Immunohistochemical study of angiogenesis In prostatic adenocarcinoma and its precursors

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M.Sc in Pathology

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بسم الله الرحمن الرحيم

﴿قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ ﴾

(البقرة :32)

Abstract:

Background: Prostate cancer(Pca) is considered to be one of most common cancers in males .Prostatic intraepithelial neoplasia (PIN) and Atypical adenomatous hyperplasia (AAH), were assumed to be precursors of prostatic adenocarcinoma. Angiogenesis facilitates progressive tumour growth by providing adequate oxygenation to the tumour.Microvessel density (MVD) is considered to be a marker of the neo-angiogenetic process ,which can be assessed on pathological slides through the evaluation of immunoreactivity to some endothelial antigens, eg.CD34.

Materials &methods: The present study done on a total 35 cases of Pca(25 cases), and AAH(5 cases), (PIN) (5 cases).Also10 cases of benign prostatic hyperplasia (BPH) used for comparison. MVD was highlighted by using CD34 immunohistochemical stain. Individual microvessels were then counted at x200 magnification, MVD was correlated with age,serum PSA and Gleason score.

Results: Most of(60%) AAH,PIN cases showed MVD(25-50),most of (68%)Pca cases showed MVD(>50).MVD showed non significant correlation with age in AAH,PIN &Pca cases ,but showed significant correlation with serum PSA level in AAH,PIN (P value <0.05) &Pca cases (P value < 0.01),also MVD showed significant correlation with Gleason score in Pca cases (P value<0.05).

Conclusion: CD34 immunostaining is a reliable method for counting the microvesseles in tumors.The microvascular density together with the Gleason's grading evaluates successfully the aggressiveness and prgnosis of prostatic carcinoma.

KEY WORDS: CD34- prostatic adenocarcinoma- microvascular density-premalignant prostatic lesions.

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List of Abbreviations

AAH	Atypical adenomatous hyperplasia
aFGF	Acidic fibroblast growth factor
BPH	Benign prostatic hyperplasia
BCH	Basal cell hyperplasia
bFGF	Basic fibroblast growth factor
CEPs	Circulating endothelial progenitor cells
DAG	Diacylglycerol
ECM	Extracellular matrix
EGF	Epidermal growth factor
HGF	Hepatocyte growth factor
HGPIN	High grade Prostatic intra-epithelial neoplasia
IL	Interleukin
IP3	Inositol 1,4,5-triphosphate
MECIF	Macrophage endothelial-cell inhibitory factor
MAP	Mitogen-activated protein
MVD	Micro-vessel density
MVC	Micro-vessel count
MMPs	Matrix metalloproteinases
PD-ECGF	Platelet derived endothelial cell growth factor

PlGF	Placenta growth factor
PLC-γ	Phospholipase C-γ
Pl3K	Phosphotidylinositol 3-kinase
PIN	Prostatic intra-epithelial neoplasia
Pca	Prostatic carcinoma
PAs	Plasminogen activators
TRUS	Transrectal ultrasound-guided needle biopsies
TUR	Trans-urethral resection
TNF-α	Tumor necrosis factor alpha
TSP-1	Thrombospondin- 1
TIMPs	Tissue inhibitors of metalloproteinases
TGF	Transforming growth factor
WHO	World Health Organization
VEGF	Vascular endothelial growth factor
VHL	Von Hippel-Lindau tumor

Introduction

Prostatic carcinoma (Pc) is the most frequent malignant tumor among men over 50 years old (Cancel-Tassin and Cussenot .,2005).

Prostate cancer is the second most common cause of cancer related deaths in the men in United States,accounting for 29,000 deaths annually (Vogelzang et al.,2005).

Tumor angiogenesis, also termed neovascularization, provides a critical component for the growth, invasion and metastasis of solid tumors including prostatic adenocarcinoma (Terrence et al., 2005).

When a new tumor reaches the size of 1 – 2 mm, its growth requires the induction of new blood vessels, which may consequently lead to the development of metastases, via the penetration of malignant cells into the circulation (Uzzan et al., 2004).

Angiogenesis promots growth because the new vessels allow exchange of nutrients,oxygen, and waste products. In addition, the endothelial cells may release important paracrine growth factors for tumor cells (Belldegrun et al., 2000).

The common pathologic approach to asses angiogenesis involve microscopic estimation of vascular density or microvascular density in tissue proved by endothelial markers in immunohistochemistry (Choi et al., 2005).

Several markers of blood vessels endothelium have been developed for routine use including CD31, CD34 and factor VIII related antigen (Uzzan et al., 2004).