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Case Report

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A rare case report of mixed uterine cancer with two distinct histological types: a spectrum of endometrioid adenocarcinoma with transitional cell carcinoma

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Abstract

Introduction: Endometrioid adenocarcinoma of the uterine corpus can coexist with squamous cell carcinoma, serous or clear cell adenocarcinoma and sarcoma. There are only 14 cases of pure transitional cell carcinoma of uterus reported till now. We report a very rare case with a mixed spectrum of endometrioid adenocarcinoma with transitional cell carcinoma. The clinical behavior of the patient depends on tumor grading and staging, though not much literature is available in this regard.

Methods: 60-year-old lady was admitted with complaints of white discharge and spotting per vaginum since last three months. She noticed obvious loss of weight as well as appetite since few months. CECT abdomen showed thickened endometrium with ill-defined enhancing mass in endometrial cavity of approximately same size as revealed by USG findings. Wertheim's hysterectomy with bilateral pelvic lymph-node dissection was done.

We received the specimen of uterus and cervix with bilateral adnexa along with bilateral external iliac and obturator lymph nodes. Uterus showed a highly necrotic, friable, large, grayish white tumor mass measuring 7.5x7 cm completely distending the endometrial cavity. Cervix and bilateral adnexae were unremarkable grossly.

Results: The endometrial tumor sections showed spectrum of patterns ranging from well differentiated (40%) along with 30% component of transitional cell carcinoma. Also 30% component of poorly differentiated endometrioid carcinoma was seen. Cervix, bilateral adnexa and regional lymph-nodes did not show evidence of metastasis.

Conclusion: This mixed endometrial tumor which presented with two tumour components is a rare entity and should be included in the differential diagnosis of uterine tumors. Thus extensive sectioning of the tumor is essential to avoid inadequate diagnosis.

Keywords: *Uterine corpus, endometrioid adenocarcinoma, transitional cell carcinoma (TCC)*

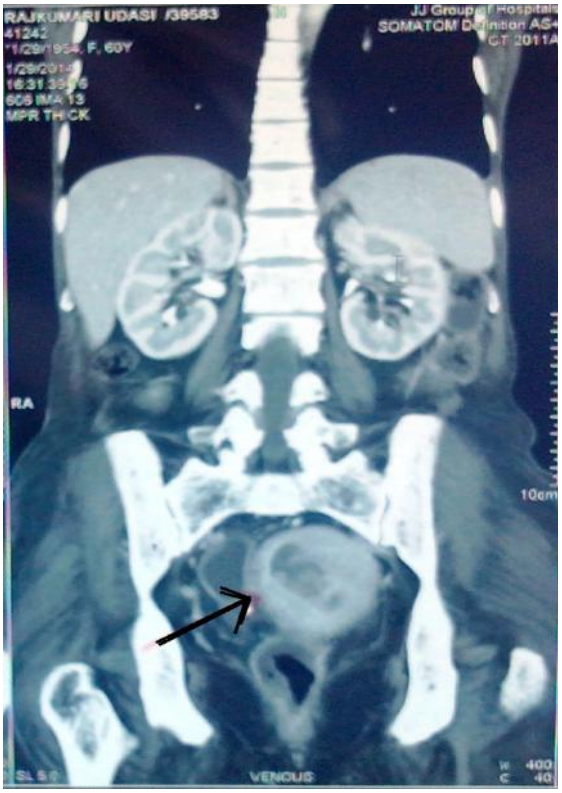
Introduction

Endometrioid adenocarcinoma of the uterine corpus with another existing histological variant is usually squamous cell carcinoma, serous or clear cell adenocarcinoma and sarcoma. There are only few reports of transitional cell carcinoma of uterus.[1] We report a patient who had mixed cancer with these two distinct histological types: a spectrum of endometrioid adenocarcinoma with transitional cell carcinoma. The clinical behavior of the patient depends on tumor grading and staging, though not much literature is available in this regard.

Case Report

A 60-year-old lady was admitted to Gynecology department on presenting with complaints of white discharge and spotting per vaginum since last three months. She attained menopause 10 years back. She noticed obvious loss of weight as well as appetite loss since few months. She was $G_4P_4L_3$. The ultrasonography abdomen with pelvis (USG) done on the same day of admission revealed a bulky uterus with a 7.5 x 6.4 x 4.3 cm mass present in endometrial cavity which was hypoechoic in nature. Contrast Enhanced Computerized Tomography (CECT) abdomen (Figure 1) showed thickened endometrium with ill-defined enhancing mass in endometrial cavity of approximately same size as revealed by USG findings. After confirmation of presence of poorly differentiated endometrioid carcinoma on biopsy, Wertheim's hysterectomy with bilateral pelvic lymph-node dissection was planned.

Figure 1: CECT abdomen showed thickened endometrium (arrow) with ill-defined enhancing 7.5 x 6.4 x 4.3 cm mass in endometrial cavity.



We received the specimen of uterus and cervix with bilateral adnexa along with bilateral external iliac and obturator lymph nodes. Also right internal iliac and right common iliac lymph nodes were received. On cutting open, uterus showed a highly necrotic, friable, large, grayish white tumor mass measuring 7.5 x 7 cm completely distending the endometrial cavity (Figure 2). Cervix and bilateral adnexa were unremarkable grossly. The tumor sections showed spectrum of patterns ranging from well differentiated (40%) along with 30% component of transitional cell carcinoma (Figure 3). Also 30% component of poorly differentiated endometrioid carcinoma was seen. (Figure 3-inset)

Figure 2: Gross appearance-Large, necrotic, friable, grayish-white tumor mass measuring 7.5 x 7 cm, completely distending the endometrial cavity.

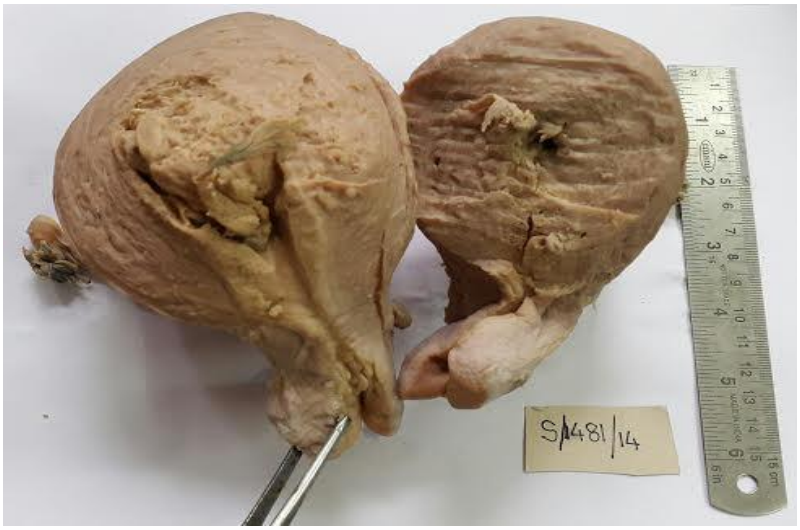
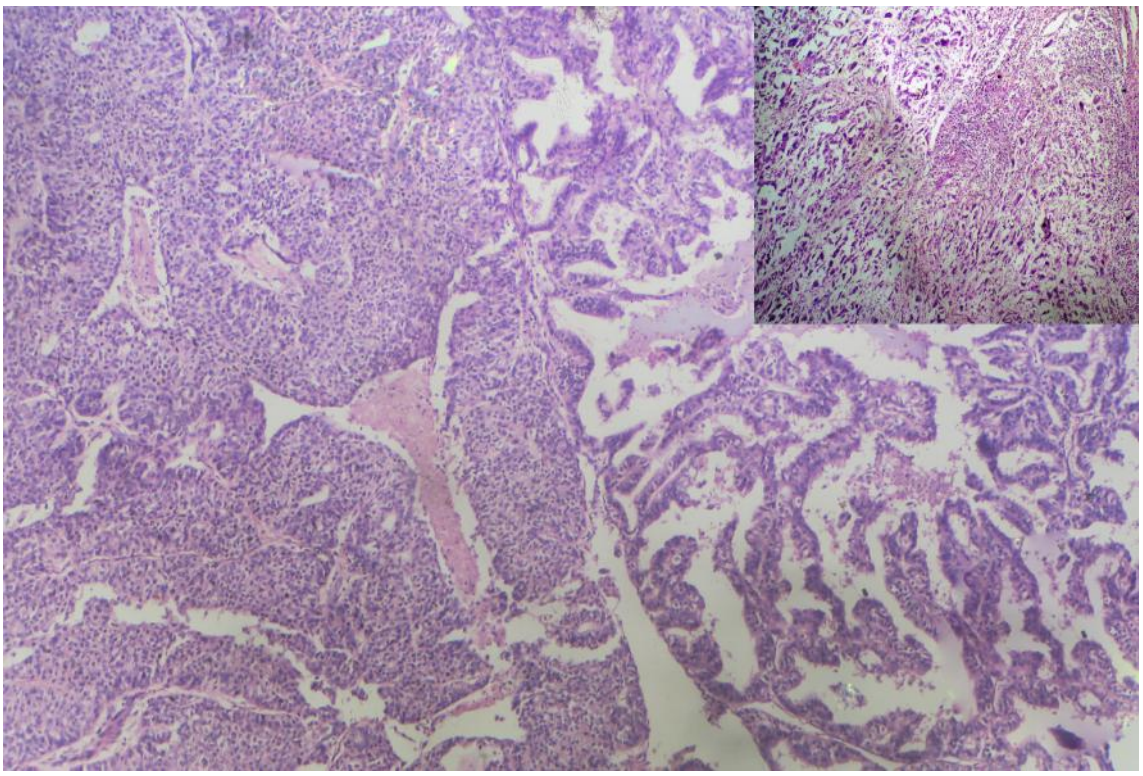


Figure 3: Microphotograph- Tissue section from endometrial mass shows well-differentiated component (*right*) with component of transitional cell carcinoma (*left*) (H&E, x 40). Also poorly differentiated endometrioid carcinoma component was seen. (Figure 3-inset) (H&E, x 100).



Well-differentiated endometrioid carcinoma (40%) was comprised of back to back arrangement of glands with little intervening stroma with occasional papillae formation. The glands were lined by columnar epithelial cells with pleomorphic, hyperchromatic and vesicular nuclei with prominent nucleoli and abundant eosinophilic cytoplasm. The poorly differentiated component (30%) displayed discohesive pattern with large, highly pleomorphic and bizarre, mitotically active cells. Numerous multinucleate tumor giant cells were seen admixed in this poorly differentiated component. Areas of necrosis were seen in the intervening tumor tissue. Also 30% component of poorly differentiated endometrioid carcinoma was seen.

Inspite of being this high grade with varied histomorphological pattern of tumor, surprisingly myometrium did not show any invasion except dense lymphocytic cell infiltrate. Lympho-vascular invasion was not seen. Cervix and bilateral adnexa were not involved by the tumor. All the 12 lymph nodes received from various sites were uninvolved by tumor. Hence, we offered the diagnosis of high grade endometrioid adenocarcinoma with transitional cell differentiation with TNM staging of T_1a N_0 M_x.

Discussion

Pure transitional cell carcinoma (TCC) of uterus is very rare. [1-3] Till now only 14 cases have been published in literature.[2] We described a case of endometrioid carcinoma of uterine corpus with transitional cell carcinoma. Transitional cell carcinoma is defined as a carcinoma in which 50% or more is composed of cells resembling urothelial transitional cells. Lesser quantities of transitional cell differentiation would qualify the tumor as a mixed carcinoma with transitional cell differentiation. Among patients with known racial origin, 50% are non- White (African, Hispanic, or Asian). The median age is 61.6 years (range 41-83 years).The main complaint at presentation is uterine bleeding. [1-3]

The histogenesis of transitional cell neoplasms of the endometrium is uncertain but may be similar to that of transitional cell neoplasms arising elsewhere in the genitourinary tract. Invasive TCCs of the urinary bladder are usually preceded by a noninvasive phase, which may be papillary or flat. Presumably, the same progression takes place in the endometrium, although benign, noninvasive forms of transitional cell neoplasia have not been described in the endometrium. TCC is admixed with other patterns of carcinoma which supports the following mechanism as the more common route for the development of transitional cell differentiation in endometrial carcinomas. In the absence of benign transitional cell metaplasia, it is more likely that the endometrial lesions develop through 'neometaplasia from müllerian epithelium' rather than developing from initially benign metaplastic transitional cell epithelium. [1]

The hypotheses for TCC in endometrium are purely speculative and await genetic testing studies. It has been suggested that the stroma of the vagina, cervix, and endometrium is important in inducing differentiation of the overlying epithelium to its characteristic appearance. The development of transitional cell differentiation may result from the 'acquisition of genetic mutations or possibly even local alterations in genomic imprinting in either the epithelial or the stromal components, with resultant alterations in the epithelial-stromal interaction and ultimately in the epithelial morphology.' [1]

In our case, endometrioid carcinoma exhibited a classical spectrum of morphology from well differentiated to highly undifferentiated giant cell-like carcinoma. Almost 100% endometrium was replaced by tumor mass. But interestingly, the tumor did not seem to invade the myometrium even after extensive sectioning. We paid special attention to sections from cornu of uterus where there are most chances of deep penetration. Bilateral ovaries, fallopian tubes and pelvic lymph-nodes were free of tumor. There was no hematogenous spread to other organs on histology which was confirmed by radiological investigations.

For the purposes of their study, Lininger RA et al (1997) [1] studied cases with mixed patterns showing any proportion of TCC and described them. They designated an endometrial tumor lesion as TCC in the endometrium when >50% of the tumor was composed of TCC. Lesions with '<50% TCC component' were qualified as endometrial carcinoma with transitional cell differentiation. [1] Based on this, as the transitional component of the tumor in our case was 30%, it was designated as endometrioid carcinoma with component of transitional cell carcinoma.

To distinguish from transitional cell carcinoma of urothelial tract, cytokeratin (CK) 7 & 20 were done in our case. There was brilliant CK 7 positivity and CK 20 negativity which confirmed it of mullerian origin or of primary endometrial origin.[1,3] Also associated endometrioid carcinoma displayed a spectrum with extremely well differentiated endometrioid carcinoma on one

hand to the presence of poorly differentiated endometrioid carcinoma cells in sheets and tumor giant cell component on the other hand. The beta hCG immunostain was performed to rule out any chorio-carcinomatous differentiation which was negative in our case.

It has been suggested by many authors that grade of carcinoma is necessary to be specified so that prognosis can be studied and followed up for treatment purpose.[4,5] The TCC component was graded according to the four-tier grading system for transitional cell neoplasms of the urinary bladder adopted by the World Health Organization.[5] In this system, transitional cell papillomas are designated Grade 0, and TCCs are graded from 1 to 3. The TCCs of the endometrium in this study were graded according to their most poorly differentiated TCC component. [4,5] The transitional cell component was of Grade 1 in our case which has good prognosis.

Conclusion

This mixed endometrial tumor is a rare entity and should be included in the differential diagnosis of uterine tumors. Thus extensive sectioning of the tumor is essential to avoid inadequate diagnosis. Immunostaining with CK 7 and CK 20 can help to know if the TCC component in endometrial lesion is primary or metastatic in origin.

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Departments of Pathology and Gynecology

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