EXPRESSIONS OF p16INK4a, P27Kip1 AND p21WAF1 IN DIFFERENTIATING PRIMARY ADENOCARCINOMA OF ENDOCERVIX FROM ENDOMETRIUM

BY

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TABLE OF CONTENTS

LIST OF TABLES

TABLE

LIST OF FIGURES

FIGURE

LIST OF ABBREVIATIONS

AIS	Adenocarcinoma in situ
CEA	Carcinoembryonic antigen
CDK	Cyclin Dependent Kinase
CDKI	Cyclin Dependent Kinase Inhibitor
DNA	Deoxyribonucleic acid
ECA	Endocervical adenocarcinoma
EMA	Endometrial adenocarcinoma
ER	Estrogen receptor
FIGO	International Federation of Gynecology and Obstetrics
H&E	Hematoxylin and eosin
HPV	Human Papilloma Virus
HSB	Hospital Sultanah Bahiyah
HUSM	Hospital Universiti Sains Malaysia
IHC	Immunohistochemistry
MI	Microsatellite instability
PCR	Polymerase chain reaction
RB	Retinoblastoma
WHO	World Health Organization

ABSTRAK

Ekspresi p16INK4a, P27Kip1 dan P21WAF1 dalam membezakan adenokarsinoma primer dari endoservix dan endometrium.

Pembezaan di antara adenokarsinoma endoservix (ECA) dan adenokarsinoma endometrium (EMA) boleh menjadi masalah pada biopsi kecil atau apabila ada tumor di dalam biopsi endometrium dan endoservix; atau apabila tumor telah merebak ke segmen bawah endometrium. Penilaian adalah terhad apabila bergantung kepada histomorfologi sahaja kerana kedua-dua tumor ini boleh mempunyai histologi yang sama.

Kami mengkaji imunohistokimia bagi p16INK4a, P27Kip1 dan P21WAF1 dalam membezakan ECA dan EMA. Kami telah menjalankan pewarnaan immunohistokimia ke atas sampel hirisan tisu dari tahun 2005 hingga 2008 dari HSBAS dan HUSM. Kadar pewarnaan immunohistokimia tadi kemudiannya di kaitkan dengan parameter patologi klinikal.

Sebanyak 40 kes ECA and 92 kes EMA telah diperiksa. p16INK4a dan P27Kip1 didapati menunjukkan ekspresi yang tinggi (([p <0.001] (80% versus 25%) and [p=0.001] (43% versus 15%)) dalam kes ECA berbanding EMA. Kes ECA juga boleh dibezakan dengan kombinasi ekspresi p16INK4a dan P27Kip1. Manakala p21WAF1 tidak dapat membezakan antara ECA dan EMA (70% versus 78%, p=0.312). Hubungan yang signifikan didapati antara ekspresi negatif p16INK4a dan histologi tahap rendah dalam

EMA (p=0.014). Di dalam kes ECA, ekspresi p21 WAF1 menunjukkan hubungan yang sinifikan dengan penglibatan korpus rahim (p=0.043), manakala ekspresi negatif p27Kip1 adalah berkaitan dengan penglibatan nodus limfa (p=0.030). Analisis multivariat menunjukkan bahawa tiada hubungan antara penglibatan nodus limfa dan ekspresi p27Kip1 dengan bangsa, tahap histologi, penglibatan salur darah, ekspresi p21WAF1 dan penglibatan korpus rahim.

Kesimpulannya, kombinasi ekspresi p16INK4a dan P27Kip1 boleh membantu dalam membezakan antara ECA daripada EMA. Pada biopsi kecil, ekspresi p21WAF1 mungkin dapat membantu dalam menentukan penglibatan korpus rahim. P27Kip1 pula boleh membantu dalam menjangkakan penglibatan nodus limfa

ABSTRACT

The distinction between an endocervical adenocarcinoma (ECA) and an endometrial adenocarcinoma (EMA) can be problematic on small biopsies or when there is tumor in both endocervical and endometrial specimens or when the tumor has extended into the lower uterine segment. The judgment is difficult to be based on histomorphology alone because these tumors can have similar histologic appearance.

We investigated the value of p16INK4a, p21WAF1 and p27kip1 immunohistochemistry for distinguishing ECA and an EMA. We immunostained tissue sections of archival samples from 2005 to 2008 from HUSM and HSB. The immunohistochemical staining scores were correlated with their clinicopathologic parameters.

There were 40 ECA and 92 EMA cases examined. We observed significant higher expressions of p16INK4a and p27kip1 ([p <0.001] (80% versus 25%) and [p=0.001] (43% versus 15%)) in ECA than in EMA. ECA could be differentiated from EMA based on the combination expressions of p16INK4a and p 27kip1. p21WAF1 expression did not differentiate these two carcinomas (70% versus 78%, p=0.312). There was significant association seen between negative p16INK4a expression and low histologic grade in EMA (p=0.014). In ECA, p21WAF1 expression shows significant association with corpus infiltration (p=0.043) while negative p27kip1 expression with lymph node invasion (p=0.030). Multivariate analysis however shows no association between lymph node invasion and p27kip1 expression adjusted by race, histologic grade, vascular invasion,

p21WAF1 expression and extension into the uterine corpus.

In conclusions, combination of p16INK4a and p27kip1 expression is helpful in differentiating ECA from EMA. In small biopsy, the expression of p21WAF1 may help in assessing the presence of corpus infiltration. P27kip1 expression is helpful in predicting presence of lymph node invasion.