EFFECTS OF IONIZING RADIATION IN ATOPIC PATIENTS EXPOSED TO RADIATION

Submitted By

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M.B.B.Ch., Faculty of Medicine, Cairo University, 1997

Master of (Dermatology), Faculty of Medicine, Cairo University, 2003

A thesis submitted in Partial Fulfillment
Of
The Requirement for the Doctor of Philosophy Degree
In
Environmental Science

Department of Environmental Medical Science
Institute of Environmental Studies and Research
Ain Shams University

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APPROVAL SHEET

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Nashwa Kamal

To

The person I love most, and to who I owe everything, to soul of my father.

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List of Abbreviations

Abb.	Meaning

AD ..... Atopic Dermatitis

ALARA ..... As Low As Reasonably Achievable

BEIR..... Biological Effects of Ionizing Radiation

CDLQI..... Children's Dermatology Life Quality Index

DFI ..... Dermatitis Family Impact

DLQ ..... Dermatology Life Quality Index

EASI ..... Eczema Area and Severity Index

EDTA..... Ethylene Diamine Tetraacitic Acid

FLG ..... Filaggrin

ICRP..... International Commission on Radiological Protection

IGA ..... Investigator's Global Assessment

IgE ..... Immunoglobulin E

IL ..... Interleukin

ITS ..... Intergenic Transcribed Spacer

LET..... Low-Linear Energy Transfer

LNT ..... Linear No-threshold

m Dixon's Agar . modified Dixon's Agar

M. ..... Malassezia

MDC ..... Macrophage-Derived Chemoattractant

NCRP ..... National Council on Radiation Protection

PCR ..... Polymerase Chain Reaction

POEM..... Patient-Oriented Eczema Measure

PRRs ..... Pattern Recognition Receptors

RBE ..... Relative Biological Effectiveness

RFLP..... Restriction fragment Length polymorphis

ROS ..... Reactive Oxygen Species

List of Abbreviations (Cont...)

Abb.	Meaning
S.aureus	*Staphylococcus aureus*
SASSAD	Six Area, Six Sign Atopic Dermatitis
SCORAD	Scoring Atopic Dermatitis index and other severity scales
SEA	Staphylococcal enterotoxin A
SEB	Staphylococcal enterotoxin B
SEC	Staphylococcal enterotoxin C
SGA	Sabouraud Glucose Agar
TAR	Cthymus and activation-regulated chemokine
Th 1	T helper 1
Th 2	T helper 2
TISS	Three Item Severity Scale
TNF	Tumor Necrosis Factor
TSST-1	Toxic shock syndrome toxin-1

ABSTRACT

Atopic dermatitis is a chronic relapsing inflammatory skin disease that arises most commonly during early infancy, and is characterized by severe pruritus, age-dependant skin manifestations, and a fluctuating clinical course.

Hereditary, environmental and immunological factors are involved in the aetiopathogenesis of AD. Also the differentiation of helper T- cells, local cytokine profile, IgE, infectious agents and superantigens are factors identified as being involved in the pathogenesis of AD.

One hundred patients with AD were selected from the outpatient clinic of the National Center for Radiation Research and Technology in Cairo, Egypt. They were divided into 2 groups; group 1 included radiation workers in the Hall of gamma irradiation unit and group 2 included workers outside controlled area and not exposed to radiation with comparable age and sex.

The severity of the disease was evaluated according to the grade of atopic dermatitis. Total and specific serum IgE was measured and Complete Blood Count was also carried out.

Four *Malassezia* species were isolated from AD patients *M. globosa*, *M. furfur*, *M. sympodialis* and *M. obtusa.* The clinical isolates consisted of two bacterial strains, *S. aureus* and *S. epidermidis*.

The significant increase of AD severity seems to be more closely related to the prevalence of *S. aureus* and Malassezia on the skin of radiation workers. This was proved by the presence of high IgE and eosinophils in radiation workers. So, the interactions of low gamma radiation and skin seems to further complicate the risk of assessments of atopic dermatitis.

Key words: Atopic dermatitis, Radiation workers, Staphylococcus, Malassezia.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory disease causing intense pruritus with typical clinical features **(Orfali *et al*., 2013).**

Atopic dermatitis (AD) is an itchy inflammatory skin disease with predilection for skin flexures. AD develops as a result of complex interaction of genetic, environmental and immunological factors. Disturbed skin function, infection and stress may be other important contributing factors. Early onset, concomitant asthma and family history of AD may predict a persistent course **(Williams and Wüthrich, 2000).**

Patients with AD usually exhibit defects in innate and acquired immune responses resulting in a heightened susceptibility to bacterial, fungal and viral infections, most notably colonization by *S. aureus*. Moreover, allergens expressed by the yeast *Malazessia furfur*, a component of normal skin flora, have also been implicated in disease pathogenesis in a subset of AD patients **(Baker, 2006).**

Microorganisms play an influential role in AD pathogenesis, interacting with disease susceptibility genes to cause initiation and/or exacerbation of disease activity. *Staphylococcus aureus* colonization of both lesions and clinically uninvolved skin has been demonstrated by many investigators. Also, the density of this organism in lesional skin correlates with the severity of inflammation; reduction in the density of *S. aureus* is associated with clinical improvement **(Williams *et al*., 1990 and Nilsson *et al*., 1992).**

Members of the genus *Malassezia*, lipophilic yeasts, colonize the skin of the head, neck, and shoulders of humans are considered to be one

of the factors that exacerbate AD, based on the finding that those patients (but not healthy subjects) have specific serum immunoglobulin E (IgE) antibodies against *Malassezia* (**Werfel and Kapp, 1998**).

The development and phenotypic expression of AD depend on a complex interaction between genetic and environmental factors **(Watson and Kapur, 2011),** including nutrition (**Wang *et al*., 2007)**.

On the other hand, the health risks of low doses of radiation could influence the occupational health of radiation workers. The worry about the indeterminate risks of low dose radiation should be integrated through collaboration between radiation biologists and epidemiologists, in order to provide an explanation of epidemiologic radiation effects.

The response of human skin to low dose radiations is a consequence of biological reactions including; genomic instability and bystander effects. This could be the predisposing factors for the emergence of premalignant skin lesions and premature skin aging; as well as higher susceptibility to bacterial and fungal infections **(Hu *et al*., 2012).**

The ultimate response of cells and tissues to radiation injury is invariably dependent on the radiation dose and the ability of the cells to repair sub-lethal damage. High radiation doses usually result in mitotic arrest and high incidence of cell death, with little chance of regenerative cellular repopulation. Lower doses of radiation fail to produce cell killing, but succeed in producing radiation induced mutations and other molecular alteration resulting in cellular abnormalities that become inherited in the genetic cell line of the cells composing the tissue and ultimately produce tissue and organ abnormalities **(El-Naggar, 2000)**.