IMMUNOHISTOCHEMICAL DETECTION OF LAMININ-1 AND Ki-67 IN RADICULAR CYSTS AND KERATOCYSTIC ODONTOGENIC TUMORS

Thesis
Submitted to the Faculty of Dentistry
Ain Shams University
In partial fulfillment of the requirements of the
Master Degree in Oral Pathology

BY

MOATAZ MOHAMED EL-KHOLY
(B.D.S.)
Ain Shams University
2003

Demonstrator of Oral Pathology
Faculty of Dentistry
MSA University

Faculty of Dentistry
Ain Shams University
2010

Supervisors

Prof. Dr. Mohamed Salah El-Din Ahmed Ayoub

Professor of Oral Pathology and
Vice Dean for post graduate studies and research,
Faculty of Dentistry,
Ain Shams University

Dr. Houry Moustafa Baghdadi

Assistant Professor of Oral Pathology,
Faculty of Dentistry,
Ain Shams University

بسم الله الرحمن الرحيم

﴿يَرْفَعِ ٱللهُ ٱلَّذِينَ ءَامَنُواْ مِنكُمْ
وَٱلَّذِينَ أُوتُواْ ٱلْعِلْمَ دَرَجَاتٍ﴾

المجادلة ١١

صدق الله العظيم

ACKNOWLEDGEMENT

First, I would like to thank ***God*** for all ***God's*** givings.

I would like to express my deepest gratitude and thanks to ***Prof. Dr. Mohamed Salah El-Din Ayoub***, Professor of Oral Pathology and Vice Dean of post-graduate studies, Faculty of Dentistry, Ain Shams University, for his constant advice, encouragement and supervision. It is difficult to find the appropriate words that would express my gratitude because I cannot by any means repay him for all that he has done.

My deepest thanks and appreciation are due to ***Dr. Houry Moustafa Baghdadi***, Assistant Professor of Oral Pathology, Faculty of Dentistry, Ain Shams University, for her precise, generous and patient supervision and her continuous encouragement.

I would also like to express my deepest gratitude and appreciation to ***Prof. Dr. Adel Mohamed Abdel Azim***, Professor of Oral Pathology and Head of Oral Pathology Department, Faculty of Dentistry, Ain Shams University, for his unlimited help and support and for allowing me to benefit from his vast knowledge.

My sincere thanks extend to ***Dr. Sahar Emad Riad***, Assistant Professor of Oral Pathology, Faculty of Dentistry, Alexandria University for her valuable help.

I would also like to express my deep thanks and appreciation to all staff members of Oral Pathology Department, Faculty of Dentistry, Modern Sciences and Arts University especially

Prof. Dr. Mamdouh Mokhtar Abdel Latif for his valuable encouragement and his continuous support to guide me patiently and ***Prof. Dr. Mona Ezzat Wali*** for her generous and constant advice.

Finally, I would like to express my sincere thanks to all the staff members of Oral Pathology Department, Faculty of Dentistry, Ain Shams University for their help during the entire course of this work.

Table of Contents

List of Abbreviations

AgNORs: Antigen nucleolar organizing regions

BM: Basement membrane

CF: Cystic fluid

DAB: Diaminobenzidine

ECM: Extracellular matrix

EGF: Epidermal growth factor

EGFr: Epithelial growth factor receptor

GM-CSF: Granulocyte-macrophage colony stimulating factor

IgA: Immunoglobulin-A

IgG: Immunoglobulin-G

IL-1: Interleukin-1

IL-6: Interleukin-6

KCOT: Keratocystic odontogenic tumor

LPs: Lipopolysaccharides

MMPs: Matrix metalloprteinases

NBCS: Nevoid basal cell carcinoma syndrome

NK: Natural killer cells

NSOKC: non-syndrome-associated Odontogenic keratocyst

OKC: Odontogenic keratocyst

PBS: Phosphate buffer saline

PCNA: Proliferating cell nuclear antigen

PGE2: Prostaglandin E2

RC: Radicular cyst

RRC: Residual radicular cyst

SOKC: Syndrome-associated Odontogenic keratocyst

SPSS: Statistical package for scientific studies

ssDNA: Single-stranded DNA

SUPs: Tissue culture supernatant

TNF-α: Tumor necrosis factor-alpha

List of Figures

List of Tables

INTRODUCTION AND REVIEW OF LITERATURE

Introduction and Review of Literature

Odontogenic cysts are those which arise from the epithelium associated with the development of teeth. The source of the epithelium is from the enamel organ, the reduced dental epithelium, epithelial rests of Malassez or the remnants of the dental lamina. Cysts are formed either in bone or soft tissue. Some cysts were found to have characteristic features that make them distinct from other lesions [(1)].

Radicular cysts (RCs) arise from the epithelial residues (rests of Malassez) in the periodontal ligament as a consequence of inflammation which usually follows the death of a dental pulp. They represent more than half of all odontogenic cysts [(2)]. Residual Radicular Cysts (RRCs) persist after removal of teeth affected by RCs. Activation and proliferation of Malassez epithelial rests and lining epithelium of RCs or RRCs are related to inflammatory processes [(3)]. RCs are characterized by a cavity lined by nonkeratinized squamous epithelium of variable thickness. These cysts are typically inflamed and, when inflammation is intense, it may destroy part of the epithelium leaving a zone of granulation tissue in its place [(4)].

The term ‘‘odontogenic keratocyst’’ was introduced in 1956 by **Philipsen**. In 1962 **Pindborg, Philipsen and Henriksen** established the following histopathologic criteria for

this lesion: (1) the lining epithelium is usually thin and uniform in thickness with little or no evidence of rete ridges (2) there is a well defined basal cell layer, the component cells of which are cuboidal or columnar in shape and often their nuclei are arranged in a palisaded arrangement (3) there is a thin spinous cell layer which often shows a direct transition from the basal cell layer (4) the cells of the spinous cell layer frequently exhibit intracellular edema (5) keratinization is predominantly parakeratotic, but it may be orthokeratotic (6) the keratin layer is often corrugated and (7) the fibrous cyst wall is generally thin and usually uninflamed [(5)].

Laminins are a family of glycoproteins that are an integral part of the structural scaffolding in almost every animal tissue. Laminins are secreted and incorporated into cell-associated extracellular matrices. Laminin is the major non-collagenous component of the basal lamina. It also has four arms that can bind to four other molecules. Laminin-1 is a major component of most basal laminae. It is a ligand for alpha 2 beta 1 integrin receptor. It plays an essential role in the assembly of basal laminae, as well as in the adhesion of cells to basal lamina [(6)].

Ki-67 antigen is the prototypic cell cycle related nuclear protein, expressed by proliferating cells in all phases of the active cell cycle (G1, S, G2 and M phase) and reaches a peak in the G2 and M phases. It is rapidly degraded after mitosis with a half life of detectable antigen being an hour or less. It is