Case Report

ABSTRACT

Dedifferentiated endometrioid carcinoma or dedifferentiated endometrioid adenocarcinoma (DEAC) is defined by the presence of undifferentiated carcinoma with endometrioid carcinoma. Undifferentiated component can be misinterpreted as solid component of high-grade endometrioid carcinoma or sarcomatous component of malignant mixed mullerian tumor. We present two cases of DEAC. Two postmenopausal women underwent hysterectomy for vaginal bleeding. Microscopically, sections from the endometrial tumors showed a biphasic growth consisting of an undifferentiated component and a glandular component with sharp transition between the two components. The undifferentiated component showed focal positivity for cytokeratin and vimentin, while glandular component was diffusely positive for cytokeratin and negative for vimentin expression.

KEY WORDS: Dedifferentiated endometrial carcinoma, dedifferentiated endometrioid carcinoma, endometrial carcinoma, malignant mixed mullerian tumor, undifferentiated carcinoma

INTRODUCTION

Undifferentiated endometrial carcinoma can present as either pure form or mixed form. Mixed form is defined by association with a differentiated component. Mixed form is also known as dedifferentiated carcinoma or combined carcinoma. Most commonly, the associated differentiated component is low-grade (Federation of Gynaecology and Obstetrics (FIGO) grade 1 or 2) endometrioid carcinoma, and occasionally grade 3 carcinoma can be present with the undifferentiated component.\(^1\) For diagnosing dedifferentiated endometrioid adenocarcinoma (DEAC) correctly, it is important to recognize the undifferentiated component, which may appear like solid component of grade 3 endometrioid carcinoma or spindle cells of carcinosarcoma. DEAC has a fulminant course and association with Lynch syndrome.\(^3\)

CASE HISTORY

Case report 1

A 48-year-old postmenopausal woman presented with vaginal bleeding for 3 months. Transvaginal ultrasonography (USG) showed thickened endometrium. Endometrial curettage revealed well-differentiated endometrioid carcinoma. The patient underwent total hysterectomy with bilateral salpingo-oophorectomy. On gross examination, uterus and cervix measured 7 cm × 4 cm × 3 cm [Figure 1a]. Endometrial surface was irregular with a tumor in the upper part of endometrial cavity. The tumor invaded more than half of the myometrium near fundus and measured 2.5 cm in largest dimension.
foci showing spindling of cells were also seen. There was sharp demarcation between the well-differentiated component and undifferentiated areas. Lymphovascular invasion was noted. The tumor had invaded more than half of myometrial thickness. Immunohistochemistry in this case was done for epithelial membrane antigen (EMA), vimentin, and CK (cytokeratin) expression. Cytokeratin showed diffuse positivity for well-differentiated part and focal, dot-like positivity for the undifferentiated component [Figure 2b]. The undifferentiated part showed weak focal positivity for EMA and the well-differentiated part showed strong positivity for EMA [Figure 2c]. Vimentin expression was negative in well-differentiated part and focal positivity was seen in the undifferentiated part [Figure 2d]. The patient was disease-free for 3 months and then lost to follow-up.

Case report 2
A 50-year-old postmenopausal woman presented with vaginal bleeding for 2 months. USG showed a mass arising from the endometrium and filling up the whole of the endometrial cavity. Total hysterectomy with bilateral salpingo-oophorectomy was performed. On gross examination, uterus and cervix measured 12 cm × 6 cm × 5 cm. The cut surface showed a growth, measuring 9 cm in largest dimension, arising from the fundus and occupying the entire endometrial cavity [Figure 1b]. Ovaries, tubes and cervix were unremarkable, stage pT1aNxMx. Microscopically, sections from the growth show histopathological features of a biphasic tumor with sharp transition between the two components. One part of the tumor showed glands arranged in confluent pattern, invading more than half of the myometrium, resembling grade 1 endometrioid carcinoma. The undifferentiated component was represented by dysplastic round to ovoid cells separated by delicate fibrovascular septa [Figure 3a]. There was high mitotic activity in the undifferentiated area. Immunohistochemistry showed the tumor cells in the glandular component to be positive for estrogen receptor (ER) (patchy) and cytokeratin [Figure 3b] and negative for vimentin [Figure 3c]. The tumor cells in the undifferentiated component showed focal intense positivity for cytokeratin; focal positivity for vimentin and was negative for ER. The patient was disease-free for 1 month after the initial diagnosis and then lost to follow-up.

DISCUSSION
Undifferentiated carcinoma of the endometrium is a poorly recognized neoplasm, defined by World Health Organization (WHO) as malignant tumor of epithelial structures that is too poorly differentiated to be placed in any other category of carcinoma.[5] As dedifferentiated carcinoma is a recently recognized tumor, the incidence rate is still not established. The prognosis of DEAC is determined by the undifferentiated component.[1] The undifferentiated component can be misinterpreted as solid component of FIGO grade 3 endometrioid carcinoma. The morphologic appearance of DEAC also resembles undifferentiated endometrial sarcoma and malignant mixed mullerian tumors (MMMTs). DEAC has a worse prognosis in comparison to high-grade endometrioid carcinoma.

The solid component of high-grade endometrioid carcinoma shows focal glandular differentiation (1%–49% according to WHO); there is usually no abrupt demarcation between solid and glandular components; the cytological features of the cells of solid component and glandular component are similar; rhabdoid features are absent; there is diffuse positivity for CK and EM and positive expression of ER. The cytological features of undifferentiated and differentiated components are distinct in DEAC.[6] Immunohistochemical expression of CK and EMA are diffusely positive in endometrioid carcinoma, whereas those are focally positive in undifferentiated component of DEAC.
The undifferentiated component of dedifferentiated carcinoma usually shows absence of claudin-4 expression, while the differentiated component shows diffuse claudin-4 expression. Claudin-4 is an epithelial tight junction protein and it is always absent in sarcoma.[7]

Undifferentiated carcinoma and DEAC are associated with DNA mismatch repair defect and Lynch syndrome.[3,4] So, diagnosing DEAC correctly has an impact on identifying the genetic condition, genetic counseling, and work-up of family members who may also be affected by the same genetic defect. Recent studies have shown that undifferentiated carcinomas are frequently positive for programmed death ligand 1, and it suggests that immunotherapy may be considered as adjuvant in undifferentiated carcinoma showing programmed death ligand 1 positivity specially because there is poor response to traditional therapy.[8]

CONCLUSION

DEC is frequently misdiagnosed as high-grade endometrioid adenocarcinoma and MMMT, but it has a fulminant clinical course, grave prognosis, and genetic defects; and misdiagnosis of this rare condition will have an adverse effect on patient’s survival.

Consent

Informed written consents were obtained from the patients for the publication of this case report along with the images.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Silva EG, Deavers MT, Bodurka DC, Malpica A. Association of low‑grade endometrioid carcinoma of the uterus and ovary with undifferentiated carcinoma: A new type of dedifferentiated carcinoma? Int J Gynecol Pathol 2006;25:52‑8.
2. Altrabulsi B, Malpica A, Deavers MT, Bodurka DC, Broaddus R, Silva EG. Undifferentiated carcinoma of the endometrium. Am J Surg Pathol 2005;29:1316‑21.
3. Zaino R, Carinelli SG, Ellenson LH, Eng C, Katabuchi H, Konichi I, et al. Epithelial tumours and precursors. In: Kurman RJ, Carcangiu ML, Herrington CS, Young RH, editors. WHO Classification of Tumours of Female Reproductive Organs. 4th ed. Lyon: IARC Press; 2014. p. 132‑3.
4. Katoh M, Shaw C, Xu Q, Van Driessche N, Morio T, Kuwayama H, et al. An orderly retreat: Dedifferentiation is a regulated process. Proc Natl Acad Sci USA 2004;107:7005‑10.
5. Silverberg SG, Mutter GL, Kurman RJ, Kubik-Huch RA, Nogales FF, Tavassoli FA. Tumours of the uterine corpus. Epithelial tumours and related lesions. In: Tavassoli FA, Devilee P, editors. World Health Organization Classification of Tumours. Pathology and Genetics. Tumors of the Breast and Female Genital Organs. Lyon: IARC Press; 2003. p. 277.
6. Tafe LJ, Garg K, Chew I, Tornos C, Soslow RA. Endometrial and ovarian carcinomas with undifferentiated components: Clinically aggressive and frequently underrecognized neoplasms. Mod Pathol 2010;23:781‑9.
7. Tessier-Cloutier B, Soslow RA, Stewart CJR, Kobel M, Lee CH. Frequent loss of claudin-4 expression in dedifferentiated and undifferentiated endometrial carcinoma. Histopathology 2018;73:299‑305.
8. Al-Hussaini M, Lataifeh I, Jaradat I, Abdeen G, Otya L, Badran O, et al. Undifferentiated endometrial carcinoma, an immunohistochemical study including PD-L1 testing of a series of cases from a single cancer center. Int J Gynecol Pathol 2018;37:564‑74.