Clinicopathologic significance of mismatch repair protein expression in endometrial cancer

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Objective

To evaluate the mismatch repair (MMR) protein expression in endometrial cancer and to assess their association with clinicopathologic outcomes.

Methods

A retrospective review of the clinico-pathologic data and clinical outcomes was performed on patients who were treated for endometrial cancer at a single center between 2014 and 2018. For the study analysis, patients with results for MMR protein immunohistochemistry were included. MMR-deficient (MMR-d) was defined as absence of expression in any of the 4 MMR proteins (MLH1, MSH2, MSH6, and PMS2). Clinical and pathologic outcomes were compared according to the MMR status.

Results

A total of 146 endometrial cancer patients with available MMR expression data were included. Of these, 41 patients (28.1%) showed absence of MMR protein expression (MMR-d). Compared with MMR-proficient (MMR-p) patients, the MMR-d patients had higher rate of pelvic and/or para-aortic lymph node metastasis and lymphovascular space invasion ($p=0.011$ and $p=0.015$, respectively). However, other clinico-pathologic variables, including stage, grade, histologic subtype, and depth of invasion, were not associated with MMR status. During the median follow-up period of 18.2 months (1-39.4), there was no difference in progression-free survival between MMR-p and MMR-d patients ($p=0.254$).

Discussion

MMR defects were associated with higher rate of lymphovascular space invasion and lymph node metastasis. However, other prognostic factors and survival outcomes were not different between MMR-p and MMR-d patients.

Table 1. Patient characteristics (N=146)

Variables	n (%)
Age at diagnosis, mean (range)	54.2 (26-81)
BMI, mean (SD), kg/m ²	25.8 +/- 4.2 (16.9-40.8)
Menopausal state	
Yes	61 (41.8)
No	85 (58.2)
DM	14 (9.6)
Hypertension	38 (26.0)
FIGO stage	
IA	88 (60.3)
IB	16 (11.0)
II	18 (12.3)
IIIA	4 (2.7)
IIIB	1 (0.7)
IIIC1	4 (2.7)
IIIC2	13 (8.9)
IV	2 (1.4)
MMR-p	105 (71.9)
MMR-d	41 (28.1)
MLH1/PMS2	28 (68.3)
MSH2/MSH6	13 (31.7)

Table 2. Clinicopathologic variables according to MMR status

Variables	MMR-p (n=105)	MMR-d (n=41)	p-value
Age at diagnosis, mean	54.2	54.2	0.997
Histologic types			0.413
Endometrioid	88 (83.8)	37 (90.2)	
Mucinous	3 (2.9)	0 (0.0)	
Serous	7 (6.7)	1 (2.4)	
Clear cell	1 (1.0)	0 (0.0)	
Others	6 (5.7)	3 (7.3)	
Grade			0.140
1	43 (41.3)	10 (24.4)	
2	38 (36.5)	21 (51.2)	
3	23 (22.1)	10 (24.4)	
Stage			0.433
IA	67 (63.8)	21 (51.2)	
IB	12 (11.4)	4 (9.8)	
II	13 (12.4)	5 (12.2)	
IIIA	3 (2.9)	1 (2.4)	
IIIB	1 (1.0)	0 (0.0)	
IIIC	8 (7.6)	9 (22.0)	
IV	1 (1.0)	1 (2.4)	
Depth of invasion			0.218
<1/2	79 (75.2)	26 (65.0)	
>1/2	26 (24.8)	14 (35.0)	
LVSI			0.015
negative	61 (66.3)	17 (43.6)	
positive	31 (33.7)	22 (56.4)	
LN metastasis			0.011
negative	96 (91.4)	31 (75.6)	
positive	9 (8.6)	10 (24.4)	

Figure 1. Survival outcomes according to MMR status