ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 10, pp.74209-74212, October, 2018

DOI: https://doi.org/10.24941/ijcr.32583.10.2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

CASE REPORT

CLEAR CELL CARCINOMA OF THE ENDOMETRIUM: A CASE REPORT AND REVIEW

Hakim A., *Mahajan R., Jaiswal I., Pandey A. and Inampudi P.

Department of Radiation Oncology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala Haryana, India

ARTICLE INFO

Article History:
Received 19th July, 2018
Received in revised form
24th August, 2018
Accepted 05th September, 2018
Published online 30th October, 2018

Key Words:
Clear Cell Carcinoma Endometrium, Post-operative, Radiotherapy.

ABSTRACT

Endometrial cancer is the most common gynecologic malignancy, and according to the Surveillance, Epidemiology and End Results (SEER) statistics for 2006 to 2010 it is the fourth most common cancer in women. More than 75% of endometrial cancers are endometrioid carcinomas, whereas 5% to 10% are serous, 1% to 5% clear cell, and 1% to 3% mucinous carcinomas. Up to 5% are other histologies, including uterine sarcomas (i.e., carcinosarcoma, leiomyosarcoma, and endometrial stromal sarcoma). Clear cell carcinoma has been considered to have a poor prognosis because of late diagnosis with advanced disease. We report a case of 74 years old postmenopausal woman who presented in our institute with complaints of bleeding per vaginum for 5 months. Patient was diagnosed as Clear cell Carcinoma of Endometrium. Patient underwent Total abdominal hysterectomy and Bilateral Salpingo-oophorectomy (TAH-BSO). Patient was referred in our Department for Radiation therapy and was treated with adjuvant radiotherapy.

Citation: ***Hakim, A., Mahajan, R., Jaiswal, I., Pandey, A. and Inampudi, P.*****, 2018.** "Clear Cell Carcinoma of the Endometrium: A case report and Review", *International Journal of Current Research*, 10, (10), 74209-74212.

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy and the fourth most common cancer in women. The mortality rate decreased from 5.3 to 4.1 deaths per 100,000 women between 1973 and 1995 and has remained more or less stable since 1995. Uterine cancer is typically a cancer of postmenopausal women between 55 and 85 years old. Incidence rates are higher in those aged 60 to 80.Lessthan 5% of the patients are younger than age 40 years. The median age at diagnosis is 62 years. Endometrial clear cell carcinoma is an uncommon variant of carcinoma of the uterus that represents only about 1%–5% of all endometrial carcinomas (Siegel *et al.,* 2013; Hecht and Mutter, 2006; Lim and Oliva, 2010). Endometrial clear cell carcinoma behaves aggressively with a high propensity for extra-uterine spread and are diagnosed in advanced stages (Clement and Young, 2004). Grossly, clear cell carcinomas often form fleshy and soft masses involving most of the endometrial surface (Fadare *et al.,* 2012). Microscopically the neoplasm can exhibit different microscopic patterns, namely solid pattern consists of sheets of clear cells intermixed with eosinophilic cells, whereas papillary, tubular and cystic patterns are mainly composed of hobnail cells with interspersed clear and eosinophilic cells (Prat *et al.,* 2007). We report a case of Clear cell carcinoma of endometrium.

Corresponding author: **Mahajan, R.,**
Department of Radiation Oncology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala Haryana, India.

CASE REPORT

A 74 years old post menopausal woman presented with complaint of bleeding per vaginum for 5 months. Patient is multiparous with no comorbities and addictions. On presentaion patient had 160 cm height and 47 kg weight. CT abdomen showed bulky cervix with fluid in endometrial cavity and bulky bilateral adnexae (Figure 1). Ultrasound abdomen and pelvis revealed heteroechoic mass lesion within endometrial cavity likely neoplastic (Figure 2). Baseline investigations Haemoglobin, blood counts, kidney function tests, liver function tests, chest radiograph were normal. Tumor marker CA-125 level was 6.7u/ml. Endometrial curettage revealed atypical cells. Patient underwent surgery, where TAH-BSO with lymphadenectomy and peritoneal washing was done. Post operatively histopathological examination revealed clear cell carcinoma of endometrium (pT3N0M0). Detailed pathological examination under 400X magnification revealed cuboidal tumor cells with clear glycogenated cytoplasm and prominent nucleoli, and tumor cells focally showing hobnail morphology (Figure 3A,B). Examination under 100X magnification shows tumor cells in nests and tubulocystic arrangement with abundant clear cytoplasm (Figure 3C, D). Patient was treated with adjuvant Radiotherapy.

DISCUSSION

Clear-cell carcinoma of the endometrium resembles renal carcinoma, but its origin from Müllerian structures is now well established.

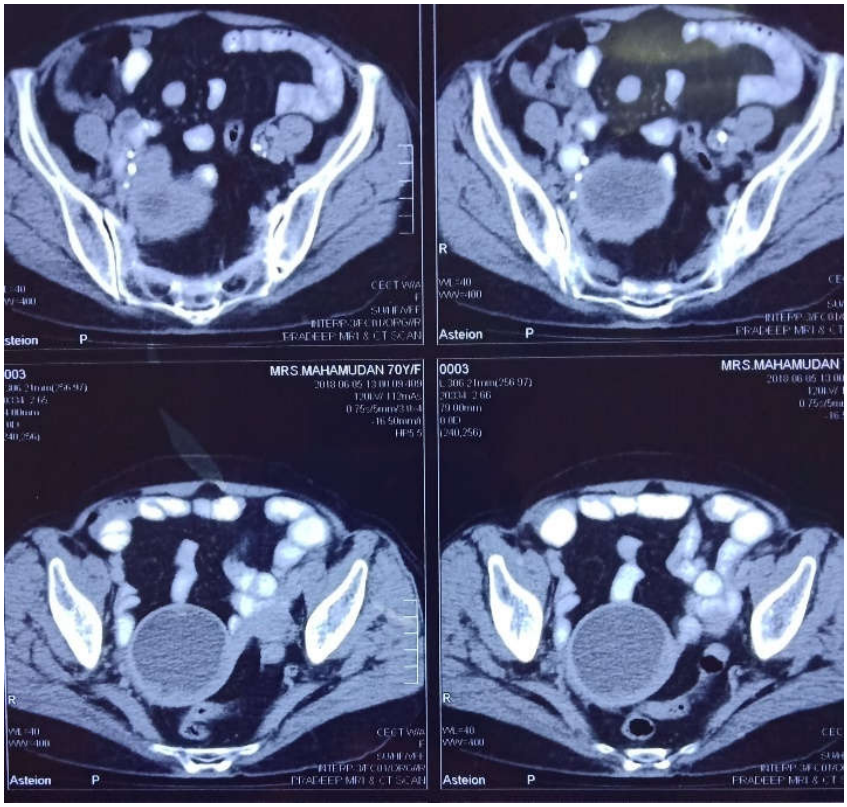

Figure 1. CT abdomen showed bulky cervix with fluid in endometrial cavity and bulky bilateral adnexae

Figure 2. Ultrasound abdomen and pelvis revealed heteroechoic mass lesion within endometrial cavity likely neoplastic

Unlike vaginal and cervical clear-cell carcinoma, it is not related to intrauterine diethylstilbestrol exposure. Clear cell carcinoma of the endometrium received attention in the 1970s, when the two pathological studies by Silverberg and De Giorgi (1973) and Kurman and Scully (1976) were published. Uterine cancer is typically a cancer of postmenopausal women between 55 and 85 years old. The median age at diagnosis is 62 years. Endometrial clear cell carcinoma is an uncommon variant of carcinoma of the uterus that represents only about 1%–5% of all endometrial carcinomas (Siegel *et al.,* 2013; Hecht and Mutter, 2006; Lim and Oliva, 2010).

In clinopathological review of one of series of 825 cases of carcinoma of endometrium diagnosed between 1955-1984, 4% cases were clear cell carcinoma of endometrium. In this series 5 years survival for clear cell carcinoma was 64% as compared to 80% in adenocarcinoma (Fadaro *et al.,* 2013). Patients with clear cell carcinoma endometrium usually presents with bleeding PV or discharge PV with duration may exceeding months. Patients may have pain abdomen, altered bowel habits and edema in advanced disease. Patients usually have history of hypertension, diabetes, obesity, use of estrogen and tamoxifen.

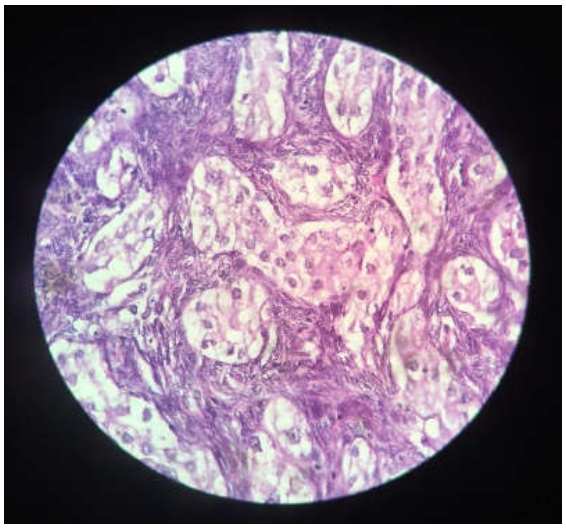

Figure 3A.400x; H&E: Section shows cuboidal tumor cells with clear glycogenated cytoplasm and prominent nucleoli

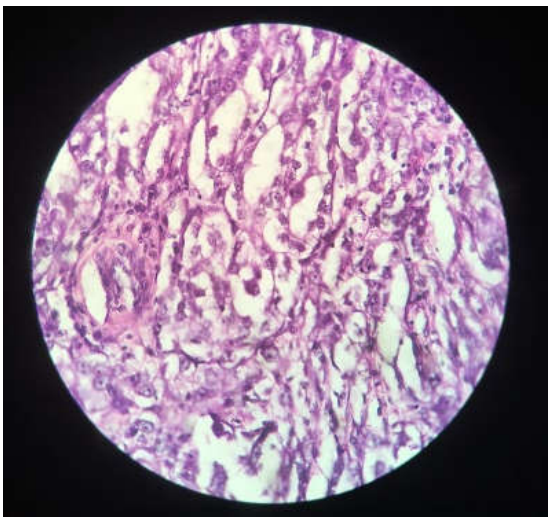

Figure 3B.400x; H&E: Section shows tumor cells focally revealing hobnail morphology

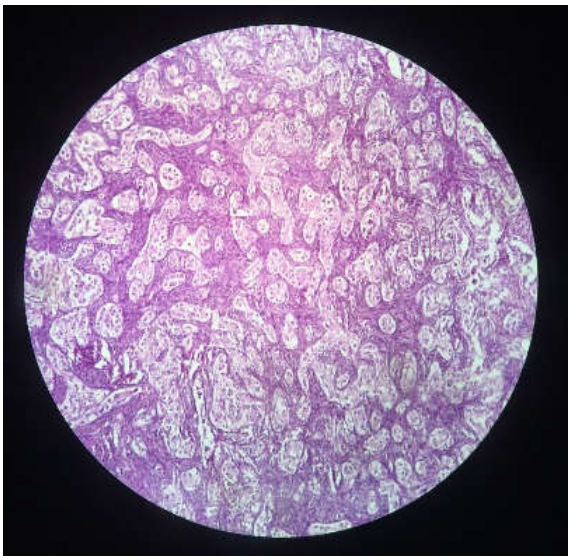

Figure 3C.100x; H&E: Section shows tumor cells with a tubulocystic arrangement

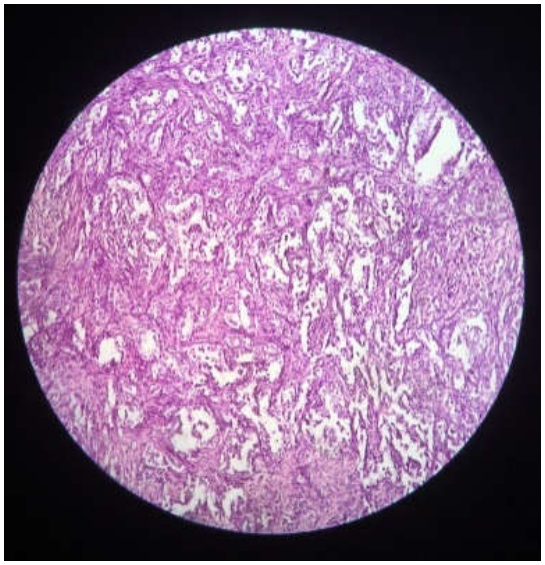

Figure 3D.100x; H&E: Section shows tumor cells in nests and tubulocystic arrangement with abundant clear cytoplasm

Patient evaluation includes history, physical examination, baseline blood investigation. Diagnosis can be made with D&C or endometrial biopsy and Trans vaginal USG. Patients require chest x-rays and CT scans to assess distant sites for metastasis. Tumor marker CA-125 levels can be moderately raised in clear cell carcinoma. Pathological features. Common *Architectural patterns are Glandular, Papillary, Solid and Cystic. Majority are* an admixture of these architectural patterns. The Glandular pattern is the most commonly encountered pattern, the glands may not be entirely confluent in most areas of the tumor, with individual glandular units being separated by stroma, or tumor cells of other architectural configurations. The glands are lined by either flat, hobnail or low cuboidal polygonal cells. Intraglandular papillations may be present. The papillary pattern includes Small rounded papillae (SRP), which is the most common papillary pattern.SRP can be seen as end tributaries of larger, fibrous-cored stem papillae, direct protrusions into round cystic/glandular spaces, or tributaries from elongated slender papillae. The Intermediate forms may also be present. The predominant cell type lining SRP is hobnail in, low cuboidal eosinophilic cells, and low cuboidal clear cells in the remainder.

Miscellaneous papillary patterns may be simple, complex or non specific. The solid pattern, characterized by diffuse sheets of cells without any architectural patterns. Solid patterns mainly have eosinophilic or clear cells. Cell membranes can be well-defined with grade 3 nuclei, these cells can be most clearly discernable, and display the highest degree of clustering, in the solid regions. Thin fibrous septae can be diffusely distributed throughout the solid regions. The cystic pattern is the least common (Gadducci *et al.,* 2010). Management of clear cell carcinoma includesa TAH-BSO (Olawaiye and Boruta, 2009; Thomas *et al.,* 2008). The standard surgical approach has traditionally been laparotomy through a midline incision, which allows full exposure of the abdomen, pelvic areas, and lymphatic sites. Surgical evaluation includes thorough examination and palpation of the pelvic and abdominal organ and variably collection of peritoneal lavage fluid or ascitis for cytologic evaluation. Laparoscopic and robotic techniques have been used for early stage I disease. Laparoscopy has advantages of shorter hospitalization and recovery time and reduction of surgical morbidity. A study by Vandeput *et al.* (2011) has shown that recurrences in early stage cancers occur irrespective of adjuvant chemotherapy, but recurrence free survival is prolonged when adjuvant

chemotherapy is administered. Anne Kim et al, in their collaborative study have shown adjuvant External beam Radiation therapy has role in early stage uterine papillary serous and clear cell carcinoma. Radiation therapy in FIGO IB-C papillary serous and clear cell carcinoma seems to play an important role in improving survival (Kim *et al.,* 2011). Murphy *et al.* (2003) in their study of 38 patients of clear cell carcinoma who underwent surgery. Adjuvant Radiation therapy was used in 22 patients. The 5- years actuarial disease free survival for the entire group was 38.4%. it was found that patients receiving adjuvant Radiation therapy did not relapse in pelvis as compared 50% in those did not receive adjuvant Radiation therapy. Clear cell carcinoma has a poor prognosis as compared endometrioid carcinoma of the endometrium (Murphy *et al.,* 2003; Malpica *et al.,* 1995; Cirisano *et al.,* 2000). Several clinical-pathological variables have been correlated with the prognosis of patients with clear cell carcinoma, including tumor stage, myometrial invasion, lymph-vascular space involvement, and patient age. Abeler *et al,* in a their study of 181patients with clear cell carcinoma, clinicalstage, pathological stage, patient age, myometrial invasion, lymph-vascular space involvement were significantly related to survival atunivariate analysis, but only patientage and pathological stage were independent prognostic variables at multivariate analysis (Abeler *et al.,* 1996).

Conclusion

Clear cell carcinoma accounts for only 1 to 5.5% of all endometrial carcinomas. Clear cell carcinoma is the disease of post menopausal women and has been considered to have a poor prognosis because of late diagnosis with advanced disease. Surgery is the main stay of treatment followed by adjuvant Radiotherapy and Chemotherapy.

REFERENCES

Abeler, V.M., Vergote, I.B., Kjorstad, K.E. and Trope, C.G. 1996. Clear cell carcinoma of the endometrium. Prognosis and metastatic pattern. *Cancer 78*: 1740-1747.

Carcangiu, M.L. and Chambers, J.T. 1995. Early pathologic stage clear cell carcinoma and uterine papillary serous carcinoma of the endometrium: comparison of clinicopathologic features and survival. *Int J Gynecol Pathol., 14*: 30-38, 1995.

Cirisano, F.D. Jr, Robboy, S.J., Dodge, R.K., Bentley, R.C., Krigman, H.R., Synan, I.S., Soper, J.T. and Clarke-Pearson, D.L. 2000. The outcome of stage I-II clinically and surgically staged papillary serous and clear cell endometrial cancers when compared with endometrioid carcinoma. *Gynecol Oncol., 77*: 55-65.

Clement, P.B., Young, R.H. 2004. Non-endometrioid carcinomas of the uterine corpus: a review of theirpathology with emphasis on recent advances and problematic aspects. *Adv Anat Pathol.,* 11: 117-142.

Fadare, O., Parkash, V., Dupont, W.D., Acs, G., Atkins, K.A., Irving, J.A., Pirog, E.C., Quade, B.J., Quddus, M.R., Rabban, J.T., Vang, R., Hecht, J.L. 2012. The Diagnosis of Endometrial Carcinomas With Clear Cells by Gynecologic Pathologists: An Assessment of Interobserver Variability and Associated Morphologic Features. *Am J Surg Pathol.,* 36: 1107-1118.

Fadaro, O., Zheng, W., Crispens, M.A., *et al*. 2013. Morphologic and Clino-pathological features. *Am. J. Cancer Res.,* 3(1):70-95.

Gadducci, A., Cosio, S., Spirito, N., Cionni, L. 2010. Clear Cell Carcinoma of the Endometrium: A Biological and Clinical Enigma. *Anticancer Research 30*: 1327-1334.

Hecht, J.L., Mutter, G.L. 2006. Molecular and pathologic aspects of endometrial carcinogenesis. *J. Clin. Oncol.,* 24:4783-91.

Kim, A., Schreiber, D., Rineer, J., Choi, K., Rotman. 2011. Impact of Adjuvant External Beam Radiation therapy in Early stage uterine papillary serous and clear Cell carcinoma. 81: 639-644.

Kurman, R.J. and Scully, R.E. 1976. Clear cell carcinoma of the endometrium: an analysis of 21 cases. Cancer *37*: 872-882.

Lim, D., Oliva, E. 2010. Nonendometrioid endometrial carcinomas. *Semin Diagn Pathol.,* 27:241-60.

Malpica, A., Tornos, C., Burke, T.W. and Silva, E.G. 1995. Low-stage clear cell carcinoma of the endometrium *Am J Surg Pathol*., *19*: 769- 774.

Murphy, K.T., Rotmensch, J., Yamada, S.D. and Mundt, A.J. 2003. Outcome and patterns of failure in pathologic stages I-IV clear-cell carcinoma of the endometrium: implications for adjuvant radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys., 55*: 1272-1276.

Olawaiye, A.B., Boruta, D.M. 2009. 2nd. Management of women with clear cell endometrial cancer: a Society of Gynecologic Oncology (SGO) review. *Gynecol Oncol.,* 113:277-83.

Prat, J., Gallardo, A., Cuatrecasas, M. and Catasus, L. 2007. Endometrial carcinoma: pathology and genetics. Pathology *39*: 72-87.

Siegel, R., Naishadham, D., Jemal, A. 2013. Cancer statistics, *CA Cancer J. Clin*., 63:11-30.

Silverberg, S.G. and De Giorgi, L.S. 1973. Clear cell carcinoma of the endometrium. *Clinical, pathologic, and ultrastructural findings.* Cancer *31*: 1127-1140.

Thomas, M., Mariani, A., Wright, J.D., Madarek, E.O., Powell, M.A., Mutch, D.G., *et al.* 2008. Surgical management and adjuvant therapy for patients with uterine clear cell carcinoma: a multi-institutional review. *Gynecol Oncol*., 08:293-7.

Vandeput, Trovit, J., Vergobe, I., Mocrman, P., *et al.* 2011. The role of adjuvant chemotherapy in surgical stages I-II serous and clear cell carcinomas and carcinosarcomas of the endometrieum: a collaborative study. *Int. J. Gynecol. cancer.*, 21(2) 332-6.

****