NUHS-MD ANDERSON PATHOLOGY UPDATE

SINGAPORE

27-29 OKTOBER 2011

DR. ANIZA HASSAN
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27-29 October 2011

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EXPRESSION OF E-CADHERIN AND β-CATENIN IN SURFACE EPITHELIAL OVARIAN CARCINOMA

Hassan Aniza[1] & Singh Mutum Samarendra[1]
Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia[1]

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Introduction

According to the World Health Organization (WHO), ovarian carcinoma represents about 30% of all cancers of the female genital tract; as common as invasive cancers of the cervix (27%) and cancers of the corpus uteri (29%) in developed nations[1]. In Kelantan, ovarian carcinoma is the third commonest cancer(8.6%) in female between 1988 to 2005, preceded by breast(19.9%) and cervix uteri(10.3%)[2].

Primary ovarian epithelial tumours are the most prevalent, accounting for almost 90% of all ovarian malignancies. They are derived from the ovarian surface epithelium and are composed of one or more distinctive types of epithelium and their behavior varies with histological subtypes. Due to their silent growth with lack of early warning symptoms, more patients tend to present at an advanced stage at the time of diagnosis[3].

Cell adhesion molecules(CAM's), are shown to be involved in tumour progression and have important roles in the molecular histology of tumours and any significant change in the expression or structure of these components leads to adherens junction disassembly, and is implicated in loss of tumour differentiation and in the development of an invasive tumour phenotype[4].

Objectives

This study aims to analyze immunoexpression of E-Cadherin and β-catenin in surface epithelial ovarian carcinoma and correlating them with histological subtype and tumour grade.

Other pertinent clinicopathological parameters that were assessed includes age, FIGO stage, presence/absence of capsular breach and peritoneal deposits.

Material & Method

This study includes data for a 13 years period from the year 1998 to 2010. This study is based on archival material of formalin-fixed, paraffin embedded blocks from hysterectomy and ovarian cystectomy specimens with final histopathological diagnosis of Primary Ovarian Carcinoma.

The demographic data and histopathological examination reports were obtained from computerized registry system and registry book from the Department of Pathology, Hospital Universiti Sains Malaysia(HUSM), Kubang Kerian, Kelantan, Malaysia. Various independent pathologists within the department had reported these specimens. The data was scrutinized to avoid duplicate of more than one entry per case.

The tumor was evaluated and scored in hot spots according to intensity and proportion of cells stained. Expression was categorized as either positive or negative using median as cutoff positivity for statistical analysis. The data was analyzed using SPSS Version 18.0. Value $p < 0.05$ was considered to be statistically significant.

Ethics

This research was granted ethical approval from the Research Ethics Committee(Human), Universiti Sains Malaysia.

Results

There was a significant association between the combination of negative expressions of both E-cadherin and β-catenin with tumour grade($p=0.038$) and FIGO stage($p=0.037$).

Both E-cadherin and β-catenin lost its expression in high grade ovarian carcinoma(84.7%). In low grade tumours, at least one of the markers were positively expressed($p=0.038$).

Most(72.2%) of the early FIGO stage(FIGO I/II) tumours maintained expression of one of the markers($p=0.037$).

There was a significant association between negative E-cadherin and β-catenin expression and serous carcinoma($p=0.004$); 90.9% of high grade serous carcinoma looses both of its E-cadherin and β-catenin expressions. This associations was not seen in mucinous, endometrioid or clear cell carcinoma.

There was no associations between the expressions of E-cadherin and β-catenin with capsular invasion and peritoneal deposits($p>0.05$).

VARIABLES	FREQUENCY	PERCENTAGE
Age(years)		
<50	40	45.5%
≥50	48	54.5%
Histological subtype		
Mucinous	14	15.9%
Serous	47	53.4%
Endometrioid	16	18.2%
Clear cell	11	12.5%
FIGO stage		
I-II	36	40.9%
III-IV	52	59.1%
Tumour Grade		
Well/Moderate	71	80.7%
Poor	17	19.3%
Capsular Invasion		
Yes	75	85.2%
No	13	14.8%
Peritoneal Deposits		
Yes	59	33.0%
No	29	67.0%

Table 1: Summary of clinicopathological parameters in ovarian cancers

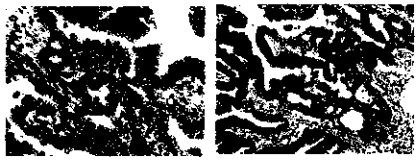

Figure 1: Image of positive E-cadherin(right) and β-catenin(left).

CHARACTERISTICS	NO. OF PATIENTS	BOTH E-CADHERIN & β-CATENIN NEGATIVE, n(%)	OTHERS, n(%)	*P VALUE
Age(years)				
<50	40	13(32.5%)	27(67.5%)	0.143
≥50	48	23(47.9%)	25(52.1%)	
Histological subtype				
Serous	47	23(48.9%)	24(51.1%)	0.137
Mucinous	14	2(14.3%)	12(85.7%)	
Endometrioid	16	6(37.5%)	10(62.5%)	
Clear cell	11	5(45.5%)	6(54.5%)	
FIGO stage				
I-II	36	10(27.8%)	26(72.2%)	0.037
III-IV	52	26(50.0%)	26(50.0%)	
Tumour Grade				
Well/Moderate	71	25(35.2%)	46(64.8%)	0.036
Poor	17	11(64.7%)	6(35.3%)	
Capsular Invasion				
Yes	75	33(44.0%)	42(56.0%)	0.157
No	13	3(23.1%)	10(76.9%)	
Peritoneal Deposits				
Yes	59	25(42.4%)	34(57.6%)	0.690
No	29	11(37.9%)	18(62.1%)	

*Pearson Chi Square Test
Table 2: Associations between combined negative expression of E-cadherin and β-catenin in ovarian carcinoma.

HISTOLOGICAL SUBTYPE	NO. OF PATIENTS	BOTH E-CADHERIN & β-CATENIN NEGATIVE, n(%)	OTHERS, n(%)	*P VALUE
SEROUS	47			
Low grade(Well/Moderate)	37	14(37.8%)	23(62.2%)	0.004
High grade(Poor)	10	9(90.0%)	10(10.0%)	

*Fisher Exact Test
Table 3: Associations between combined negative E-cadherin and β-catenin in serous subtype of ovarian carcinoma according to tumour grade

Conclusions

Ovarian carcinomas with both negative E-cadherin and β-catenin expressions might behave more aggressive clinically as they tend to have higher grade and stage.

Reference

1. Tavassoli FA and Devilee P(2003), World Health Organizations Classifications of Tumours Pathology and Genetics Tumours of the Breast and Female Genital Organs.
2. Kelantan Cancer Registry

3.Fabiro-Rodriguez C(2008), Epithelial ovarian cancer and E-cadherin-catenin complex in Handbook of Immunohistochemistry and in situ hybridization of Human Carcinoma: Molecular Genetics, Gastrointestinal Carcinoma and Ovarian Carcinoma.

4. Smith and Pihanelli(1997)
IHC

Acknowledgements

1. A very special and heartfelt thanks to my dear friends and colleagues in the Department of Pathology, School of Medical Sciences, HUSM, who has always been helpful.
2. These study was a project under the HUSM, Short Term Grant, PPSP/304/813/10044.