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DEDIFFERENTIATED ENDOMETRIAL CARCINOMA ASSOCIATED WITH ENDOMETRIAL POLYPS WITH STROMAL ATYPIA – A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT:
DEDIFFERENTIATED ENDOMETRIAL CARCINOMA IS A RARE OCCURRENCE IN UTERINE MALIGNANCIES. THIS HISTOPATHOLOGICAL SUBTYPE IS RELATIVELY NEW IN TUMOUR CLASSIFICATIONS AND MOLECULAR ALTERATIONS ARE IN CONTINUOUS DEVELOPMENT. WE DESCRIBE A 61-YEAR-OLD WOMAN WITH THIS DIAGNOSIS ASSOCIATING TWO ENDOMETRIAL POLYPS WITH STROMAL ATYPIA. THIS TYPE OF ASSOCIATION HAS NOT BEEN PREVIOUSLY REPORTED AND DIFFERENTIAL DIAGNOSIS IS OF THE UTMOST IMPORTANCE. WE EXCLUDED OTHER POTENTIAL DIAGNOSES SUCH AS MIXED CARCINOMA OR CARCINOSARCOMA. OUR AIM WAS TO BRING RECOGNITION TO THIS RELATIVELY NEW LESION AND REVIEW THE LITERATURE.

KEY WORDS: DEDIFFERENTIATED, ENDOMETRIAL, CARCINOMA.

INTRODUCTION

Dedifferentiated endometrial carcinoma is a relatively rare entity defined by the association of an undifferentiated component with a low-grade endometrioid component (FIGO grade 1 or 2) [6]. It accounts for approximately 9% of endometrial carcinomas [7] and is

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[6] WHO classification of tumours editorial board, *Female Genital Tumours*.
[7] Vroobel and Attygalle, "Sarcomatous Transformation in Undifferentiated/Dedifferentiated Endometrial Carcinoma."

usually associated with poor prognosis. Considering that new molecular subgroups have been proposed by the TCGA and WHO [8] for endometrial carcinomas, this rare entity has also been investigated. Reported cases have shown a heterogenous display of molecular alterations with different percentages in all four subgroups [9].

Endometrial polyps with stromal atypia are considered rare occurrences in postmenopausal women in which the atypical stroma is thought to be a degenerative or reactive process [10]. Studies are limited regarding this lesion, but its importance lies in the differential diagnosis. Malignancies must be excluded in this situation: carcinosarcoma or adenosarcoma.

MAIN TEXT

A 61-year-old female patient was referred to our clinic for surgical consult and treatment after accusing multiple abundant metrorrhagias and receiving a diagnosis of endometrioid endometrial carcinoma on a curettage in another institution. Patient history revealed heart failure NYHA II, paroxysmal atrial fibrillation under treatment, liver steatosis, a left renal cyst and gallbladder lithiasis. Clinical examination showed morbid obesity, with no other visible changes. A cardiology consult was performed and subsequent medication was established. CT examination revealed an enlarged uterus with the highest diameter of 20 mm with no secondary involvement of lymph nodes, lung, liver or bone. Total hysterectomy with bilateral adnexectomy with radical lymph node removal was performed.

Gross examination revealed an 8/6/6 cm endometrial tumour that occupied more than a half of the myometrium. Additionally, we found two endometrial polyps, closely connected to the endometrial tumour, measuring 5/3/2 cm and 3,5/4/1 cm respectively (Figure 1.). Histopathological examination revealed that the endometrial tumour consisted of two malignant populations: a low-grade (FIGO grade 2) endometrioid component (70%) and an undifferentiated component (30%) (Figure 2.A). Our findings were similar to other case reports, except for the presence of the two polyps [11].

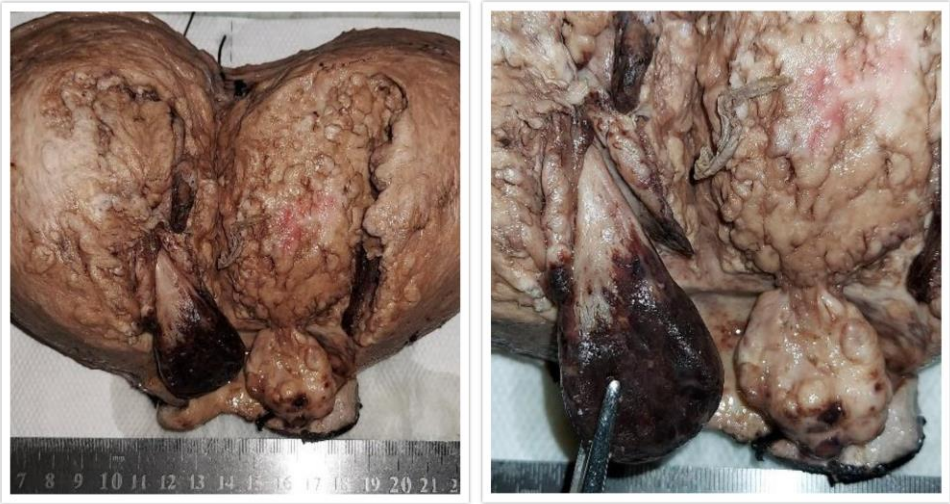

Figure 1.

[8] Hoang et al., "Interobserver Agreement in Endometrial Carcinoma Histotype Diagnosis Varies Depending on The Cancer Genome Atlas (TCGA)-Based Molecular Subgroup."
[9] Busca et al., "Undifferentiated Endometrial Carcinoma Arising in the Background of High-grade Endometrial Carcinoma – Expanding the Definition of Dedifferentiated Endometrial Carcinoma."
[10] Tai and Tavassoli, "Endometrial Polyps With Atypical (Bizarre) Stromal Cells."
[11] Han et al., "Dedifferentiated Endometrioid Carcinoma of the Uterus."

According to standardized pathological protocol, we reported several histopathologic parameters as follows: lympho-vascular invasion – present; uterine serosa involvement – absent; cervical stroma involvement – absent; lower uterine segment involvement – present.

Pattern of tumour invasion was reported as `adenomyosis involvement` (Figure 2.D). All resection margins and all lymph nodes were negative. Preliminary histopathological diagnosis was dedifferentiated endometrial carcinoma with TNM staging: pT1b pN0 LV1 R0, FIGO IB. On microscopic examination, the two endometrial polyps revealed tumour invasion and, in addition, their stroma showed pleomorphic, multinucleated stromal cells, warranting a differential diagnosis with a potential sarcomatous component (Figure 2.B, 2.C).

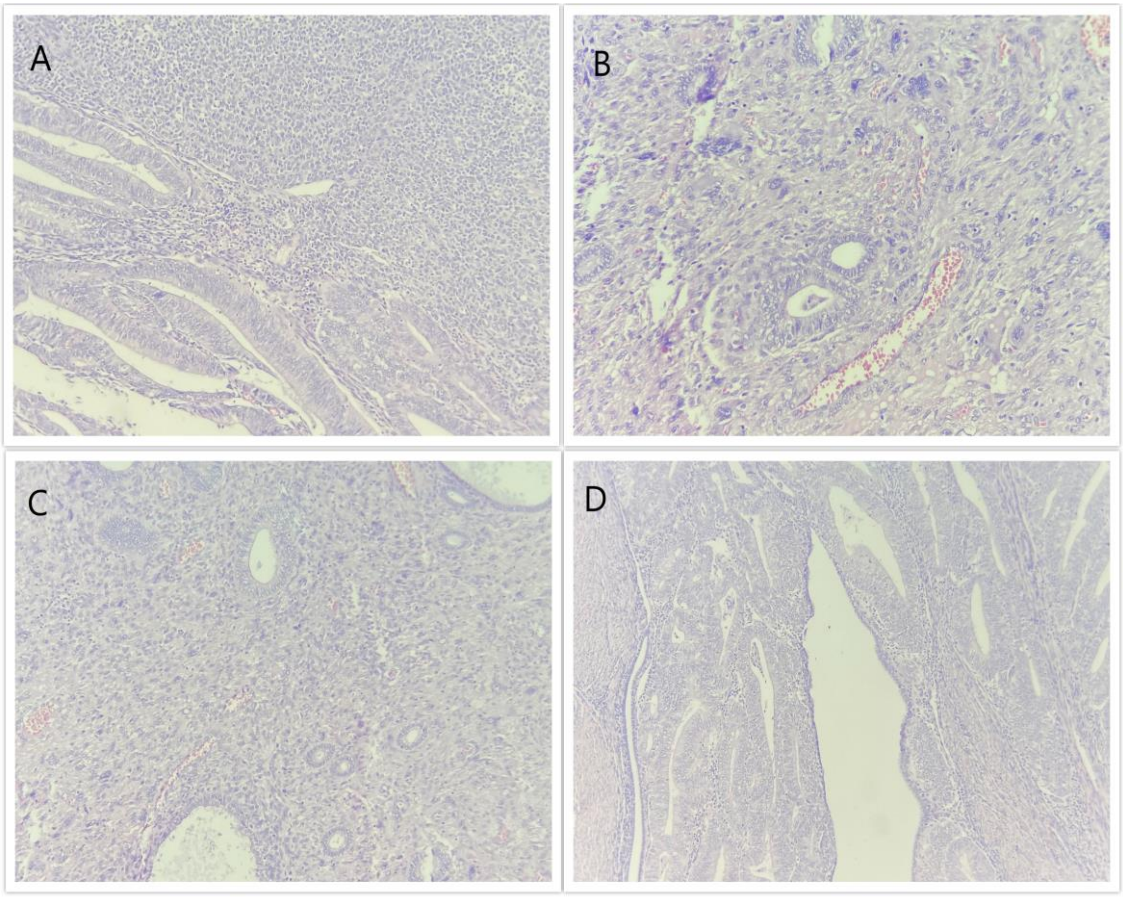

Figure 2.

An immunohistochemical panel was selected in order to evaluate all prognostic parameters and to exclude other differential diagnoses such as mixed endometrial carcinoma or carcinosarcoma. Genetic testing for POLE mutation was not available for this case. We performed ER (Figure 3.F) and PR (Figure 3.D) that were positive in 95% of tumour nuclei in the endometrioid component and negative in the undifferentiated component. Hormone receptor negativity in the undifferentiated component is a relatively constant finding, further confirming the diagnosis [12].

MLH1 (Figure 3.C), MSH2, PMS2 and MSH6 were positive in both components (MSS molecular subgroup – microsatellite stability). Surprisingly, most dedifferentiated

[12] Yiğit et al., "Dedifferentiated Endometrioid Adenocarcinoma; Clinicopathologic and Immunohistochemical Features of Five Cases."

endometrial carcinomas show microsatellite instability – MSI or are connected to the Lynch syndrome. Therefore, these subtypes are good candidates for immunotherapy and frequently express the immunohistochemical marker PD-L1 [13].

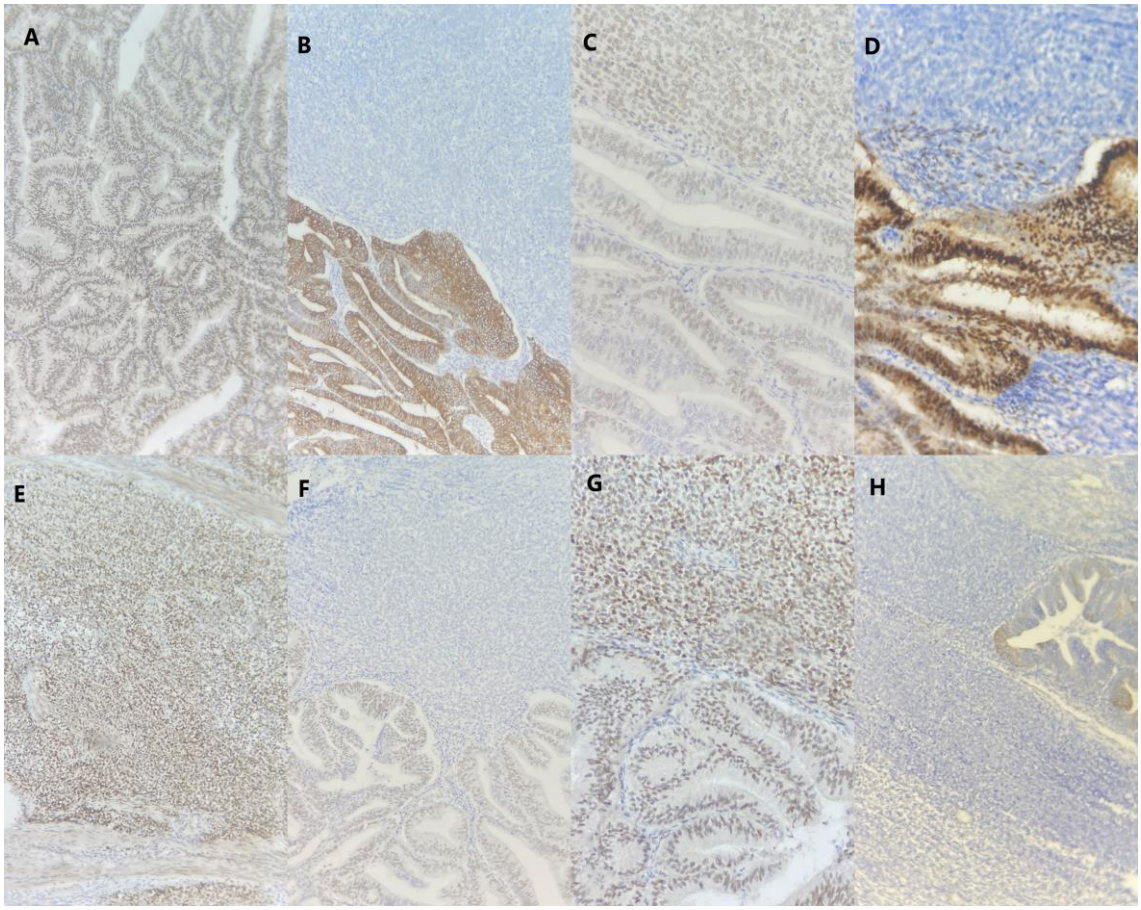

Figure 3.

P53 was overexpressed in both components (Figure 3.A, 3E), in more than 90% of tumour nuclei (p53abn molecular subgroup). WHO states that dedifferentiated endometrial carcinomas usually belong to the copy-number low subgroup, followed less frequently by the POLE-mutated subgroup and the TP53-mutated subgroup (p53abn). One recent study classified undifferentiated and dedifferentiated endometrial carcinoma according to the four TCGA molecular subgroups, showing that the p53abn molecular subgroup was identified in 18.6% of cases [14]. EMA (Figure 3.B) and CK8/18 (Figure 3.H) were positive in the endometrioid component, and only focally positive in the undifferentiated component. HER2 was negative in both components. Ki67 was positive in 90% (Figure 3.G) of tumour nuclei in both components.

In addition, we performed immunohistochemical testing in the endometrial polyps with atypical stroma. SMA (Figure 4.D.) and Vimentin (Figure 4.B.) were positive in the atypical stromal cells. CD10 was focally positive in the stromal cells (Figure 4.A). AE1-AE3 (Figure

[13] Ono et al., "Dedifferentiated Endometrial Carcinoma Could Be A Target for Immune Checkpoint Inhibitors (Anti PD-1/PD-L1 Antibodies)."
[14] Travaglino et al., "TCGA Molecular Subgroups in Endometrial Undifferentiated/Dedifferentiated Carcinoma."

4.E) was negative in the atypical stromal cells. Ki67 (Figure 4.C.) was positive in 4% of nuclei in the atypical stromal cells. Consequently, we excluded other sarcomatous components. Stromal atypia in endometrial polyps is rare and usually identified in patients that followed tamoxifen treatment[15]. Since this is not the case with our patient, we concluded that the atypical stromal cells should be interpreted as degenerative in a post menopause patient.

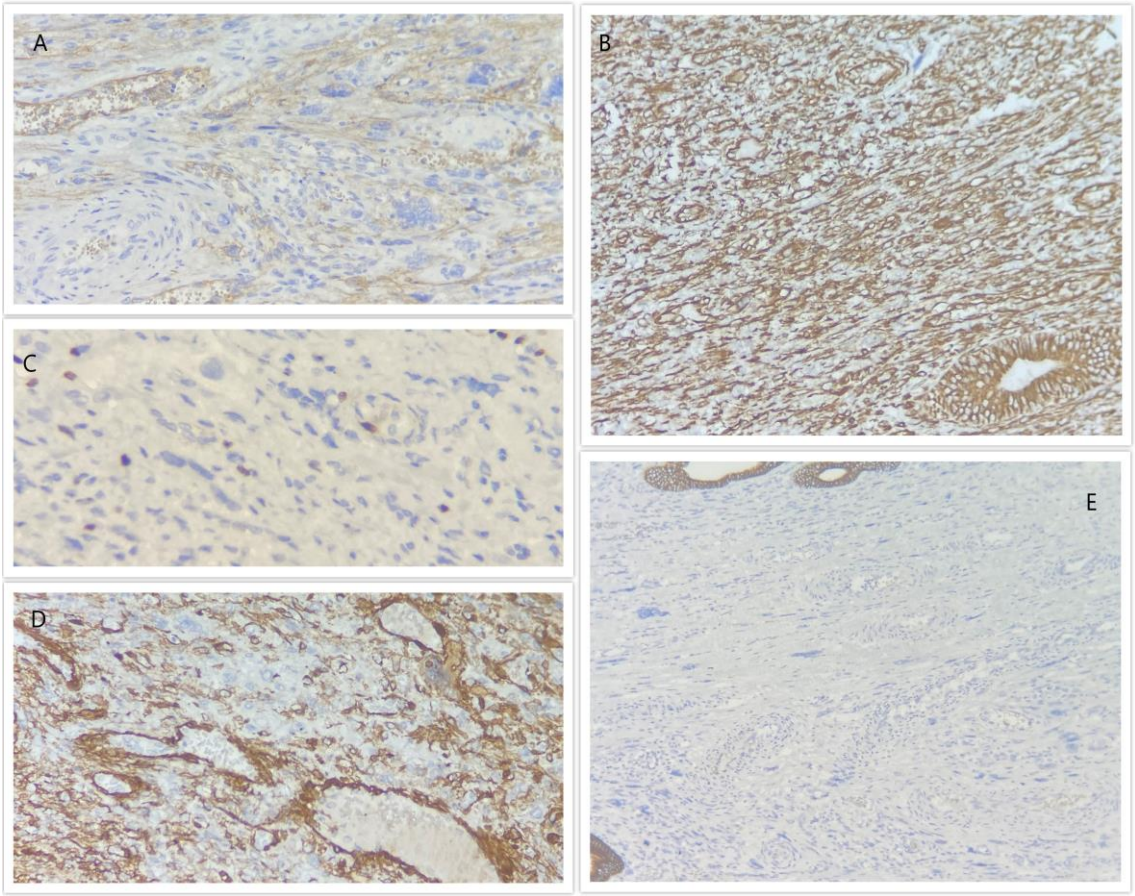

Figure 4.

Final histopathological and immunohistochemical diagnosis was *dedifferentiated endometrial carcinoma, MSS, p53abn, associated with endometrial polyps with stromal atypia*.

CONCLUSION

The rarity of our case is represented by various factors: the histopathological subtype, the microsatellite stability, belonging to the p53abn molecular subgroup and the association with two endometrial polyps with stromal atypia.

Dedifferentiated endometrial carcinomas are rare histopathological subtypes and have a very poor prognosis. One should always have in mind the differential diagnoses for the undifferentiated component such as high-grade (FIGO3) endometrioid carcinoma, which has a very different clinical behaviour. To our knowledge, this is one of a few case reports of

[15] Öztürk et al., "Case Report of Atypical Endometrial Stromal Cells in an Endometrial Polyp and Osteoclastic like Giant Cells in Leiomyoma in the Same Patient."

dedifferentiated endometrial carcinoma associated with endometrial polyps with stromal atypia in our country.

I undersign, certificate that I have the written consent of the identifiable person or his/her legal guardian in order to present the cases in this scientific paper. All authors equally contributed to this research. All authors report no potential conflict of interest.

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