IMMUNOHISTOCHEMICAL EXPRESSION OF CYCLIN D1 IN ENDOMETRIAL CARCINOMA.

Samar Mohammed El Sheikh, Mohammed Farouk El-Shazly,* Marwa Mohamed Abd El-Aziz, Aya Mohamed saied Abd El Aal
Department of Pathology, Department of clinical oncology,* Faculty of Medicine, Alexandria University, Alexandria, Egypt

Introduction

EC is considered as one of the most common malignant tumors of the female reproductive tract. EC is most typically diagnosed after menopause, with a peak incidence of 60 to 70 years. Risk factors include obesity, nulliparity, hormonal imbalance and genetic predisposition. Molecular classification of EC includes POLE mutated type, hypermutated type with MSI instability and p53 mutant type. Prognostic factors of EC include: stage and its parameters, endometrial thickness, p53 status, MMR status. The tumor stage is determined by: Histological subtype and grade, Uterine serosal involvement, Adnexal involvement, Parametrial invasion, Myometrial invasion, Cervical stromal invasion, Vaginal involvement, Lymphovascular space invasion (LVI) and Lymph node involvement. Cyclin D1 is a crucial regulator of cell cycle progression and participates in DNA synthesis. Cyclin D1 regulates the G1-S phase transition by both CDK-dependent and CDK-independent pathways. During cell cycle progression most oxidative DNA lesions occurring in the G1 phase are repaired by MMR proteins. Persistent expression of cyclin D1 during S-phase increases the mutational burden and promotes microsatellite instability due to inability of MMR proteins to bind to PCNA, persistently occupied by p21.

Aim of the work

To evaluate the immunohistochemical expression of Cyclin D1 in endometrial carcinoma tissue samples and to correlate the pattern of expression of Cyclin D1 with different clinicopathologic parameters.

Material and Methods

This study was conducted on 45 retrospective cases of EC. Paraffin blocks and relevant data for all cases were retrospectively collected from the archives of Pathology and Oncology Departments, Faculty of Medicine, Alexandria University, in the period between January 2020 and December 2022. In the present study, the work protocol entailed the following: Collection of clinical data, Pathological examination, Staging of EC according to FIGO staging system 2023, Immunohistochemical examination and Statistical analysis of collected data. Positive and negative controls were included in all runs. Assessment of Cyclin D1 immunostaining was done by four methods as follows: Cyclin D1 combined H score, density of Cyclin D1 immunostaining, predominant intensity and highest intensity of Cyclin D1 immunostaining. The staining pattern of p53 was determined as follows: Wild type, Mutant positive, Mutant null and Mutant cytoplasmic pattern.

MMR staining was categorized into either deficient or proficient pattern as deficient or proficient. Staining for any MMR protein is considered intact with any nuclear staining that shows an intensity similar to or higher than the surrounding stromal fibroblasts which act as internal positive control.

Results

Table 1: Correlation between H-score and density of Cyclin D1 expression with different pathologic parameters.

		Cyclin D1 combined H-score			Density of Cyclin D1		
	N	Mean (± SD)	Test of significance	p	Mean (± SD)	Test of significance	P
Histology subtype							
Endometrioid	40	76.33 ± 67.64	U= 59.50	0.148	31.93 ± 22.43	U= 60.50	0.158
Non Endometrioid	5	35.0 ± 28.94			18.0 ± 13.04		
Histology grade							
1	14	45.43 ± 42.50	H=1.620	0.445	20.07 ± 15.34	H=6.672	0.036
2	19	74.74 ± 47.27			34.21 ± 16.69		
3	7	142.43 ± 108.59			49.43 ± 34.96		
FIGO Stage							
I	29	76.72 ± 64.35	H= 1.586	0.452	33.10 ± 21.56	H=2.012	0.366
II	8	48.38 ± 42.39			22.0 ± 14.71		
III	5	106.0± 100.46			39.0 ± 31.50		
P53 expression							
Wild	40	76.03 ±67.70	U= 64.00	0.207	32.02 ±22.46	U=58.500	0.137
Mutant	5	37.40 ±31.64			17.20 ±11.26		
MMR status							
All proficient	28	56.11 ±58.53	U= 142.0*	0.024*	25.39 ± 19.67	U= 152.0*	0.043*
Deficient	17	97.47 ± 70.17			59. 23.55		

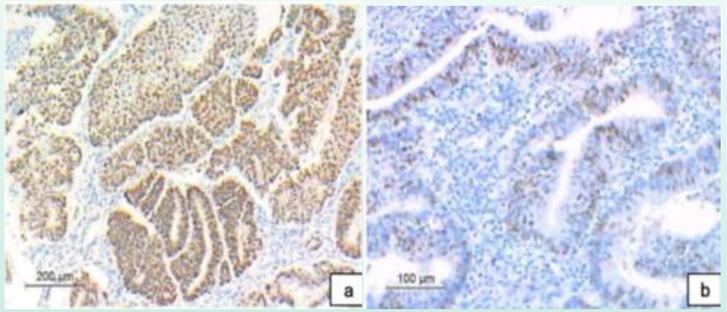

Figure 1:
Cyclin D1 expression:
(a) A predominantly strong intensity in >90% of the nuclei in EEC.
(b) A predominantly moderate intensity in >50% of the nuclei.

Conclusion

Since Cyclin D1 expression is significantly higher in MMR deficient cases, Cyclin D1 can be used to predict the MMR deficient status using either of the following: H score>65, density>20 and strong intensity (being the predominant or the highest intensity).

Only the density of Cyclin D1 showed a statistically significant correlation with the FIGO grade in EEC.