Study of $p27^{Kip1}$ as an Emerging Prognostic Marker for Breast Duct Carcinomas

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بسم الله الرحمن الرحيم

"وما أوتيتم من العلم الا قليلا"

صدق الله العظيم

Abstract

$p27^{kip1}$ is an inhibitor of cyclin dependent kinase involved in cell cycle regulation. The present work aimed at studying the value of p27 expression as a potential prognostic marker in breast duct carcinomas. p27 immunodetection was estimated and correlated with other clinicopathological prognostic factors (tumor size, tumor grade and lymph nodal status) and with other known well established prognostic biological markers (ER, PR and HER2/neu). Our results revealed the significant association of decreased p27 level of expression with a more aggressive tumor phenotype, concluding that p27 could be useful in the assessment of prognosis, especially in those cases in which the commonly used parameters are insufficient, and might ultimately influence the therapy of this disease.

Key Words: Breast duct carcinoma – Prognostic factor – Cell cycle inhibitor – p27

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LIST OF CONTENTS

Page

Introduction ……..……..……..…..1

Aim of the work ……..……..……..…..4

Review of Literature……..…..…..…….6

- *Breast carcinoma*…….……...7
  - *Normal histological structure of the breast*…….7
  - *Incidence of breast cancer*……10
  - *Risk factors of breast cancer*……12
  - *WHO classification of tumours of the breast*…… 20
  - *Prognostic and predictive factors*…… 24
- *The cyclin dependent kinase inhibitor p27^{kip1}*…… 48
  - *P27 regulation in normal & malignant cells*…… 52
  - *P27 localization and D cyclin CDK assembly*…… 58
  - *Cytoplasmic p27, migration and metastasis*…… 59
  - *Prognostic studies of p27 in human cancers*…… 60

Materials and Methods……...……..…….....67

Results……...…….....78

Discussion……....151

Summary & Conclusion…….....171

References……...……....177

Arabic Summary…….....……...210

LIST OF FIGURES

Page

Figure 1: Anatomy of the breast (Wendie and Thomas, 2006).....9
Figure 2: Normal histology of the human breast, a lobe and a TDLU (Tabár et al., 1998)…….....9
Figure 3: Regulation of the cell cycle (Kong et al, 2003)…….49
Figure 4: p27 phosphorylation and degradation (Medscape, 2008)…..56
Figure 5: Distribution of studied cases according to age……80
Figure 6: Distribution of tumour grades among the studied cases……..…81
Figure 7: Grade 2 invasive duct carcinoma showing tubular and glandular formation. X200.....82
Figure 8: Same case above exhibiting moderate cellular pleomorphism, anaplasia and occasional mitosis. X400……..……....82
Figure 9: Grade 2 IDC, showing evident tubular formation. X200.....83
Figure 10: Grade 2 IDC exhibiting moderate cellular pleomorphism and anaplasia. X400.....83
Figure 11: High grade IDC, exhibiting marked degree of anaplasia and frequent mitosis. Abnormal mitotic figures are detected. X400...……84
Figure 12: Grade 3 invasive duct carcinoma associated with comedo type DCIS. X200.....84
Figure 13: Distribution according to tumour size (T).....85
Figure 14: Distribution according to tumour type…….....86
Figure 15: Invasive duct carcinoma grade2, associated with DCIS component of solid and cribriform types. X100.....87
Figure 16: Invasive duct carcinoma associated with DCIS component comedo, solid and papillary (arrow) types. X200.....87
Figure 17: Invasive duct carcinoma showing multiple lymphovascular emboli (arrows). X200.....88
Figure 18: Evident perineural permeation by malignant ductal cells of IDC. X200…….....88
Figure 19: Distribution according to lymph nodal status.....89
Figure 20: Distribution according to tumour stage.....91
Figure 21: Distribution according to hormone receptor status.....93
Figure 22: Invasive duct carcinoma strongly expressing ER. X200.....94
Figure 23: Grade 2 IDC with positive ER staining of strong intensity and high proportion X400.....94
Figure 24: Invasive duct carcinoma associated with DCIS component showing weak positive reaction to PR with moderate intensity

of staining. Positive internal control in one normal breast lobule is demonstrated (arrow). X100……95
Figure 25: High grade IDC showing weak positive reaction to ER with positive internal control seen in nearby normal breast lobule (arrow). X200……95
Figure 26: Moderately positive ER reaction with weak staining intensity in grade 2 IDC. X200……96
Figure 27: Grade 2 IDC showing positive PR staining reaction with strong intensity. X200……96
Figure 28: Grade 3 IDC showing negative reaction to ER. Positive internal control is demonstrated in nearby normal breast lobule (arrows). X400……...97
Figure 29: Distribution according to HER2/neu expression.....98
Figure 30: Invasive duct carcinoma strongly positive for HER2/neu (score 3). X200……...99
Figure 31: Strong positive reaction for HER2/neu in a case of high grade IDC. Tumour cell in mitosis are seen (arrows). X400…….99
Figure 32: Strong Her2/neu positive reaction in a case of IDC associated with comedo DCIS. X200……100
Figure 33: Invasive duct carcinoma with equivocal reaction to HER2/neu (score 2). X100……100
Figure 34: Invasive duct carcinoma with equivocal HER2/neu reaction (score 2). X200……101
Figure 35: Invasive duct carcinoma with faint complete membranous equivocal reaction to HER2/neu (score 2). X200…….101
Figure 36: Invasive duct carcinoma showing incomplete membranous reaction for HER2/neu (score 1). X400……102
Figure 37: Invasive duct carcinoma with negative staining for HER2/neu (score 0). X200……102
Figure 38: Median percentage among studied tumour types.....104
Figure 39: Correlation between p27 expression and tumour type…....107
Figure 40: Correlation between p27 expression and tumour grade…...108
Figure 41: Correlation between p27 expression and tumour size…..…110
Figure 42: Correlation between p27 expression and lymph nodal status……112
Figure 43: Correlation between p27 expression and tumour stage..…114
Figure 44: Correlation between p27 expression and ER and PR status…….....116
Figure 45: Correlation between p27 expression and HER2/neu status……...118
Figure 46: Correlation between tumour type and p27 intensity of staining……...120

Figure 47: Correlation between tumour grade and intensity of p27 staining……...122
Figure 48: Correlation between tumour size and intensity of p27 staining…….....124
Figure 49: Correlation between lymph nodal status and p27 intensity…….....126
Figure 50: Correlation between tumour stage and p27 intensity…….128
Figure 51: Correlation between ER status and p27 intensity……131
Figure 52: Correlation between ER/PR status and p27 intensity……..132
Figure 53: Correlation between HER2/neu expression and p27 intensity…….....134
Figure 54: Correlation between tumour size and p27 cytoplasmic reaction……138
Figure 55: Correlation between tumour stage and p27 cytoplasmic reaction……141
Figure 56: Correlation between hormone receptor status and p27 cytoplasmic reaction…….143
Figure 57: Correlation between HER2/neu status and p27 cytoplasmic reaction…….144
Figure 58: Grade 2 invasive duct carcinoma strongly expressing p27 (90%) with strong intensity reaction. X200……..145
Figure 59: High expression of p27 among tumour cells (90%). Noticed tumour cells in mitosis did not show nuclear expression for p27 (arrows). X400……..145
Figure 60: Grade 2 invasive duct carcinoma expressing p27 (88.3%) with strong intensity reaction. X200…….146
Figure 61: High grade invasive duct carcinoma showing low expression for p27 (15%). Associated lymphocytic exudate shows strong p27 reaction as an internal positive control (arrows). X100……146
Figure 62: High grade invasive duct carcinoma with low expression of nuclear p27 (15%). Internal positive control is demonstrated in nearby lymphocytes. Faint cytoplasmic reaction is noticed.X200……...…….....147
Figure 63: IDC with comedo DCIS component showing moderate p27 expression (67%) with moderate intensity. X100.....147
Figure 64: DCIS highly expressing nuclear p27 (89%) with strong intensity reaction. X400……...148
Figure 65: Invasive duct carcinoma showing expressed nuclear p27 (64.5%) with moderate intensity reaction. X400…….148

Figure 66: Mildly expressed nuclear p27 (23%) with moderate staining intensity in a case of invasive duct carcinoma.X200……..….149
Figure 67: High grade invasive duct carcinoma showing low p27 expression (12.5%) with evident strong cytoplasmic reaction. X400…….149
Figure 68: Invasive duct carcinoma with very low p27 expression (12%). X400…….150

LIST OF TABLES

Page

Table 1: TNM staging system of breast cancer, 6th edition……..28
Table 2: Bloom Richardson scores in breast cancer…….....34
Table 3: Bloom-Richardson combined score and grades…….....35
Table 4: Allred score……41
Table 5: HER2/neu score used to evaluate Hercept Test…….46
Table 6: Age distribution among the studied cases.....79
Table 7: Distribution of tumour grades among the studied cases….....81
Table 8: Distribution of lymph nodal status among studied cases.....89
Table 9: Distribution of tumour stage among studied cases……90
Table 10: Hormone receptor status in cases studied……....92
Table 11: Median percentage of p27 among studied tumour types ……..…….....104
Table 12: Correlation of p27 expression with tumour type ……106
Table 13: Correlation between p27 expression and tumour grade ……..108
Table 14: Correlation between p27 expression and tumour size….....109
Table 15: Correlation between p27 expression and LN status....……..111
Table 16: Correlation between p27 expression and tumour stage……113
Table 17: Correlation between P27 expression and ER status.....115
Table 18: Correlation between p27 expression and PR status….....115
Table 19: Correlation between p27 expression and HER2/neu status…….....117
Table 20: Distribution of studied cases according to p27 intensity….....119
Table 21: Correlation between tumour type and intensity of p27 staining……120
Table 22: Correlation between tumour grade and p27 intensity of staining……121
Table 23: Correlation between tumour size and intensity of p27 staining……123
Table 24: Correlation between lymph nodal status and intensity of p27staining…….....125
Table 25: Correlation between tumour stage and p27 staining intensity…….....127
Table 26: Correlation between ER status and p27 intensity……..130
Table 27: Correlation between PR status and p27 intensity……..130
Table 28: Correlation between ER/PR status and p27 intensity……131

Table 29: Correlation between HER2/neu status and p27 intensity.....133
Table 30: Correlation between tumour type and presence of p27 cytoplasmic reaction……135
Table 31: Correlation between tumour grade and presence of p27 cytoplasmic reaction……136
Table 32: Correlation between tumour size and p27 cytoplasmic reaction……137
Table 33: Correlation between lymph nodal status and presence of p27 cytoplasmic reaction……..139
Table 34: Correlation between tumour stage and p27 cytoplasmic reaction…….....140
Table 35: Correlation between ER status and p27 cytoplasmic reaction……142
Table 36: Correlation between PR status and p27 cytoplasmic reaction.....142
Table 37: Correlation between ER/PR status and p27 cytoplasmic reaction……..143
Table 38: Correlation between HER2/neu status and p27 cytoplasmic reaction……...144

LIST OF ABBREVIATIONS

Abl 1: Abelson murine leukemia viral oncogene homolog 1
AG : Adenine Guanine
AKT: protein family, which members are also called protein kinases B (PKB) plays an important role in mammalian cellular signaling. Ak" in Akt was a temporary classification name for a mouse strain developing spontaneous thymic lymphomas. The "t" stands for 'transforming'
BCL-2: B-cell CLL/lymphoma 2
BR grade: Bloom Richardson grade
BRCA1: Breast cancer susceptibility gene 1
BRCA2: Breast cancer susceptibility gene 2
C : Cytosine
CD: Cathepsin-D
CDKs: Cyclin dependent kinases
CDKN1B: Cyclin-dependent kinase inhibitor 1B
CKS1B: cyclin-dependent kinase subunit 1B
c-erb-b2: erythroblastic leukemia viral oncogene homolog 2
CHEK2: Cell-cycle checkpoint kinase gene 2
CIS: Carcinoma insitu
CISH: Chromogenic In situ Hybridization
CML: Chronic myelogenous leukaemia
CUL 1: Cullin 1
DCIS: Ductal carcinoma insitu
Del : Deletion
DFS: Disease free survival
DNA: Deoxy ribonucleic acid
EGFR: Epidermal growth factor receptor
ER: Estrogen receptor
FISH: Fluorescence In situ hybridization
FoxO: Forkhead box class O family
Fyn: Proto-oncogene tyrosine-protein kinase Fyn
G0: Gap 0 (Resting phase).
G1: Growth phase 1 (Gap 1).
G2: Growth phase 2 (Gap 2).
GCSF: Granulocyte colony stimulating factor
HER-2/neu: Human Epidermal growth factor Receptor 2
HR: Hazard ratio
HRT: Hormone replacement therapy

ICD-O-3: International Classification of Diseases for Oncology, third revision
IDC: Invasive duct carcinoma
IHC: Immunohistochemistry
INK4: Inhibitors of kinase 4
Ins : Insertion
IRES: Internal ribosome entry site
Ki-67: Antigen identified by monoclonal antibody Ki-67
KIP: Kinase Inhibitor Protein
Lck: Leukocyte-specific protein tyrosine kinase
Lyn: V-yes-1 Yamaguchi sarcoma viral related oncogene homolog
M: Mitosis
MEK: Mitogen-activated protein kinase kinase kinase 1, also known as MAP3K1
MEN: Multiple endocrine neoplasia
MIB1: Mindbomb homolog 1 (Drosophila), commonly used monoclonal antibody to detect the Ki-67 antigen
miRNAs: micro ribonucleic acids
MIs: Mitotic indices
mRNA: messenger ribonucleic acid
MYC: myelocytomatosis oncogene
NLS: Nuclear localization signal
NSCLC: Non-small cell lung cancers
p: Short arm of the chromosome
PCBs: Polychlorinated biphenyls
PI3Ks: Phosphoinositide 3-kinases
PML: promyelocytic leukaemia protein
PR: Progesterone receptor
PS1 and PS2: Presenilin genes 1 and 2
PSA: Prostate specific antigen
PTB: Polypyrimidine tract-binding protein
PTEN: Phosphatase and tensin homolog
q: long arm of chromosome
RAS: Rat Sarcoma gene
RB: Retinoblastoma gene
RhoA: Ras homolog gene family, member A
RNA: Ribonucleic acid
SCF complex: Skp1, a Cullin subunit, an F-box protein, and the Roc1/Rbx1 protein
Skp1 and 2: S-phase kinase-associated protein 1 and 2
SPF: S-phase fraction
S-phase: Phase of synthesis
Src: Sarcoma inducing gene of Rous sarcoma virus

T : Tyrosine
TDLU: Terminal Duct-Lobular Unit
TGFβ: Transforming growth factor β
Thr: Threonine
TLIs: Thymidine-labeling indices
Tyr: Tyrosine
Ubc: Ubiquitin-conjugating enzyme
uPA: Urokinase plasminogen activator
UTR: Untranslated Region, refers to either of two sections on each side of a coding sequence on a strand of mRNA.