

Infraorbital pigmentation; Clinical and Histopathological Assessment

Thesis

*Submitted for partial Fulfillment of
Master Degree in Dermatology, Venereology and Andrology*

Presented by

Dalia Badr El-Din Abd El-Hafiz
(M.B, B.Ch)

Under The Supervision of

Prof. Dr. Nader Fouad Ragab
*Professor of Dermatology, Venereology and
Andrology
Faculty of Medicine, Ain Shams University*

Prof.Dr.Marwa Abd El-Rehim Abdallah
*Professor of Dermatology, Venereology and
Andrology
Faculty of Medicine, Ain Shams University*

Dr.Hatem Ayman Tawfeek
*Assistance lecturer of Ophthalmology
Faculty of Medicine-Ain Shams University*

Faculty of Medicine – Ain Shams University

2010

Abstract

Background: Dark circles refer to the conditions that present with bilateral, round, homogeneous pigment macules on the infraorbital regions. Although it is not a medical concern, it can be a cosmetic concern for a large number of individuals. Moreover, possible causes have not been elucidated.

Objective: to study the etiology of infraorbital pigmentation through clinical and histopathology assessment.

Patients & Methods: Thirty female patients with dark circles under the eye (IOP group) were included in our study and they were compared with 15 healthy individuals (control group). Clinical examination was done to exclude patients with systemic illness especially hepatic or renal disease and hemoglobin level assessment was done to evaluate the relation of anemia with dark circles. Eyelid biopsy specimens from IOP group and control group were examined histopathologically after Masson-Fontana silver stain (to detect the level of dermal melanin deposition and count

it) and Perl's potassium ferrocyanide (to detect haemosidren deposition).

Results: patients of IOP group showed significantly higher rate of stress, hair fall, family history of IOP and anemia. By histopathological assesament, IOP group showed vacuolated keratinocytes, focal acanthosis and perivasular sub-epidermal inflammatory infiltrates. Masson-Fontana silver stain showed; larger size and number of melanophages which were present more in the mid dermis in addition to upper and deep dermis than control group which showed smaller size and number of melanophages in the more superficial part of the dermis. Perl's potassium ferrocyanide stain detected no haemosidren deposition

Conclusions: In conclusion, the main reason for IOP is dermal melanin deposition which is present in melanophages. No other pigment could be detected in the dermis even in case of venous congestion. Deposition of the dermal melanin may be secondary to certain keratinocyte dysfunction. The cause of keratinocytes dysfunctions is yet to be determined, it may be due to release of reactive oxygen species which may be increased with venous congestion as a result of

stress or eye strain and; ultraviolet B may play role in mediating vacuolar degeneration.

Key words: Infraorbital pigmentation, Periorbital pigmentation, Dark circles, Histopathological assesment, Treatment.

Acknowledgement

First, I always feel indebted to “**ALLAH**” the most beneficent and merciful.

Words cannot express the depth of my gratitude to **Prof. Dr. Nader Fouad Ragab** Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, for his valuable suggestions, generous assistance, kind support and continuous encouragement throughout this work.

My great appreciation and thanks to **Dr. Marwa Abd El-Rehim Abdallah**, Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, for her unlimited help, kind support, valuable supervision, guidance and advice.

My great thanks to **Dr. Hatem Ayman Tawfeek**, Assistance lecturer of Ophthalmology, Faculty of Medicine, Ain Shams University, for his unlimited help, guidance and advice.

Finally, I would like to thank all members of my family, my patients and all members of EL-Demerdash and Om El-Masreen hospital who participated in one way or another in accomplishment of this work.

List of Abbreviations

List of Abbreviations

ACD	Allergic contact dermatitis
AD	Atopic dermatitis
α-MSH	Alfa melanocytic stimulating hormone
bFGF	Basic fibroblast growth factor
β-MSH	Beta-melanocytic stimulating hormone
BaSo4	Barium sulfate
CALM	Cafe-au-lait macule
Co2 laser	Carbon dioxid laser
DA	Deoxy- arbutin
DC	Dark circles
DCT	DoPA chrome tautomerase
DHI	5,6-Dihydroxyindole
DHICA	5,6-Dihydroxyindole-2-carboxylic acid
DOPA	3,4-Dihydroxy-L-phenylalanine
ER	Endoplasmic reticulum
ET-1	Endothelin-1
HGF	Hepatocyte growth factor
HPF	High power field

List of Abbreviations (continued)

ICD	Irritant contact dermatitis
I O P	Infraorbital pigmentation
LIF	Leukemia inhibitory factor
Mc	Melanocytes
MC1-R	Melanocortin 1 receptor
MgO	Magnesium oxide
MSH	Melanocyte-stimulating hormone
Nd:YAG laser	Neodymium doped Yttrium aluminium garnet
NF	Neurofibromatosis
NGF	Nerve growth factor
ODM	Oculodermal melanocytosis
PABA	Para-aminobenzoic acid
PBC	primary biliary cirrhosis
PD	papillary dermis
PKA	protein kinase A
PKC	protein kinase C
POMC	proopiomelanocortin
POP	Periorbital pigmentation
PG	Prostaglandin
QSNd: YAG	Q-switched neodymium doped Yttrium aluminium garnet

List of Abbreviations (continued)

RAPK	Reticulate acropigmentation of Kitamura
RD	Reticular dermis
RM	Riehl's Melanosis
SCF	Stem cell factor
TiO₂	Titanium dioxide
TSH	Thyroid stimulating hormone
TYR	Tyrosinase
TYRP1	Tyrosinase-related protein1
UVR	Ultraviolet ray
UVA	Ultraviolet A
UVB	Ultraviolet B
VC-IP	Tetra-isopalmitoyl ascorbic acid
ZnO	Zinc oxide

List of Contents

List of Contents

<i>Subject</i>	<i>Page</i>
Introduction	1
Review of literature	
Chapter 1: Anatomy and Histology of the Eyelid	4
Chapter 2: Pathogenesis of Pigmentation.....	27
Chapter 3: Infraorbital pigmentation (IOP)	33
History of Infraorbital pigmentation	33
Causes of Infraorbital pigmentation.....	35
Chapter 4: Treatment of IOP	80
Patients and methods	108
Results.....	114
Discussion	132
Summary and conclusion.....	146
References.....	152
Arabic summary.....	193

List of Tables

List of Tables

	<i>Subject</i>	<i>Page</i>
Table 1:	Demographic characteristics of the study group.	115
Table 2:	Comparing clinical data between IOP group and control group.	122
Table 3 :	Histopathological assessment of the IOP specimens.	127
Table 4:	Comparison between IOP group and control group according to the level of pigmentation.	128
Table 5:	Comparison between IOP group and control group according to the number of cells in the eyelid skin sections.	129

List of Figures

List of Figures

	<i>Subject</i>	<i>Page</i>
Figure 1:	Surface anatomy of the eyelid	6
Figure 2:	Sagital section of the eyelid.	7
Figure 3:	Anatomy of orbicularis oculi muscle	9
Figure 4:	Deeper eyelid dissection and orbital anatomy	11
Figure 5:	Orbital septum	12
Figure 6:	Blood vessels of the eyelid	16
Figure 7:	Anatomy and histology of the eyelid	20
Figure 8:	Immunolabelling of normal human epidermis with an antibody to S100 protein reveals dendritic cells in the basal layer (melanocytes) and in suprabasal layer (Langerhans cells)	22
Figure 9:	Schematic presentation of a melanocyte; the engine for melanin production. The four developmental stages of melanosomes are shown as they move toward the periphery of the cell within the dendrites	29

List of Figures (continued)

Figure 10	Scheme of signaling pathways within the epidermal melanin unit and mechanisms by which keratinocyte-derived factors act on human melanocyte proliferation and differentiation	32
Figure 11:	Dark circles due to tear trough depression before and after blepheroptasty	45
Figure 12:	Patient with skin type III presenting with grade I pigmentation.	118
Figure 13:	Patient' skin type III with IOP grade III (dark brown)	118
Figure 14:	Patient with skin type III presenting with grade I pigmentation and tear trough deformity.	119
Figure 15:	Patient with skin type III presenting with grade II pigmentation.	119
Figure 16:	Patient with skin type IV presenting with grade II pigmentation.	120
Figure 17:	Patient with skin type III presenting with grade III pigmentation associated with venous congestion due to chronic nasal allergy, it appears as "allergic shiners".	120

List of Figures (continued)

Figure 18:	IOP section stained with H&E (x400) showing; focal acanthosis and vacuolated keratiocytes.	124
Figure 19:	IOP section stained with H&E(x400) showing; four to five epidermal cell layers and melanophages in the upper dermis.	124
Figure 20:	Melanophages are seen in the upper dermis extending to deep dermis by Masson-Fontana stain.	126
Figure 21:	IOP section stained with Masson-Fontana silver stain (x400) showing; melanophages in the upper dermis extending to mid dermis with median number of cells (27).	126
Figure 22	Control section stained with Masson-Fontana silver stain (x400) showing; melanophages in the upper dermis with median number of cells (7) which is smaller than melanophages of IOP section.	127
Figure 23	Comparison between IOP group and control group according to the degree of pigmentation.	129

List of Figures (continued)

Figure 24	Comparison between IOP group and control group according to the number of melanophages in the eyelid skin sections.	130
Figure 25.A:	Congested spleen stained with Perl's potassium ferrocyanide stain (x400) showing iron deposition (positive control for haemosidren deposition).	131
Figure 25.B:	IOP section showing the dermis stained with Perl's potassium ferrocyanide stain (x400). No iron deposition is seen compared to congested spleen (25. A).	131

Introduction

Infraorbital pigmentation (IOP) is one of the main aesthetic facial concerns that affects individuals of any age, both genders and all races (**Yaar and Gilchrest, 2001**).

IOP interfere with the face appearance, giving the patient a tired, sad, or hangover look. Disguising a lesion is almost mandatory for some individuals who depend on a well-cared and positive appearance for their work or social activities (**Gupta and Gupta, 2001**). Many people also describe the IOP as dark circles under the eyes "DC", "Tired Look", "Eyelid Bags", "Puffy Eyes" and "Eye Bags" (**Seckel, 2007**).

IOP is defined as bilateral, round, homogeneous pigmented macules on the infraorbital regions (**Watanabe et al., 2006**). The condition usually starts after puberty and progresses thereafter. There are many contributing factors that may exacerbate the condition such as weight loss, exhaustion, late hour's eye strain and stress (**Hacker, 1996**). The skin below the lower eyelid is first involved and with age pigmentation progresses to the area of
