mass in the bladder

Method: Case Report

Case: A 51 years old female presented with enlarging abdominal with gradual pain. The result of transabdominal sonography were multiple cysts with solid mass, suspected solid cystic ovarian neoplasm and ascites. The patient prepared for laparotomy; optimal debulking surgery, mass resection from bladder. Cytology examination was performed from ascitic fluid and it was confirmed by histopathology examination.

Result: Microscopic features on cytology examination of ascitic fluid smear was suggest carcinoma. Histological examination was confirmed the diagnosis and the result was ovarian clear cell carcinoma.

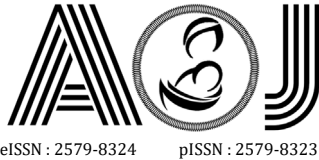
Discussion: Ovarian clear cell carcinoma is a rare subtype of epithelial ovarian cancer and comprises about 5-10% of ovarian carcinomas. Clear cell carcinoma tends to occur in the fifth to seventh decades. Cytology examination showed the cellular smear consists of groups of epithelial cells with large nucleus, hyperchromatic, pale-staining, vacuolated cytoplasm. There is also eosinophilic, extracellular substance. The presence of a tumor in ascitic fluid and the label mass in the bladder can categorize become IIB. This determined based on the FIGO's ovarian tumor staging system.

Keywords: ovarian clear cell carcinoma; ascitic fluid.

INTRODUCTION

Clear cell carcinoma (CCC) of the ovary is a malignant tumour composed of an admixture of clear, eosinophilic and hobnail cells, displaying a combination of tubulocystic, papillary and solid patterns.¹ Clear cell carcinoma is a rare subtype of epithelial ovarian cancer (EOC) and comprises about 5–10% of ovarian carcinomas.² Clear cell carcinoma mostly occurs in the fifth to seventh decades of life. About 50-70% have associated with pelvic endometriosis and/or endometriosis involving the ovary (25%).³⁻⁵ Patients typically present with symptoms related to an enlarging abdominal mass, 2-10% associated with a paraneoplastic syndrome consisting of hypercalcemia and 20-45% with venous thromboembolism.^{4,6,7} The cytomorphological characteristic of clear cell carcinoma of the ovary were described in peritoneal fluid and ascitic samples. The major cytological features to be considered were finding of clear cell and

Received : June 9th, 2021Accepted : June 29th, 2021Correspondence : Muthia Kamelia, email: muthiakamelia@gmail.com



eISSN : 2579-8324

pISSN : 2579-8323

Address for Correspondence:Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127**Website:**<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

eosinophilic globular cytoplasm, hyaline extracellular substances with formation of “raspberry bodies”. The ‘raspberry’ body or ‘mirror ball pattern’ is a cluster of tumour cell with eosinophilic, hyaline globular substance in the centre. In all reported studies, this eosinophilic substance is clearly visible only Giemsa-stained samples.⁵ Peritoneal cytology has an important role in the diagnosis and staging of abdominal and gynaecologic neoplasms. A positive peritoneal fluid for ovarian carcinoma will upstage the diagnosis to an International Federation of Obstetricians and Gynaecologists (FIGO) to become stage IC. The presence of grossly evident peritoneal dissemination can be confirmed by histopathologic samples.⁸ The following will describe a case report of ovarian clear cell carcinoma which detected in ascitic fluid on a 51 years old female patient. In this patient, a cytological examination of ascitic fluid was confirmed by histopathological examination of the tumour tissue.

METHODS

A 51 years old female patient was admitted to the emergency department of Dr. M. Djamil Padang Hospital on September 26, 2020 at 6.30 PM with the main complaint of weakness. From recent illness history, the patient complained of no appetite since 2 weeks before admission to the hospital, vomiting, a little urinating and having irregular bowel movements. The patient also feels enlarging abdominal alternating abdominal pain since 1 month before entering the hospital. There is no bleeding from genital, no history of pain during intercourse. The patient experienced a drastic weight loss since 2 month ago. She had no had her menstruation since 5 years ago. The patient is married but does not have children.

From her past medical history, she didn't had history of heart disease, lung disease, hypertension and diabetes mellitus. From her medical history, the patient has had alternative treatment and once to the Obstetric Gynaecologic Specialist. The patient underwent an ultrasound examination of the Abdomen on September 19, 2020 at the Pariaman Regional General Hospital with result: multiple cysts with solid mass, suspected solid cystic ovarian neoplasm, ascites, thickening of the gallbladder wall is suspected of hypoalbuminemia. Initial view of left Chronic Kidney Disease (Fig 1.1). The patient also check tumour marker CA125 on September 22, 2020 with results was 385,17 U/ml (0-35 U/ml). From family history, she didn't have history of hereditary, infectious and psychiatric diseases.

Physical examination showed the general state was moderate, compos mentis cooperative, blood pressure was 130/70 mmHg, pulse rate was 88x/minute, respiratory rate was 20x/minute, temperature was 36,6°C, conjunctiva was anemic, no icteric of sclera. Thoracic examination: cardiomegaly (-), and lung: vesicular, rhonchi -/-, wheezing -/-. Abdominal examination: inspection: distended, like a frog's stomach, shifting dullness (+), pressure pain (+), loose pain (-), scar (-). Extremities: edema (-). From the laboratory test in the Emergency Room, she had haemoglobin 8,4 mg/dl, haematocrit 26%, leucocytes 11.190/mm³, platelets 555.000/mm³. Prothrombin Time/Activated Partial Thromboplastin

Received : June 9th, 2021Accepted : June 29th, 2021Correspondence : Muthia Kamelia, email: muthiakamelia@gmail.com

Time: 10,3/35,7 second, albumin/globulin: 2,9/3,8 gr/dl. Urea/creatinine: 85/3,8 mg/dl. Randomized Blood Sugar 80 mg/dl. Electrolyte: Sodium/Potassium/Chloride: 123/4,6/88 mEq/L. Calcium 9,4 mg/dl. Working diagnosed was cystic ovarian neoplasm suspect Malignancy + Anemia + hypoalbuminemia + Acute Kidney Injury + electrolyte imbalance. Therapy: monitor general condition and vital sign, IVFD RL 20 drops per minute, inj. 2x50mg ranitidine and internal medicine consultation.



Figure 1. Abdominal Ultrasonography

The results of the internal medicine consultation obtained a diagnosis of mild anemia et causa chronic disease, hypoalbuminemia et causa malnutrition, stage III Acute Kidney Injury (DD/ Acute on Chronic Kidney Disease), low intake et causa hyponatremia. Therapy: IVFD NaCl 0.9% 8 hours/kolf, bicarbonate natrium 3x500mg (peroral), folic acid 1x5mg (peroral), check electrolytes and creatinine, urea every three days, check peripheral blood smears if there are no signs of haemolytic, 1 bag PRC transfusion is allowed per day, target Haemoglobin > 10gr/dl. Check urinalysis and consultation with clinical nutrition. Patients are treated together.

After being given a blood transfusion of 3 bags and 1 kolf of albumin infusion, the patient planned optimal debulking surgery. The patient underwent exploratory laparotomy on October 5 at 06.00 PM and on October 6, 2020 a reddish sample of 10cc cytological ascitic fluid was received. From cytology examination, it shows that the cellular smear consists of groups of epithelial cells with a large nucleus (increased N/C ratio), hyperchromatic, clear cytoplasm, the presence of intracytoplasmic vacuoles with several nuclei pushed aside. There was also eosinophilic, extracellular substance. Cytopathological diagnosis was carcinoma metastases to ascitic fluid (Fig. 1.2).

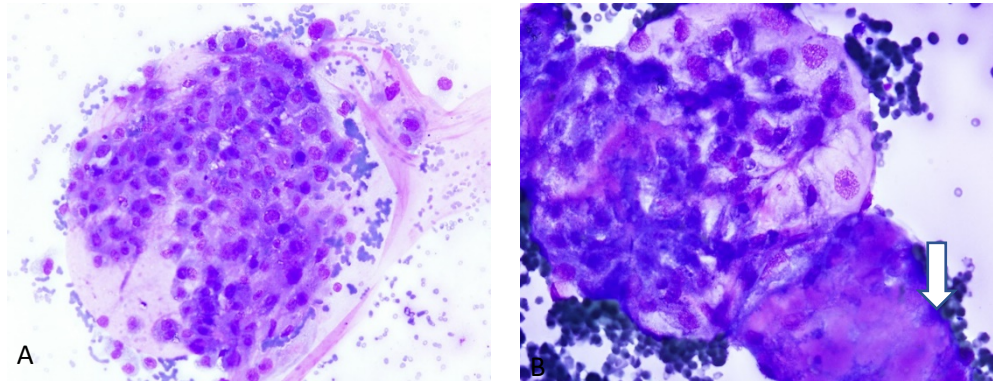


Figure 2. Cytology of tumours. A) it shows a cluster of epithelial cells with a large nucleus (increased N/C ratio), hyperchromatic, clear cytoplasm, the presence of intracytoplasmic vacuoles with several nuclei pushed aside, 20x, Giemsa. B) eosinophilic, extracellular substance (arrow), 40x, Giemsa.

Histopathological tissue from 4 tissue pockets that were received. There were from right ovary label, left ovary label, mass on the bladder label and uterine label (Figure 3).



Figure 3. Macroscopic of tumour. A) the right ovary: section of brownish-white ovarian tissue that has been split, semisolid, 12x8x4 cm in size, cut of surface is a multiple cavities fluid filled cyst with white to brown mass, diameter of cavity in range of 1-7 cm, some thick and thin wall. B) the left ovary: a piece of brownish white ovarian tissue, 6x4x2 cm in size, a cut of surface of a cyst with multiple cavities filled with clear fluid, there is a brownish white mass, 0,5-5 cm in diameter, with thin and thick walls. C) the uterine and cervix: a piece of uterine tissue with a cervix with both adnexal, measuring 8,5x7,5x4cm, cut of surface: uterine cavum was distended with diameter 6 cm and thinning uterine wall.

Microscopic features (Fig 1.4) from the label of the right ovary and left ovary were pieces of ovarian tissue in the form of a cyst wall, the surface is covered with proliferating epithelial cells with a polygonal shape, clear-eosinophilic cytoplasm, large nucleus, partly hyperchromatic, partly vesicular, prominent nucleoli, mitosis can be found, some cells with a hobnail appearance. These cells were arranged to form papillary structures, tubulocystic and solid and infiltrating between the fibrocollagen stroma. There was also focus necrosis and bleeding. From the label of the mass in the bladder, microscopic there were 2 pieces of tissue

with fibrocollagen stroma consist of proliferating tumor cells as in the right and left ovary. There was no visible bladder mucosa. From the endometrium, microscopic there was endometrial tissue with a dense stroma consisting of atrophic endometrial glands, glands lined with columnar epithelium. From the cervix, microscopic, there was pieces of cervical tissue with a surface covered with columnar epithelium, nuclei in basal and clear cytoplasm. In the fibrocollagen stroma beneath it, there are glands that are cystically dilated, lined with columnar-flat epithelial cells. From the parametrium, microscopic there is a tissue consisting of smooth muscle tissue, loose fibrocollagen tissue and a little fatty tissue containing capillaries. No malignant tumor cells were seen.

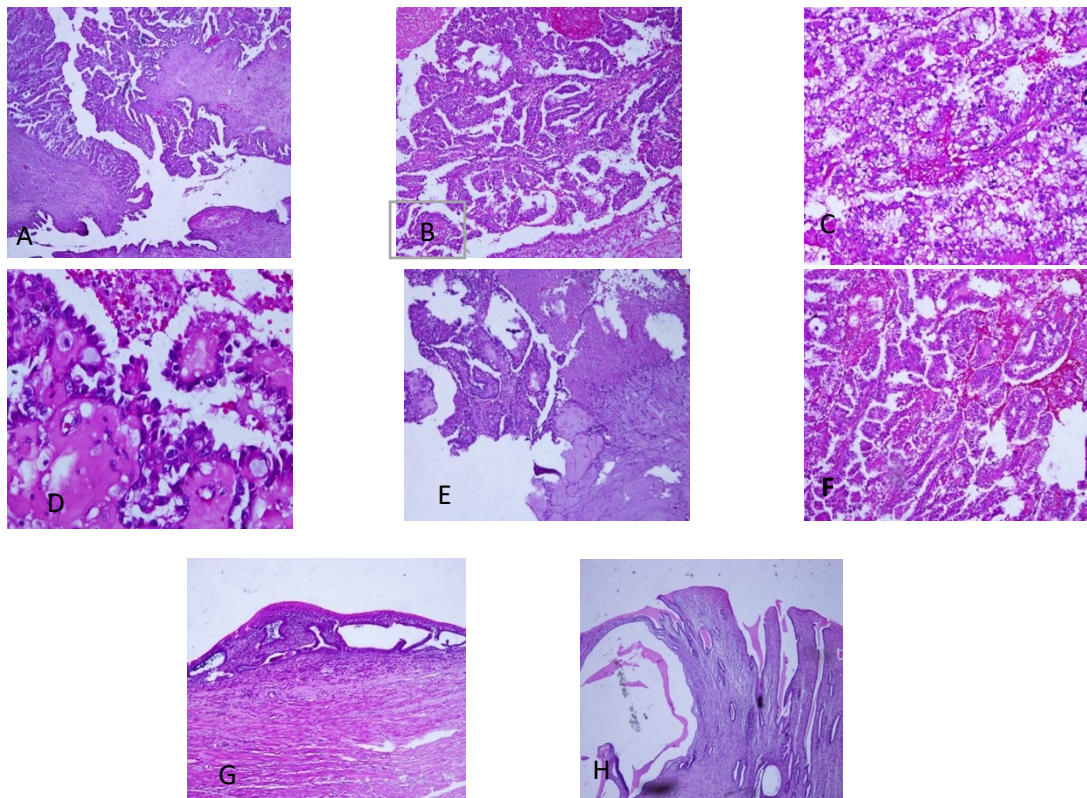
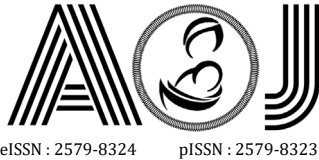


Figure 4. Microscopic of Tumor. The tumors show a papillary pattern (A, HE, 100x), tubulocystic pattern (B, HE, 200x), and solid pattern (C, HE, 200x). The neoplastic cells are consist of clear cell and hobnail cell, polygonal, with a clear-eosinophilic cytoplasm, large nucleus, partly hyperchromatic, partly vesicular with prominent nucleoli (D, HE, 400x). The same microscopic features are also found on left ovary (E, HE, 100x) and from label of mass in the bladder (F, HE, 200x). The microscopic features of uterine corpus show an endometrial tissue with a dense stroma consisting of atrophic endometrial glands (G, HE, 100x). On the cervix, there is a piece of cervical tissue with a surface covered with columnar epithelium, nuclei in basal, with clear cytoplasm. There are glands that are cystically dilated.



eISSN : 2579-8324

pISSN : 2579-8323

Address for Correspondence:Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127**Website:**<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>**RESULTS**

The conclusion from cytopathologic examination was carcinoma metastases to ascitic fluid and the histopathologic examination was Bilateral Ovarian Clear Cell Carcinoma, High grade minimum PT2bNxMx with a tumor involves the tissue on the mass label in the bladder. Case of ovarian clear cell carcinoma in this patient were categorized as stage IIB according to the FIGO's ovarian tumor staging system, where there is involvement of one or both ovaries with pelvic extension (below the pelvic brim).

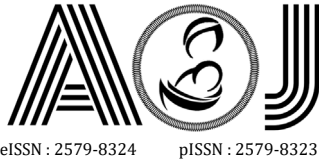
DISCUSSION

A case of 51 years old female patient was reported, she was diagnosed histopathological as an ovarian clear cell carcinoma and from cytology examination of ascitic fluid which showed a carcinoma. Ovarian clear cell carcinoma is a rare subtype of epithelial ovarian cancer and comprises about 5–10% of ovarian carcinomas.² Clear cell carcinoma tends to occur in the fifth to seventh decades, with mean patient age is 56 years.^{4,5} The similar studies were reported by Joo et al from 48 women patients ovarian CCC with mean age 53 years.² Tang et al also reported a study from 130 women patient with ovarian clear cell carcinoma, the mean age at diagnosis was 51,54 years (range 31-75 years).⁹

The patient presented with complaint enlargement of abdomen with gradual pain and loss of weight. Similar with study that conducted by Tang et al, 38% (50 cases) had abdominal distention/mass, 31% (43 cases) feel abdominal pain.⁹ The most common symptom of ovarian cancer is enlarged abdomen accompanied by pain. These symptoms are caused by an enlargement effect tumour mass and mass compression on the surrounding organ structured. Other symptoms which can also accompany is weight loss, decreased appetite and fatigue. This caused by the cachexia cancer process involves a series of cytokine formation processes by cancer cells.¹⁰

In this patient, after transabdominal sonography was found ascites. Ascites is the excess accumulation of fluid in the peritoneal cavity. The peritoneal membrane is rich in lymphatic tissue. The lymphatic system circulates fluid, proteins and other macromolecules back into the vascular circulation. These lymphatic portals are particularly abundant on the omental and sub-diaphragmatic peritoneal surfaces and their obstruction by tumour cells has been suggested as a mechanism for ascites. In addition, malignant ascites has a high protein concentration that is secondary to increased capillary permeability. This decreases the plasma to peritoneal oncotic pressure difference, so that the direction of fluid flow is into the peritoneal cavity.¹¹ The studies from Joo et al. and Tang et al. was found ascites in 44 cases (60,6%) and 52 cases (40%), respectively.^{2,9}

Received : June 9th, 2021Accepted : June 29th, 2021Correspondence : Muthia Kamelia, email: muthiakamelia@gmail.com



eISSN : 2579-8324

pISSN : 2579-8323

Address for Correspondence:Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127**Website:**<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

From cytology examination in this case showed the cellular smear consists of groups of epithelial cells with a large nucleus (increased N/C ratio), hyperchromatic, clear cytoplasm, vacuoles with several nuclei eccentric. There is also eosinophilic, extracellular substance. According to the literature, the cytology features of ovarian clear cell carcinoma is the presence of the cells with abundant, pale-staining, finely granular, and vacuolated cytoplasm and eosinophilic, globular, and hyaline extracellular substance with formation of so called raspberry bodies.¹² The similar study was also reported by Vrdoljak-Mozetic et al, which found 4 cases (33,3%) of 12 samples from peritoneal fluid showing “raspberry bodies”.⁵

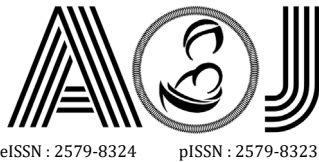
It was confirmed by histopathology examination, from microscopic there is pieces of ovarian tissue in the form of a cyst wall, the surface is covered with proliferating epithelial cells with a polygonal shape, with a clear eosinophilic cytoplasm, a large nucleus, partly hyperchromatic, partly vesicular, prominent nucleoli, mitosis can be found, some cells with a hobnail appearance. These cells are arranged to form papillary structures, tubulocystic and solid and grow to infiltrate between the connective tissue stroma. There is also focus necrosis and bleeding. This histopathological finding was suitable with literatures, CCC displays tubulocystic, papillary, and solid architecture, frequently admixed. The tubulocystic pattern exhibits tubules and cyst, sometimes with dense eosinophilic secretion, lined by a single layer of hobnail, cuboidal, or attenuated and deceptively benign-appearing cells. The papillary pattern comprises simple, non-branching papillae with round stromal cores seen in cross-section. Stromal hyalinization is frequent. The solid pattern of CCC is characterized by sheets of polyhedral cells with abundant, clear cytoplasm separated by delicate fibrovascular septa or dense fibrotic stroma. Nuclei are large and monomorphic with rounded to angulated contour, hyperchromatic, prominent nucleoli and (rarely) nuclear pseudoinclusions.^{4,6,7,12-14}

The presence of a tumour in ascitic fluid or peritoneal wash and also tumor cells on the mass label in the bladder that refers to pelvic extension made categorize tumour become T2b (FIGO stage IIB). This is determined based on TNM classification correspond to the FIGO's ovarian tumour staging system. About 54-69% of ovarian CCC present in FIGO stage I and 9-17% in stage II.¹⁴ In this case, ovarian CCC occurred in both ovaries, this is in accordance with the literature that 8% of ovarian CCC are bilateral with 4% of stage I cases are bilateral. The 5 years survival rate for patient with stage I ovarian CCC is 69%, stage II 55%, stage III 14% and stage IV 4%.^{7,14}

CONCLUSION

We have reported a case of malignancy in a 51 years old female patient diagnosed with ovarian clear cell carcinoma. Microscopic features on cytology examination of peritoneal fluid suggests carcinoma. Histological examination was performed to confirm the diagnosis, and the result is ovarian clear cell carcinoma. Peritoneal cytology has an important role in the

Received : June 9th, 2021Accepted : June 29th, 2021Correspondence : Muthia Kamelia, email: muthiakamelia@gmail.com



eISSN : 2579-8324

pISSN : 2579-8323

Address for Correspondence:Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127**Website:**<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

diagnosis and staging of gynecologic neoplasm. Peritoneal washing is recommended for patients who undergo laparotomy for gynecologic neoplasm. The “raspberry bodies” are the major cytological characteristics of CCC.

REFERENCES

1. Damiani D, Suci V, Genestie C, Vielh P. Cytomorphology of ovarian clear cell carcinomas in peritoneal effusions. *Cytopathology*. 2016 Dec;27(6):427–32.
2. Joo HL, Shin YR, Rha SE, Park CS, Shim DJ, Kim K. Preoperative discrimination of tumour stage in clear cell carcinoma of the ovary using computed tomography and magnetic resonance imaging. *Eur J Radiol*. 2018;109:19–26.
3. Moriya T, editor. *Pathology of female cancers: precursor and early-stage breast, ovarian and uterine carcinomas*. Singapore: Springer Singapore; 2018. 211 p.
4. Nucci MR, Oliva E, editors. *Gynecologic pathology*. Edinburgh: Churchill Livingstone; 2009. 710 p.
5. Vrdoljak-Mozetič D, Stanković T, Krašević M, Verša-Ostojić D, Štemberger-Papić S, Rupčić S. Intraoperative cytology of clear cell carcinoma of the ovary. *Cytopathology*. 2006;17(6):390–5.
6. Crum CP, Laury AR, Hirsch MS. *Gynecologic and obstetric pathology: high-yield pathology*. Philadelphia: Elsevier; 2016. 821 p.
7. Mutter GL, Prat J, editors. *Pathology of the female reproductive tract*. 3., rev. ed. London: Churchill Livingstone; 2014. 873 p.
8. Bibbo M, Wilbur DC. *Comprehensive cytopathology*. London etc.: Elsevier Health Stock; 2015. 1074 p.
9. Tang H, Liu Y, Wang X, Guan L, Chen W, Jiang H, et al. Clear cell carcinoma of the ovary: Clinicopathologic features and outcomes in a Chinese cohort. *Medicine*. 2018;97(21):e10881.
10. Martin ML, Halling K, Eek D, Reaney M. “Lower abdominal pains, as if I was being squeezed...in a clamp”: a qualitative analysis of symptoms, patient-perceived side effects and impacts of ovarian cancer. *Patient*. 2020;13(2):189–200.
11. Kipps E, Tan DSP, Kaye SB. Meeting the challenge of ascites in ovarian cancer: new avenues for therapy and research. *Nat Rev Cancer*. 2013;13(4):273–82.
12. WHO classification of tumours editorial board, editors. *WHO classification of Tumours: Female genital tumours*. 5th Ed. 2020. 631 p.
13. Goldblum JR, Lamps LW, McKenney JK, Myers JL, Ackerman LV, Rosai J, editors. *Rosai and Ackerman’s surgical pathology*. Eleventh edition. Philadelphia, PA: Elsevier; 2018. 1025–1040 p.

Received : June 9th, 2021Accepted : June 29th, 2021Correspondence : Muthia Kamelia, email: muthiakamelia@gmail.com



eISSN : 2579-8324

pISSN : 2579-8323

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL**Address for Correspondence:**Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127**Website:**<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

14. Kurman RJ, Hedrick Ellenson L, Ronnett BM, editors. Blaustein's pathology of the female genital tract. Cham: Springer International Publishing; 2019. 1472 p.
15. Oda K, Hamanishi J, Matsuo K, Hasegawa K. Genomics to immunotherapy of ovarian clear cell carcinoma: Unique opportunities for management. *Gynecol Oncol.* 2018 Nov;151(2):381-389. doi: 10.1016/j.ygyno.2018.09.001. Epub 2018 Sep 12. PMID: 30217369; PMCID: PMC7526052.
16. Fadare O, Parkash V. Pathology of Endometrioid and Clear Cell Carcinoma of the Ovary. *Surg Pathol Clin.* 2019 Jun;12(2):529-564. doi: 10.1016/j.path.2019.01.009. PMID: 31097114.
17. Fujiwara K, Shintani D, Nishikawa T. Clear-cell carcinoma of the ovary. *Ann Oncol.* 2016 Apr;27 Suppl 1:i50-i52. doi: 10.1093/annonc/mdw086. PMID: 27141072.
18. Fujiwara K, Shintani D, Nishikawa T. Clear-cell carcinoma of the ovary. *Ann Oncol.* 2016 Apr;27 Suppl 1:i50-i52. doi: 10.1093/annonc/mdw086. PMID: 27141072.
19. Mabuchi S, Sugiyama T, Kimura T. Clear cell carcinoma of the ovary: molecular insights and future therapeutic perspectives. *J Gynecol Oncol.* 2016 May;27(3):e31. doi: 10.3802/jgo.2016.27.e31. PMID: 27029752; PMCID: PMC4823362.
20. Mabuchi S, Sugiyama T, Kimura T. Clear cell carcinoma of the ovary: molecular insights and future therapeutic perspectives. *J Gynecol Oncol.* 2016 May;27(3):e31. doi: 10.3802/jgo.2016.27.e31. PMID: 27029752; PMCID: PMC4823362.

Received : June 9th, 2021Accepted : June 29th, 2021Correspondence : Muthia Kamelia, email: muthiakamelia@gmail.com