Gynecologic Oncology Reports 53 (2024) 101370

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Primary peritoneal clear cell carcinoma arising in the setting of abdominal wall Endometriosis: A case report and review of the literature

Cameron M. Harris [a,*], Miller P. Singleton [b], Theresa Samulski [c], Leslie H. Clark [d]

[a] University of North Carolina School of Medicine, Chapel Hill, NC 27599, USA
[b] Department of Obstetrics and Gynecology, University of North Carolina, Chapel Hill, NC 27599, USA
[c] Department of Pathology, University of North Carolina, Chapel Hill, NC 27599, USA
[d] Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of North Carolina School of Medicine, Chapel Hill, NC 27599, USA

ARTICLE INFO

Keywords:
Clear cell carcinoma
Primary peritoneal cancer
Endometriosis

1. Introduction

Endometriosis is an inflammatory disease characterized by functioning endometrial tissue outside of the uterus. The abdominal wall is a common site of extraperitoneal endometriosis. The probability of developing surgical scar endometriosis is approximately 0.03–1 % (Castagnino et al., 2021). Hypothesized pathogenesis of abdominal wall endometriosis is iatrogenic transplantation of endometrial tissue during a surgical procedure such as a cesarean delivery, laparotomy, laparoscopy, amniocentesis, or inguinal herniorrhaphy (Behbehani et al., 2020) Table 1.

Malignant transformation of abdominal wall endometriosis is rare, occurring at an incidence of 0.3–1.0 %.(Castagnino et al., 2021) Resultant adenocarcinomas are slow growing, presenting on average 21 years after initial surgery.(Bahall et al., 2022) Approximately 80 % of endometriosis-associated malignancies locate to the ovary, while the remaining 20 % are in extra-gonadal sites.(Giannella et al., 2020) The most common subtypes of extra-peritoneal malignant endometriosis are endometrioid carcinoma (69.1 %) and sarcoma (25 %), with clear cell carcinoma comprising only 4.5 % of cases.(Bats et al., 2008) In this report, we describe the case of a patient who was found to have primary peritoneal clear cell carcinoma arising from abdominal wall endometriosis.

2. Case

The patient is a 46-year-old female who underwent a total laparoscopic hysterectomy and bilateral salpingectomy for abnormal uterine bleeding 6 years prior to her current presentation. Intraoperative findings were notable for significant abdominal wall endometriosis, but pathology from surgery was all benign. The patient presented to an orthopedic clinic with 2 weeks of acute-on-chronic right-sided lower back pain and abdominal discomfort. Work up included magnetic resonance imaging (MRI) of the lumbar spine which partially revealed a complex abnormal signal of the right upper pelvis. Subsequent computed tomography (CT) of the abdomen and pelvis with contrast revealed a right lower quadrant (RLQ) mass measuring 4.8 x 5.1 x 4.6 cm with adjacent small volume ascites. The mass appeared to abut the right iliacus and right oblique muscles and exert mass effect on the ascending colon (Fig. 1). Notably, no suspicious adnexal lesions were identified.

At a general surgery consult two weeks later, the patient reported abdominal pressure and soreness with a palpable RLQ mass. She otherwise denied night sweats, fevers, weight loss, lymphadenopathy, or bowel changes. The patient underwent ultrasound-guided core biopsy which revealed metastatic high-grade carcinoma consistent with clear-cell carcinoma of gynecologic origin. Immunohistochemistry demonstrated positive CK7, PAX8, Napsin, weak nonspecific staining with inhibin, and wild-type pattern p53 and was negative for CK20, CDX2, TTF-1, estrogen receptor, P16, WT-1, and calretinin. Tumor markers obtained included CA125 and CA19-9 which were elevated at 70 and

* Corresponding author at: Cleveland Clinic Foundation, Department of Obstetrics and Gynecology, 9500 Euclid Avenue, Cleveland, OH 44195.
E-mail address: harrisc40@ccf.org (C.M. Harris).

https://doi.org/10.1016/j.gore.2024.101370
Received 13 January 2024; Received in revised form 13 March 2024; Accepted 17 March 2024
Available online 19 March 2024

47.32, respectively. The patient was subsequently referred to Gynecologic Oncology. At her initial consult, physical exam was notable for a soft, nondistended, nontender abdomen with a fixed RLQ mass 2 cm medial to the anterior superior iliac spine (ASIS), no lymphadenopathy, normal appearing vagina, and no discrete adnexal fullness. She underwent an exploratory laparotomy, bilateral oophorectomy, appendectomy, omental biopsy, and right pelvic tumor resection for a complete surgical cytoreduction. Intraoperative findings were notable for a 6 cm right abdominal wall mass overlying the iliacus and lateral edge of psoas muscles and femoral nerve with close involvement of the internal oblique muscles laterally. There was no evidence of colonic involvement. The appendix was normal but contained endometriosis and was adherent to the right ovary. Her postoperative course was uncomplicated, and she was discharged on postoperative day one.

Final pathology of the abdominal wall mass confirmed clear cell adenocarcinoma of gynecologic origin involving fibroadipose tissue and associated skeletal muscle. All surgical margins were negative. Further immunohistochemical evaluation was performed and demonstrated tumor cells that were positive for CK7, PAX8, Napsin A, and P504S. Tumor cells were negative for WT1 and ER. P53 demonstrated a wild-type staining pattern. MLH1, MSH2, PMS2 and MSH6 were intact. Endometriosis involved the peritoneum and appendix but was not intimately associated with the abdominal wall mass. Bilateral ovaries were benign (Fig. 2). Given the clinical history of endometriosis and peritoneal involvement, findings were compatible with clear cell adenocarcinoma of primary peritoneal origin arising in the setting of endometriosis which clinically appeared to be arising near a trocar site from her prior laparoscopic hysterectomy.

The case was discussed at a multidisciplinary tumor board and staged as a FIGO Stage IIIC clear cell carcinoma of primary peritoneal origin with an R0 primary cytoreductive surgery. The patient was recommended for 6 cycles of platinum/taxane/bevacizumab therapy with consideration of radiation for local control. She received three cycles of adjuvant carboplatin, paclitaxel, and bevacizumab at which point she declined additional cytotoxic therapy. She underwent external beam radiation for a total of 4500 cGy over 5.5 weeks. Her treatment was complicated by grade 3 neutropenia which resolved spontaneously. She entered post-treatment surveillance. Germline genetic testing revealed a variant of uncertain significance (VUS) in the ATM gene. Somatic tumor testing revealed multiple mutations. Of those potentially actionable, an ATM slice site mutation at 2124 + 1G > T and PIK3CA amplification were noted. Other findings included CCND3 amplification, FGF12

Table 1
Literature review for cases of clear cell carcinoma arising from abdominal wall endometriosis.

Author/ Year	Tumor Marker	IHC	Treatment	Pelvic RT	Follow-up Outcome
Bahall 2022	CA125 (1200 U/mL), CA15-3 (425.8 U/mL), CEA (10.2 U/mL)	+ CK7, CK20, ER, p53 - WT-1	Cytoreductive surgery; 6 cycles paclitaxel and carboplatin	No	NED at 32 months post-treatment
	Not Reported	+ CK7, PAX8 - ER, WT-1, CK20	Surgical resection including lymphadenectomy and BSO; 6 cycles paclitaxel and carboplatin	No	Recurrence following 6 cycles chemotherapy
Castagnino 2021	CEA (1.8), CA19-9 (84), CA 125 (49.8)	+ PAX8, Ber Ep4, CK7 - WT-1, ER	Total annex hysterectomy with lymphadenectomy; 6 cycles carboplatin and paclitaxel plus bevacizumab	No	Not Reported
Gianella 2020	Not Reported	Not Reported	Front-line chemotherapy with 8 cycles carboplatin and paclitaxel weekly; 3 cycles gemcitabine; pegylated liposomal doxorubicin	Yes for pelvic skeletal metastases	Death after 7 months
Behbahani 2019	Not Reported	Not Reported	Mass resection, partial anterior bladder cyctectomy, BSO; 2 cycles liposomal doxorubicin followed by gemcitabine	No	Not Reported
Gentile 2017	Normal CA 125, CA 19–9, CEA, alpha-fetoprotein	+ D AE1AE3, CK7 - CD34, CK20, ER, WT-1, vimentin	Mass resection, lymphadenectomy of inguinal and external iliac chains	No	NED at 8 months postoperatively
Marques 2017	Normal CA 125	Not Reported	Mass resection, hysterectomy, bilateral oophorectomy; 6 cycles carboplatin and paclitaxel	No	NED at 36 months
Ruiz 2015	Not Reported	Not Reported	TAH, BSO, mass resection; 6 cycles carboplatin and paclitaxel	Yes after mass recurrence at 6 months	6 months following TAH/BSO/mass resection and adjuvant chemo with new mass treated with targeted radiation. Follow-up CT following radiation with resolution of mass
	Elevated CEA (96.5) and CA125 (81), normal CA 19–9	Not Reported	Mass excision, TAH, BSO, bilateral inguinal and internal iliac lymphadenectomy	Yes	NED without reported follow-up time
Liu 2014	Normal CA125 (22.1)	Not Reported	Mass excision, partial bladder excision, hysterectomy, bilateral adnexectomy, omentectomy, lymph node dissection; 3 cycles carboplatin and paclitaxel; refused further chemo and pursued Chinese herbal therapy	No	Recurrence after 10 months with death at 1 year
Bats 2007	Not Reported	Not Reported	3 cycles carboplatin and paclitaxel followed by total hysterectomy with BSO	No	Right external iliac node metastasis, refuses further treatment with radiation therapy
Alberto 2006	Normal CA-125	+ CAM 5.2, cytokeratin 7 - cytokeratin 20, vascular and mesothelial markers	Wide local excision of mass; 6 cycles of taxol/carboplatin	Yes	Not Reported

NED (no evidence of disease), TAH (total abdominal hysterectomy), BSO (bilateral salpingo-oopherectomy.

amplification – equivocal, GATA6 amplification, PRKC1 amplification, RAD21 amplification – equivocal, SGK1 alteration, TERC amplification and VEGFA amplification. Loss of heterozygosity score was 9.1 %. The tumor was negative for microsatellite instability, and PDL1 expression negative. She has been followed with tumor markers and serial CT scans since therapy and remains without evidence of disease at 6 months of post-treatment follow up.

3. Discussion

Sampson et al. defined three criteria for diagnosing endometriosis-derived neoplasms: endometriosis in proximity to the neoplasm, absence of another primary site neoplasm, and histologic evidence of endometrial origin.(Sampson, 1925) However, clinical suspicion for endometrial origin is high if there is co-existence of endometriotic tissue and carcinoma with glandular transformation given the possibility of sampling error or replacement of endometrial tissue with malignancy. While the pathophysiology remains unclear, some studies imply oxidative stress can lead to epigenetic alterations which predispose cells to malignant transformation.(Scutiero et al., 2017) Risk factors include unopposed or excess estrogen, exposure to carcinogens or cocarcinogens (including dioxin and polychlorinated biphenyls), and genetic anomalies.(Bats et al., 2008; Alberto et al., 2006) A study by Wiegand et al. found that the tumor-suppressor gene ARID1A is frequently disrupted in ovarian clear cell (46 %) and endometrial (30 %) carcinomas and may contribute to transformation of endometriosis into cancer.(Wiegand, 2010) While the case presented did not include an ARID1A mutation, the contribution of her germline VUS in ATM is unclear.

3.1. Patient presentation

Abdominal wall clear cell adenocarcinoma is similar to other cancers of the female reproductive tract; all are deeply invasive and generally carry a poor prognosis.(Bahall et al., 2022) Patients often present with nonspecific symptoms related to mass effect of the tumor which can be mistaken for benign conditions such as endometriosis, hernia, abscess, or hematomas. Premenopausal women may experience cyclical abdominal pain which reflects hormonally active endometriotic foci.

Review of the literature suggests that common presenting symptoms in this population include an abdominal wall mass, nonspecific pelvic pain, or a long-standing history of endometriosis or significant dysmenorrhea. Previous cesarean delivery occurred in 11 of 12 evaluated cases.(Bahall et al.,2022;Bats et al.,2008;Behbehani et al., 2020; Castagnino et al.,2021;Giannella et al.,2020);(Alberto et al., 2006; Wiegand, 2010; Gentile et al., 2018; Marques et al., 2017; Ruiz et al., 2015; Liu et al., 2014) Exam findings often consisted of a palpable large, immobile, and nontender mass arising from a previous incision site and without identified lymphadenitis. Imaging typically demonstrates a heterogenous, multiseptated, and enhancing mass with varying infiltration of the surrounding structures including rectus or ilacus muscles, bladder, or subcutaneous fat.

3.2. Histology/Pathology

Biomarkers including CA-125, CEA, and CA19-9 have not demonstrated diagnostic efficacy. CA-125 is a nonspecific biomarker which can be elevated in both gynecologic malignancies and advanced endometriosis.(Bats et al., 2008) While some cases, including this case, noted elevated tumor markers, most cases had no elevation of CA-125, CA 19–9, and CEA.(Castagnino et al., 2021; Bahall et al., 2022; Alberto et al., 2006);(Gentile et al., 2018; Marques et al., 2017; Ruiz et al., 2015; Liu et al., 2014), Histologically, clear cell carcinoma exhibits mixed papillary, tubulocystic, or solid patterns with intraluminal mucin, intracytoplasmic vacuoles, eosinophilic hyaline mucin, stromal hyalinization, and nuclear atypia.(Fadare and Parkash, 2019).

Immunohistochemically, both ovarian and extra-peritoneal clear cell carcinomas have equivalent IHC marker expression. The typical immunophenotype for clear cell carcinoma (CCC) is HNF1β, Napsin A, CK7, PAX8, and AMACR positive. ER-alpha, WT-1, and PR are typically negative. P53 is aberrant in approximately 25 % of cases.(Fadare and Parkash, 2019) In differentiating from metastatic clear cell renal cell carcinoma (CCRCC), CCRCC frequently shows distinctive nested alveolar pattern with interalveolar stromal vascularity in contrast to CCC in which tubulocystic patterns, small rounded papillae, and hobnail cells are characteristic. Additionally, Napsin A, CK7, and p504S are less frequently expressed in CCRCC. In our case, tumor cells were positive for CK7, PAX8, Napsin A, and P504S, negative for WT-1 and ER, wild-type staining p53, and low probability of microsatellite instability; thereby the sample was determined to be a CCC of gynecologic origin. Other similar cases stained CK7, PAX8, CAM 5.2, and Ber Ep4 positive and CK20, ER, WT-1, CD34, and vimentin negative.(Castagnino et al., 2021; Bahall et al., 2022; Alberto et al., 2006; Gentile et al., 2018).

Many cases, including ours, do not show direct evidence of endometriosis involving the abdominal wall mass. In our case, endometriotic origin was inferred given her history of significant abdominal wall endometriosis, operative findings of endometriosis involving the peritoneum and appendix, and no evidence of another primary site tumor on imaging suggesting alternate etiology. Various cases reported

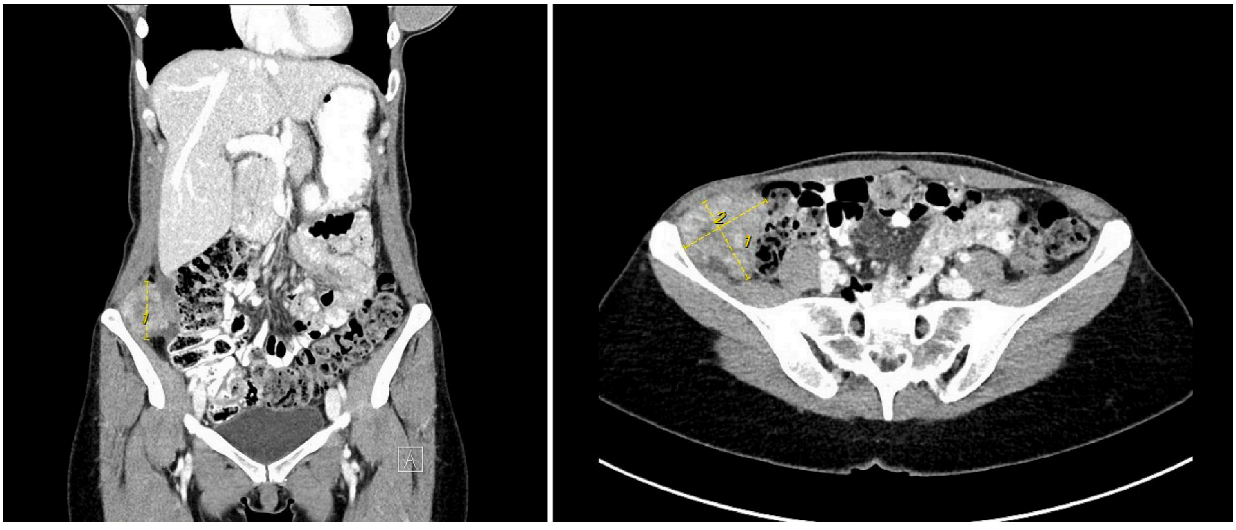

Fig. 1. CT findings demonstrating a new right lower quadrant mass.

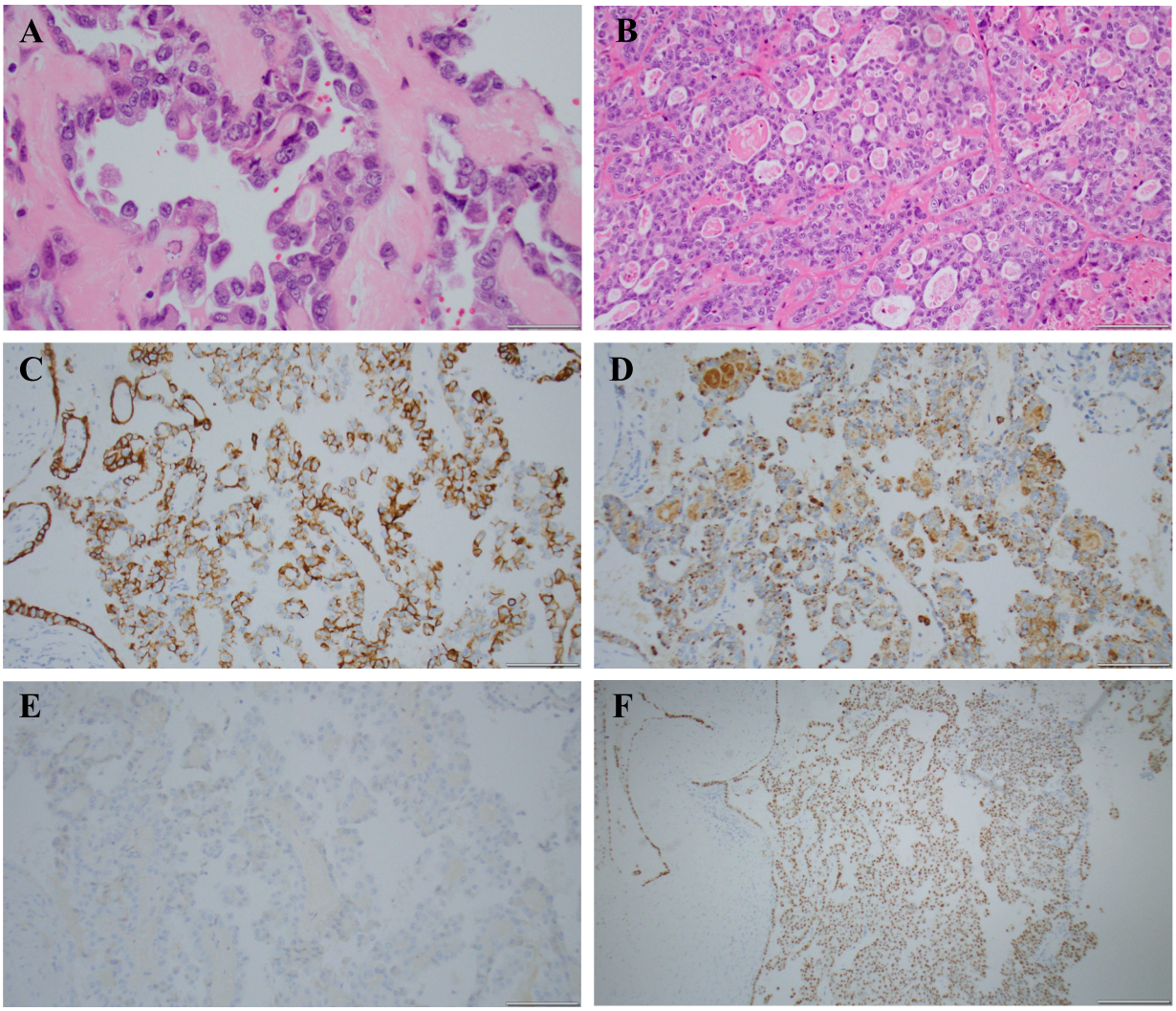

Fig. 2. Histology and Immunohistochemistry. **(A)** Papillary pattern with rounded papillae with hyalinized cores and characteristic hobnailing. **(B)** Tubulocystic pattern with glandular structures in a hyalinized background. Cells demonstrate eosinophilic to clear cytoplasm with variable nuclear pleomorphism. **(C)** Tumor cells diffusely positive for CK7. **(D)** Tumor cells were diffusely positive for Napsin-A. **(E)** Tumor cells were negative for WT-1, ER. **(F)** Tumor cells were diffusely positive for PAX-8.

hemorrhagic cysts or aggregates of hemosiderin-laden macrophages suggestive of a "burnt out" endometriosis.(Bahall et al., 2022; Bats et al., 2008).

3.3. Treatment

Clear cell carcinoma can be difficult to treat, with increased rates of delayed presentation, platinum-based chemoresistance,(Sugiyama, 2000) local invasion into surrounding structures, and lymphatic metastasis.(Liu et al., 2014) Prognosis of clear cell carcinoma of the abdominal wall is often poor with lymph node metastasis commonly involving inguinal node. The mean survival time from diagnosis is 30 months.(Bahall et al., 2022) Consensus for surgery includes primary resection with many cases also performing total hysterectomy and inguinal and iliac lymphadenectomy. Reconstruction of the abdominal wall with mesh may be required if there is extensive involvement of the abdominal wall.

There is no consensus on a standardized chemotherapy regimen for intraabdominal clear cell carcinoma of endometriotic origin, and therefore treatment typically follows the guidelines for ovarian clear cell carcinoma. The current standard of care for treatment of all epithelial ovarian cancer is combination of adjuvant platinum-based chemotherapy with combination carboplatin (AUC 5–6) and paclitaxel (175 mg/m2) with some preferring the addition of bevacizumab (15 mg/kg).(You, et al., 2022; Burger et al., 2011; Walker et al., 2019) Specifically in clear cell ovarian cancers, bevacizumab has shown promise in multiple studies which prompted its use in this case.(Seki, et al., 2022; Tate, et al., 2021) Alternative chemotherapy regimens reported in similar cases include gemcitabine and pegylated liposomal doxorubicin following platinum resistance.(Giannella et al., 2020).

The role of radiation in these cases is also limited. Given the locally aggressive nature of the patient's tumor and relative chemo-resistance of clear cell carcinomas, radiation was considered and recommended by the multidisciplinary tumor board conference. Stereotactic body radiotherapy has been shown effective in cases of ovarian cancer.(Macchia et al., 2020) Post-chemotherapy radiation therapy was performed in three cases in which there was no evidence of recurrence on follow-up. (Alberto et al., 2006; Ruiz et al., 2015).

Despite aggressive treatment, clear cell carcinoma arising from abdominal wall endometriosis carries a poor prognosis. Given the rare nature of this disease process, additional clinical and molecular data is needed to help treatment guidelines.

4. Conclusions

Clear cell carcinoma arising from abdominal wall endometriosis is a rare disease and poses diagnostic and therapeutic challenges given the paucity of available literature surrounding the specific pathology. Clinical history coupled with characteristic histology and immunohistochemical stains can often aid in identification. Given the various proposed treatments and heterogeneity in outcomes across, there is limited data to offer standardized guidelines for care. This report detailing the work up, diagnosis, and treatment of a patient with clear cell carcinoma arising from abdominal wall endometriosis will add to the existing body of literature to promote further investigation and improve patient care.

CRediT authorship contribution statement

Cameron Harris: conceptualization, writing of original draft, review and editing, investigation. **Miller Singleton:** reviewing and editing. **Theresa Samulski:** reviewing and editing. **Leslie Clark:** conceptualization, writing the original draft, reviewing and editing, providing supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

Informed consent was obtained from the patient for publication of this case report. A copy of the consent is available for the Editor of this journal upon request.

References

Alberto, V.O., Lynch, M., Labbei, F.N., Jeffers, M., 2006. Primary abdominal wall clear cell carcinoma arising in a Caesarean section scar endometriosis. Ir J Med Sci. 175 (1), 69–71. https://doi.org/10.1007/BF03169006. PMID: 16615235.

Bahall, V., De Barry, L., Rampersad, A., 2022. Clear cell carcinoma arising from abdominal wall endometriosis-a report on two cases and literature review. World J Surg Oncol. 20 (1), 86. https://doi.org/10.1186/s12957-022-02553-x. PMID: 35292079; PMCID: PMC8922864.

Bats, A.S., Zafrani, Y., Pautier, P., Duvillard, P., Morice, P., 2008. Malignant transformation of abdominal wall endometriosis to clear cell carcinoma: case report and review of the literature. Fertil Steril. 90 (4), 1197. https://doi.org/10.1016/j.fertnstert.2007.08.080. Epub 2007 Dec 20 PMID: 18082734.

Behbehani S, Magtibay P, Chen L, Wasson M. Clear Cell Carcinoma of the Anterior Abdominal Wall Secondary to Iatrogenic Endometriosis. J Minim Invasive Gynecol. 2020 Sep-Oct;27(6):1230-1231. doi: 10.1016/j.jmig.2019.12.016. Epub 2019 Dec 30. PMID: 31899266.

Burger, R.A., Brady, M.F., Bookman, M.A., et al., 2011. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med. 365 (26), 2473–2483. https://doi.org/10.1056/NEJMoa1104390.

Castagnino, B., Angeramo, C.A., Sadava, E.E., 2021. Clear Cell Carcinoma Arising from Endometriosis in the Abdominal Wall. J Gastrointest Surg. 25 (10), 2707–2709. https://doi.org/10.1007/s11605-021-04992-5. Epub 2021 Mar 26 PMID: 33772402.

Fadare, O., Parkash, V., 2019. Pathology of endometrioid and clear cell carcinoma of the ovary. Surgical Pathology Clinics 12 (2), 529–564.

Gentile, J.K.A., Migliore, R., Kistenmacker, F.J.N., Oliveira, M.M., Garcia, R.B., Bin, F.C., Souza, P.M.S.B., Assef, J.C., 2018. Malignant transformation of abdominal wall endometriosis to clear cell carcinoma: case report. Sao Paulo Med J. 136 (6), 586–590. https://doi.org/10.1590/1516-3180.2017.0103300417. Epub 2017 Nov 6 PMID: 29116312.

Giannella L, Serri M, Maccaroni E, DI Giuseppe J, Carpini GD, Berardi R, Sopracordevole F, Ciavattini A. Endometriosis-associated Clear Cell Carcinoma of the Abdominal Wall After Caesarean Section: A Case Report and Review of the Literature. In Vivo. 2020 Jul-Aug;34(4):2147-2152. doi: 10.21873/invivo.12021. PMID: 32606196; PMCID: PMC7439887.

Liu, H., Leng, J., Lang, J., Cui, Q., 2014. Clear cell carcinoma arising from abdominal wall endometriosis: a unique case with bladder and lymph node metastasis. World J Surg Oncol. 5 (12), 51. https://doi.org/10.1186/1477-7819-12-51. PMID: 24597651; PMCID: PMC3973880.

Macchia, G., Lazzari, R., Colombo, N., et al., 2020. A Large, Multicenter, Retrospective Study on Efficacy and Safety of Stereotactic Body Radiotherapy (SBRT) in Oligometastatic Ovarian Cancer (MITO RT1 Study): A Collaboration of MITO, AIRO GYN, and MaNGO Groups. Oncologist. 25 (2), e311–e320. https://doi.org/10.1634/theoncologist.2019-0309.

Marques, C., Silva, T.S., Dias, M.F., 2017. Clear cell carcinoma arising from abdominal wall endometriosis - Brief report and review of the literature. Gynecol Oncol Rep. 14 (20), 78–80. https://doi.org/10.1016/j.gore.2017.03.008. PMID: 28367489; PMCID: PMC5362132.

Ruiz, M.P., Wallace, D.L., Connell, M.T., 2015. Transformation of abdominal wall endometriosis to clear cell carcinoma. Case Reports in Obstetrics and Gynecology 2015.

Sampson, J.A., 1925. Endometrial carcinoma of the ovary, arising in endometrial tissue in that organ. Arch Surg. 10 (1), 1–72. https://doi.org/10.1001/archsurg.1925.01120100007001.

Scutiero, G., Iannone, P., Bernardi, G., Bonaccorsi, G., Spadaro, S., Volta, C.A., et al., 2017. Oxidative stress and endometriosis: a systematic review of the literature. Oxid Med Cell Longev. 2017, 7265238. https://doi.org/10.1155/2017/7265238.

Seki, Toshiyuki, et al. "Bevacizumab in first-line chemotherapy to improve the survival outcome for advanced ovarian clear cell carcinoma: A multicenter, retrospective analysis." (2022): 5502-5502.

Sugiyama, T., et al., 2000. Clinical characteristics of clear cell carcinoma of the ovary: a distinct histologic type with poor prognosis and resistance to platinum-based chemotherapy. Cancer: Interdisciplinary International Journal of the American Cancer Society 88 (11), 2584–2589.

Tate, Shinichi et al. "Bevacizumab in First-Line Chemotherapy Improves Progression-Free Survival for Advanced Ovarian Clear Cell Carcinoma." *Cancers* vol. 13,13 3177. 25 Jun. 2021, doi:10.3390/cancers13133177.

Walker JL, Brady MF, Wenzel L, et al. Randomized Trial of Intravenous Versus Intraperitoneal Chemotherapy Plus Bevacizumab in Advanced Ovarian Carcinoma: An NRG Oncology/Gynecologic Oncology Group Study [published correction appears in J Clin Oncol. 2019 Sep 1;37(25):2299]. *J Clin Oncol.* 2019;37(16):1380-1390. doi:10.1200/JCO.18.01568.

Wiegand, K.C., et al., 2010. ARID1A mutations in endometriosis-associated ovarian carcinomas. New England Journal of Medicine 363 (16), 1532–1543.

You, Benoit et al. "Identification of Patients With Ovarian Cancer Experiencing the Highest Benefit From Bevacizumab in the First-Line Setting on the Basis of Their Tumor-Intrinsic Chemosensitivity (KELIM): The GOG-0218 Validation Study." *Journal of clinical oncology: official journal of the American Society of Clinical Oncology* vol. 40,34 (2022): 3965-3974. doi:10.1200/JCO.22.01207.