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Yue Huang
Third Hospital of Shanxi Medical University
Hongxin Yu
Third Hospital of Shanxi Medical University
Yaqian Feng
Third Hospital of Shanxi Medical University
Qi Guo
Third Hospital of Shanxi Medical University
Xiaoxue Wang
Third Hospital of Shanxi Medical University
Lina Hu
Third Hospital of Shanxi Medical University
Jingfen Sun
Third Hospital of Shanxi Medical University
Haixia Shang
shanghaixia@sxbqeh.com.cn
Third Hospital of Shanxi Medical University

Case Report

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A Case Report on Endometrial Dedifferentiated Carcinoma with a Comprehensive Literature Review

Yue Huang[1#],Hongxin Yu[2#],Yaqian Feng[3], Qi Guo[4],Xiaoxue Wang[5] ,Lina Hu[3*] ,Jingfen Sun[2*],Haixia Shang[1*]

1 Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

2 Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

3 Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

4 Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

5 Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

2* Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

3* Department of Gynecology,Third Hospital of Shanxi Medical University/Shanxi Bethune Hospital,Taiyuan,Shanxi Sheng,China

#These authors contributed equally to this work.

*Corresponding author

Haixia Shang

Third Hospital of Shanxi Medical University, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences，Tongji Shanxi Hospital，Taiyuan, 030032, China,E-mail: shanghaixia@sxbqeh.com.cn

Short Title: Dedifferentiated Endometrial Carcinoma Misdiagnosed as Cervical Neuroendocrine Carcinoma

Keywords: endometrial dedifferentiated carcinoma; case report;pathological features; diagnosis and treatment.

Abstract

Objective: To illustrate the diagnostic pitfalls and key histopathologic clues in a rare case of International Federation of Gynecology and Obstetrics (FIGO) stage IA dedifferentiated endometrial carcinoma initially mistaken for cervical high-grade neuroendocrine carcinoma.

Case presentation: A 33-year-old woman presented with 7 years of intermittent postcoital bleeding. Cervical cytology showed high-grade squamous intraepithelial lesion despite negative HPV testing. Colposcopic biopsies of the cervix and endocervical canal revealed poorly differentiated carcinoma; immunohistochemistry favoured highgrade neuroendocrine carcinoma with possible adenocarcinoma admixture, leading to a pre-operative diagnosis of FIGO IB2 cervical neuroendocrine carcinoma. Laparoscopic radical hysterectomy with pelvic lymphadenectomy was performed. Definitive pathologic examination of the surgical specimen re-classified the tumour as dedifferentiated endometrial carcinoma, stage IA.

Conclusion: This case underscores the importance of comprehensive tissue sampling and judicious use of immunohistochemistry to avoid misclassifying uterine dedifferentiated carcinoma as cervical neuroendocrine malignancy, thereby ensuring appropriate surgical staging and adjuvant management.

Background

Endometrial dedifferentiated carcinoma (EDC) is a rare and exceptionally aggressive subtype of endometrial cancer first recognized in 2006 [1]. It is defined by the intimate admixture of a low-grade (FIGO grade 1–2) endometrioid adenocarcinoma and a solid, high-grade undifferentiated component; even when the latter constitutes as little as 20 % of the tumour volume, it dictates the fulminant clinical behaviour [2,3]. Patients typically present with abnormal uterine bleeding and a rapidly expanding uterine mass, yet the histological diagnosis is easily missed because the low-grade component may dominate the biopsy material, while the undifferentiated foci—often discohesive sheets of epithelioid or rhabdoid cells—are under-sampled . Misclassification as conventional grade 2/3 endometrioid carcinoma or even as carcinosarcoma is common, leading to under-treatment and poor outcome [1, 4]. Accurate identification of EDC is therefore critical, as this neoplasm carries a significantly worse prognosis than pure high-grade endometrioid carcinoma, with early extrauterine spread, frequent vascular invasion, and a median survival measured in months despite multimodal therapy [1, 4].Here we presented an uncommon case of FIGO stage IA dedifferentiated endometrial carcinoma that was initially misdiagnosed as high-grade neuroendocrine carcinoma of the cervix.

Case presentation

A 33-year-old Chinese woman, gravida 0, was referred for evaluation of persistent post-coital bleeding. Menarche occurred at age 17; menses were oligomenorrhoeic and required cyclic oral dydrogesterone to induce withdrawal bleeding. She had used traditional Chinese medicine intermittently without relief.

Physical examination showed vital signs were normal.Speculum examination revealed a 2 cm ulcerated mass replacing the anterior lip of the cervix; no vaginal parametrial involvement was appreciated.

Laboratory data showed that HPV DNA was negative (repeated twice, 2017 and 2024); ThinPrep cytology (first ever, 2024) was high-grade squamous intraepithelial lesion; Colposcopic biopsies (3, 9, 12 o’ clock plus endocervical curettage) were poorly differentiated carcinoma with brisk mitotic activity. Immunohistochemistry (IHC) performed at the referring hospital was interpreted as neuroendocrine carcinoma: synaptophysin diffusely positive, chromogranin-A focal, p40 negative, Ki67 index 90%.

Trans-vaginal ultrasound imaging showed 19 × 17 × 16 mm heterogeneous, hyper-vascular solid lesion arising from the anterior cervix. Contrast-enhanced pelvic CT showed irregular cervical wall thickening; no evidence of parametrial invasion or lymph-node enlargement.

The case report was approved by the Ethics Committee of the Third Clinical Medical College of Shanxi Medical University (YXLL-2025-294). Patient identities have been anonymised and informed consent obtained.

Pre-operative diagnosis was cervical high-grade neuroendocrine carcinoma,FIGO 2018 stage IB2.

Therapeutic intervention was radical surgery selected by the patient after fertility counselling. Laparoscopic radical hysterectomy with bilateral salpingo-oophorectomy and systematic pelvic lymphadenectomy was performed without intra-operative complications. Gross inspection revealed a cauliflower-like 2 cm tumour occupying the cervical canal and extending to the posterior wall of the lower uterine segment. Adjuvant treatment was initiated 20 days after surgery. Four cycles of paclitaxel–carboplatin (TC) were delivered every 3 weeks; cycles 3 and 4 were combined with bevacizumab. External-beam pelvic radiotherapy was subsequently completed.

Pathological findings showed tumour size was 1.6 × 0.8 × 0.6 cm, limited to the isthmic–cervical junction. Depth of myometrial invasion was one-third of the myometrial thickness. Lymphovascular space invasion was absent and all 28 pelvic nodes were negative. Endometrium was complex hyperplasia with squamous metaplasia.

Immunohistochemistry was performed. Endometrioid component showed that AE1/AE3, Vimentin, ER, PR, PAX-8, INI-1, SMARCA4 and mismatch-repair proteins (MLH1, PMS2, MSH2, MSH6) were positive; neuroendocrine markers (Syn,CgA, CD56) were negative; p53 showed wild-type staining; and Ki-67 index was ~40% in hot-spot areas

Undifferentiated component showed that AE1/AE3, Vimentin, ER[Figure1], and PAX-8 remained positive; PR and P16 became positive partially[Figure2-3]; mismatch-repair proteins (PMS2, MLH1, MSH2, MSH6) were positive[Figure4-7]; neuroendocrine markers were only focally and weakly positive; EMA was lost; p53 again indicated wild-type[Figure 8]; Ki-67 index rose to ~80% in hot-spot areas[Figure 9]..

Final diagnosis was dedifferentiated endometrial carcinoma, FIGO 2021 stage IA(pT1a N0 M0).

At 7 months post-treatment, the patient remains disease-free; surveillance imaging is unremarkable and serum tumour markers (CEA, CA19-9 and CA-125) are all within normal limits.

Discussion

Dedifferentiated endometrial carcinoma (EDC) is among the most aggressive uterine malignancies, yet its deceptively biphasic composition frequently leads to under-recognition, particularly when small biopsies sample only the undifferentiated component[1][2]. The present case illustrates two major pitfalls: (i) a cervical-centred growth pattern that masqueraded as a primary cervical neoplasm, and (ii) diffuse synaptophysin expression that prompted an erroneous diagnosis of high-grade neuroendocrine carcinoma. These issues are not unique; up to 40 % of EDCs are initially misclassified, resulting in protocol deviations that may compromise survival[3][4].

The tumour’s topography was the first confounder. EDC usually arises in the uterine fundus, but isolated examples originating in the lower uterine segment or endocervical canal have been described [5]. When the lesion protrudes through the cervical os, bleeding is easily attributed to a cervical primary, especially in young women who are still being screened cytologically. The negative high-risk HPV status should have raised suspicion; neuroendocrine carcinomas of the cervix are almost always HPV-related, whereas EDC shows no such association [6][7].

The second confounder was immunophenotype. The referring laboratory interpreted diffuse synaptophysin positivity as evidence of neuroendocrine differentiation. However, synaptophysin (and, less commonly, chromogranin) can be expressed non-specifically in a variety of high-grade gynaecological carcinomas, including the undifferentiated compartment of EDC [8]. Key iscriminatory markers were therefore the retained PAX-8, ER and PR, and the absence of TTF-1, p16 block positivity and HPV RNA, effectively excluding small-cell carcinoma of either cervical or pulmonary origin [9]. Loss of EMA in the undifferentiated component further aligned with the literature profile of EDC [10].

Accurate classification is not merely academic. Stage-for-stage, EDC carries a five-fold higher hazard of recurrence than FIGO grade 3 endometrioid carcinoma, and even women with apparent stage IA disease may harbour occult extrauterine spread [1] [11] . Our patient had deep myometrial invasion (one-third thickness), yet enjoyed favourable anatomy—tumour confined to the uterine isthmus, no lymphovascular space invasion and 28 negative pelvic nodes. On this basis we offered adjuvant chemotherapy plus bevacizumab followed by pelvic radiotherapy, a sequence modelled on the GOG-258 paradigm for high-risk endometrial cancer [12] . Whether bevacizumab adds meaningful benefit in EDC is unknown, but angiogenic gene signatures are enriched in the undifferentiated component and provide a biological rationale [13] . Close surveillance is mandatory; the median time to recurrence in contemporary series is [2][14] .

Fertility-sparing considerations deserve special comment. EDC has been reported in women as young as 24 years [15] ; hence the diagnosis must be entertained even in reproductive-age patients. When the tumour is confined to an endometrial polyp or superficial myometrium, theoretical fertility options (progesterone therapy plus/minus oncologic metrectomy) have been proposed, but no successful live births have been documented [16] . In our patient, deep myometrial invasion and an endocervical component mandated radical surgery; oocyte retrieval was precluded by the emergent nature of the procedure, underscoring the need for rapid multidisciplinary review once EDC is suspected.

In summary, this case emphasises that EDC can present at the cervix, express neuroendocrine markers, and afflict young women. Recognition requires integration of HPV status, topography, a broad immunohistochemical panel and, whenever feasible, expert gynaecological pathology review. Correct identification allows appropriate surgical staging and individualised adjuvant therapy, offering the best— albeit guarded—chance for cure.

Conclusion:

This case underscores the importance of comprehensive tissue sampling and judicious use of immunohistochemistry to avoid misclassifying uterine dedifferentiated carcinoma as cervical neuroendocrine malignancy, thereby ensuring appropriate surgical staging and adjuvant management.

List of abbreviations

EDC:Endometrial dedifferentiated carcinoma ; IHC:Immunohistochemistry ; TC: paclitaxel–carboplatin

Declarations

Statement of Ethics: The case report was approved by the Ethics Committee of the Third Clinical Medical College of Shanxi Medical University (YXLL-2023-053). Patient identities have been anonymised and written informed consent has been obtained.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Conflict of Interest Statement: The authors declare that they have no conflicts of interest regarding the publication ofthis study.

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Figure Legends

Fig . Legend text.

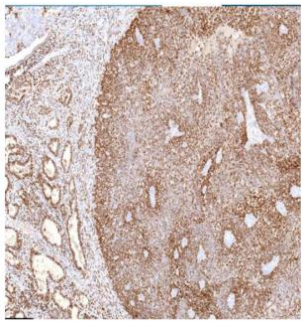


Figure 1 : ER IHC 10×

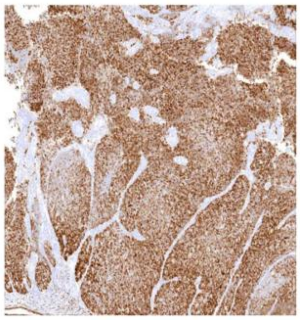


Figure 2 : PR IHC 10×

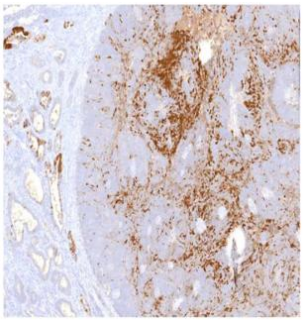


Figure 3 : p16 IHC 10×

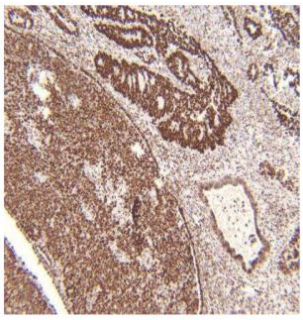


Figure 4 : PMS2 IHC 10×

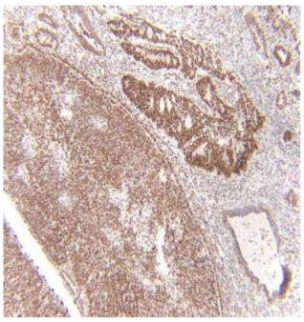


Figure 5 : MLH1 IHC 10×

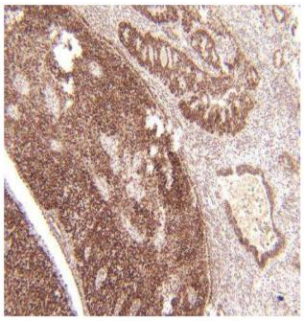


Figure 6 : MSH2 IHC 10×

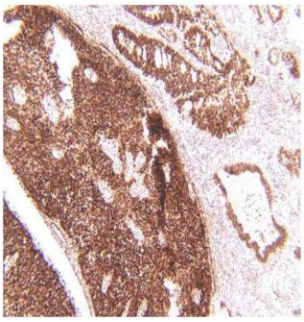


Figure 7 : MSH6 IHC 10×

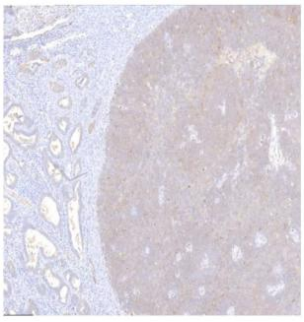


Figure 8 : p53 IHC 10×

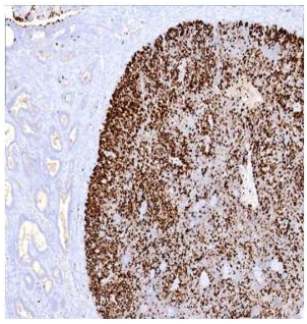


Figure 9 : Ki-67 IHC 10×

Figure 1–9. Immunohistochemical features of dedifferentiated endometrial carcinoma.Figures 1-2show ER and PR are retained in the endometrioid component and partially retained in the undifferentiated component, ,While Figures 3 show p16 demonstrates a nonblock-type staining pattern. Figures 4 show retained PMS2 expression. Figures 5-7 show retained nuclear expression of MLH1, MSH2, and MSH6, supporting mismatch repair proficiency. Figures 8 show wild-type p53 expression. Figures 9 show an increased Ki-67 proliferative index. Original magnification, ×10.