The Journal of Obstetrics and Gynecology of India (March–April 2025) 75 (Suppl 1):5552–5555
https://doi.org/10.1007/s13224-024-02007-2

CASE REPORT

Case Report on Dedifferentiated Carcinoma of Endometrium and It's Histopathological Characteristics

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Received: 30 December 2023 / Accepted: 27 May 2024 / Published online: 10 July 2024

Abstract

The DEAC, a rare entity, has an unfavorable clinical outcome. The role of adjuvant therapy is also controversial in this high-risk variety. The current FIGO grading may also lead to misdiagnosis of DEAC as FIGO grade 2 or 3 endometroid carcinoma, owing to histological insufficiency in assessing the details of solid component within a tumor. The recognition of UC component as a solid patternless growth is extremely important for a correct diagnosis of DEAC. Hereby, a 51-year-old female is presented with chief complaint of postmenopausal bleeding, with D&C report of a poorly differentiated carcinoma of endometrium. Complete comprehensive surgical staging was performed. The final HPE revealed 85–90% UC and 10–15% moderately differentiated endometroid carcinoma, which was finally IHC-proven as well. The disease was found metastatic to adnexa and retroperitoneal lymph nodes. Postoperatively patient was given chemotherapy as adjuvant therapy and she is asymptomatic on follow-up.

Keywords Dedifferentiated endometrioid adenocarcinoma · Undifferentiated carcinoma · DNA mismatch repair proteins · Immunohistochemistry (IHC)

Abbreviations

DEAC	Dedifferentiated endometrioid adenocarcinoma
EmC	Endometrioid adenocarcinoma carcinoma
UC	Undifferentiated carcinoma
FIGO	International Federation of Gynecology and Obstetrics
HPE	Histopathology examination
IHC	Immunohistochemistry
SC	Serous carcinoma
MMMT	Malignant mixed mullerian tumour
MMR	Mismatch repair

Introduction

Dedifferentiated endometrioid adenocarcinoma (DEAC) has two fundamental elements, low-grade endometrioid adenocarcinoma (EmC) and undifferentiated carcinoma (UC). The low-grade component in these tumours is usually the International Federation of Gynaecology and Obstetrics (FIGO) grade 1 or 2 endometrioid adenocarcinoma. Undifferentiated carcinoma (UC) component histologically characteristically displays solid, pattern less growth and clinically has a major significance. It is an aggressive tumour, with 58% of affected women presenting at FIGO stages III or IV [1]. The current FIGO grading system of endometrioid adenocarcinoma (EmC), grades tumours by the proportion of solid components within a tumour, without further details on the histologic features of solid areas, resulting in a misdiagnosis of DEAC as a FIGO grade 2 or 3 endometrioid carcinoma. However, differentiating between the two histology is essential for the provision of an appropriate management option for the patients as well as explaining the expected prognosis. The DEAC has a worse clinical outcome than even a high-grade endometrioid adenocarcinoma. The recognition of the UC component is critically important for a correct diagnosis of DEAC. The various studies in the literature emphasized that there are reproducible, distinctive histological features

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of UC. We present a rare case scenario of DEAC with an emphasized discussion on its characteristic clinicopathological features and management.

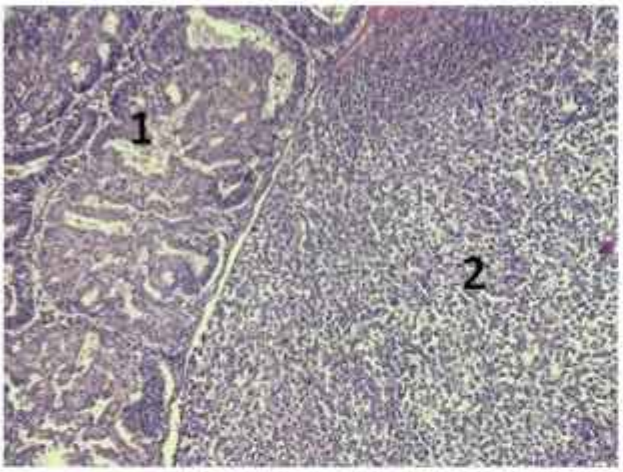

Fig. 1 Microscopic image showing UC (2) with solid discohesive cells pattern less growth with abrupt transition to low-grade EmC (1)

Case Summary

51 years female, para 2 live 2 with a BMI 23 kg/m^2, presented with chief complaints of post-menopausal bleeding for 4 months. She had diabetes mellitus and hypertension as medical comorbidities. The dilatation and curettage of the endometrium revealed a report of poorly differentiated carcinoma of the endometrium. The pre-operative imaging showed a disease involving the uterus invading the full thickness of its wall. There was no evidence of any enlarged lymph nodes in the pelvic or para-aortic region. Subsequently, the patient underwent comprehensive surgical staging as definitive management including hysterectomy, bilateral salpingo-oophorectomy with bilateral pelvic, and para-aortic lymphadenectomy with total omentectomy.

The gross examination of the specimen revealed a large polypoidal mass occupying the endometrial cavity and extending into the lower uterine segment. The tumour appeared to invade deep into the underlying myometrium and lower uterine segment. There was no cervical involvement. Microscopically, the tumour displayed an undifferentiated carcinoma (UC) component made up of sheets of discohesive cells with areas of necrosis, directly adjacent to a well-differentiated endometroid carcinoma. The UC component did not show any glandular, squamous, or serous/clear cell differentiation. The high-grade (UC) component comprised the bulk of the tumour. The boundary between

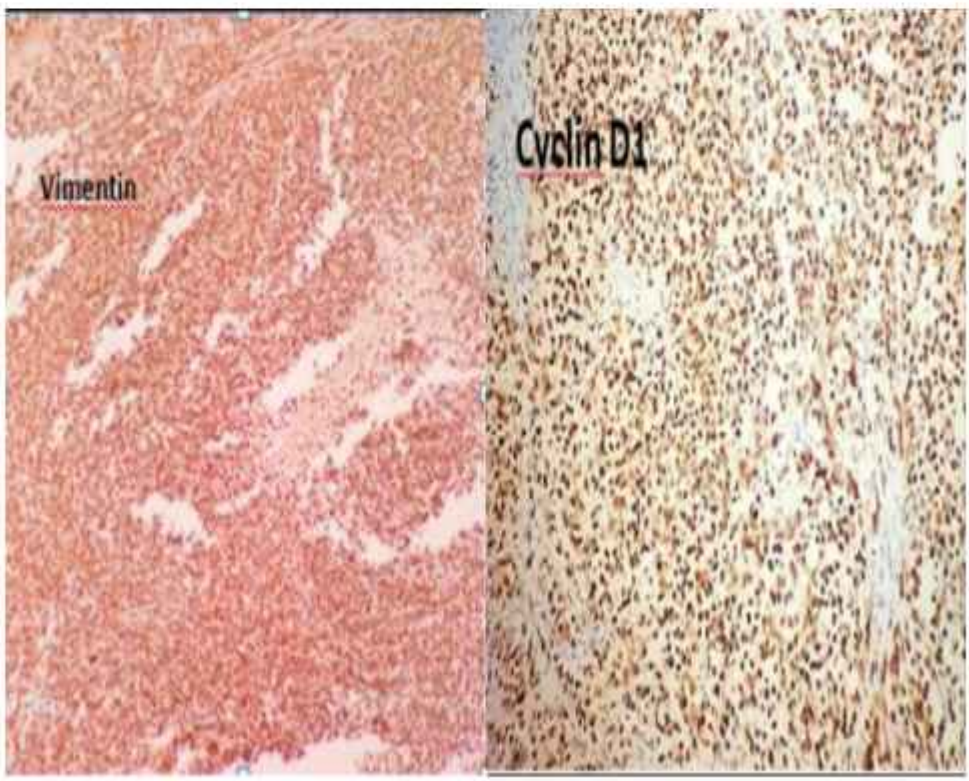

Fig. 2 IHC features of UC with diffuse positivity of vimentin, cyclin D1

the two components was abrupt with no definitive overlap or transition (Fig. 1).

The final histopathology report (HPE) revealed a tumour with two distinct components:

- 85–90% area shows discohesive monotonous epitheloid cells arranged in sheets
- 10–15% area shows moderately differentiated endometrioid carcinoma

Immunohistochemistry (IHC) panel markers results:

- Diffuse positive in Glandular component: CK, EMA, CK7, ER, PR.
- Diffuse positive in undifferentiated component: Vimentin, Cyclin D1 (Fig. 2).
- Patchy positive in undifferentiated component: CK, EMA, synaptophysin.
- Negative in undifferentiated component: ER, PR.
- P53 nuclear positive in undifferentiated component.

The final histopathology report: Dedifferentiated carcinoma of the endometrium

Further, the HPE report showed disease metastasis to bilateral ovaries along with a single pelvic and para-aortic lymph node positivity. The left parametria was also positive for a foci of metastasis, confirming it to be a case of FIGO stage IIIC2. Interestingly, all the metastatic sites had only undifferentiated components. Loss of DNA mismatch repair (MMR) proteins was observed in UC components. Further genetic evaluation found a germline MSH2 mutation consistent with Lynch syndrome. The post-operative course was uneventful. The patient was advised six cycles of chemotherapy (carboplatin with paclitaxel). Presently, the patient has been on follow-up for the last six months.

Discussion

The biological behaviour of DEAC is known to be determined by the UC component even when this component represents only 20% of the entire neoplasms, thus, conforming with its aggressive outcome. Our index case had approximately 90% UC of the entire neoplasm. DEAC primarily occurs during the 6th and 7th decades. Our patient was 51 years old, by the disease epidemiology. Even though UC components of DEACs are variably positive for keratins, EMA, and ER, they are mostly negative for PAX-8. Inadvertently, the undifferentiated component in DEAC is often misdiagnosed as grade 3 EmC, serous carcinoma (SC), malignant mixed Mullerian tumour (MMMT), undifferentiated endometrial sarcoma, poorly differentiated neuroendocrine carcinoma or malignant lymphoma. However, in grade 3 EmC, the tumour cells are morphologically similar to carcinoma cells in glandular areas; solid sheets or nests, and conspicuous glandular structures might also coexist. In SC, the glandular component with papillary features, slit-like lumens, background endometrial atrophy, and architectural-cytological discordance can also support the diagnosis. MMMT is a biphasic tumour composed of high-grade carcinoma, usually a serous carcinoma and a sarcomatous component that is typically reminiscent of a pleomorphic sarcoma.

The IHC markers, PAX-8, CK, EMA, ER, and PR were strongly and diffusely expressed in the low-grade EmC component, whereas the UC component was diffusely positive for vimentin and focally positive for CK, EMA, and neuroendocrine markers such as synaptophysin, chromogranin A, and CD 56 are rarely positive [2]. Our case HPE/IHC also correlated to similar findings.

The loss of DNA mismatch repair (MMR) proteins was observed relatively commonly in UC components associated with Lynch syndrome in some studies. So, an evaluation for MMR protein is warranted in these cases. Also, according to the literature, endometrioid tumours involving the lower uterine segment are commonly found to be associated with Lynch syndrome cases. The patient had a germline MSH2 mutation, consistent with Lynch syndrome. These results, together with the previous studies, suggest that MMR protein testing should be performed in patients with undifferentiated and dedifferentiated carcinomas [3].

In a study by Hamilton et al. [4], the disease-free survival for a 5-year was 80% for stage I/II, 29% for stage III, and only 10% for stage IV. The overall survival for a 5-year was 84% for stage I/II, 38% for stage III and 12% for stage IV. The literature suggests that adjuvant chemotherapy or radiotherapy and a lower FIGO stage of the malignancy have good clinical outcomes. The role of hormonal therapy is doubtful owing to negative ER and PR. The studies in literature stated that DEAC can present with a disease metastatic to bone or with distant metastases, even if the disease in the pelvis is restricted. They also observed only undifferentiated components at the metastatic site, corroborating to findings in our study.

Future studies are required relating to the origin of these undifferentiated tumour cell lines and their biological behaviour, as it usually behaves as a case of lymphoma or plasmacytoma cell lines. The role of adjuvant therapy as chemotherapy, radiotherapy, or immunotherapy needs an exhaustive evaluation. The contribution of extensive surgical staging for such an advanced stage with a poor prognosis needs to be extensively assessed.

Conclusion

The diagnosis of DEAC is purely based on its distinctive histological features of undifferentiated components. MMR testing should be performed for these patients due to a high incidence of abnormal profiles. The standard treatment guidelines for this rare pathology should be further discussed and designed.

Funding Not applicable.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest and nothing to disclose.

Ethical Approval Research involving human participants and/or animals: Ethical committee approval not required, as it is a retrospective original case report.

Informed Consent Informed consent was obtained from the participant included in the study.

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