



## Dedifferentiated Endometrial Carcinoma: A Rare Uterine Malignancy

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### Editorial

Dedifferentiation represents the presence of a high-grade neoplasm which can occur de novo, or be juxtaposed to, or arise as a recurrence of previously well-differentiated tumor. Usually, dedifferentiation can be observed in bone and soft-tissue tumors and it was considered as a histological indicator of tumor progression.

More recently, dedifferentiation also has been recognized in a variety of malignant epithelial neoplasms such as salivary gland carcinomas, including adenoid cystic carcinoma, mucoepidermoid carcinoma, myoepithelial carcinoma, and acinic cell carcinoma.

As well as, dedifferentiated carcinomas had been reported in gastrointestinal tract, pancreas and urinary tract.

Dedifferentiated Endometrial Carcinoma (DEC) is an uterine or ovarian neoplasm containing both Low-Grade Endometrioid Carcinoma (LGEC) and a solid undifferentiated component (Undifferentiated Carcinoma). According to studies of Silva et al, DEC is an aggressive tumor even when the UC component represents only 20% of the entire neoplasm.

### DEC Frequently is Misdiagnosed as G3 Endometrioid Carcinoma

It is very important to distinguish G3 endometrioid carcinoma from DECs which have an aggressive behavior and can be considered as a malignancy with a poorer prognosis than G3 endometrioid carcinoma. Many reports, in fact, have demonstrated that differentiating in endometrial carcinoma have fulminant clinical outcomes and poorer prognosis than high-grade endometrioid carcinoma.

Thus, the recognition of the undifferentiated component associated with low-grade endometrioid adenocarcinoma is very important. A range of differentials needs to be considered and ruled out on the basis of the clinical profile, morphology, and immunohistochemical features of this tumor.

The UC component was characterized by the solid growth of tumor cells, with large necrotic areas, instead, gland formation, trabecular or nested growth pattern characteristically are absent. The cells in the UC had a monomorphic appearance, presented as sheets of dyscohesive round to ovoid cells with prominent eosinophilic nucleoli, coarse chromatin, significant atypia and numerous mitotic figures, which was separated by delicate fibrovascular septa.

In some cases the UC cell component may show dyscohesive round rhabdoid features. In these occurrences the neoplasm can be misdiagnosed as Malignant Mixed Mullerian tumor.

On immunohistochemical analysis, the differentiated components express strongly, diffusely positive with EMA and ER and Ca-125, on the contrary, the undifferentiated areas show almost complete loss of expression of these markers. As well as strong, diffuse staining for cytokeratins can be observed in the differentiated components, but with focal and strong staining in the undifferentiated areas. Both the differentiated and undifferentiated areas show strongly positive staining for PR, but the positive cells of the undifferentiated areas was much lower.

In some instances UC component can express immunoreactivity for neuroendocrine markers, such as Chromogranin A, Synaptophysin, suggesting erroneous diagnosis of neuroendocrine neoplasm.

In line with other high grade neoplasms, undifferentiated component of endometrial dedifferentiated carcinoma shows iper-expression of p53 and p16, suggesting that abnormalities of these proteins may be implicated in the process of dedifferentiation.

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In my previous investigation, I confirmed the more recent hypothesis of Shia et al, who suggested that DECs having an

architectural heterogeneity and should be characterized by high Microsatellite Instability (MSI).