Quantitation of mast cells and collagen fibers in skin tags

Thesis

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By

Dalia Hesham Mohamed Mohamed

(M. B. B. Ch)

Supervised by

Dr. Omar Soliman El Safouri
Assistant Professor of dermatology
Faculty of Medicine
Cairo University

Dr. Marwa Mohamed Fawzi
Lecturer of dermatology
Faculty of Medicine
Cairo University

Dr. Zeinab Mohamed El Maadawi
Lecturer of histology
Faculty of Medicine
Cairo University

Faculty of Medicine
Cairo University

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Abstract

Background: Skin tags are common benign skin tumours usually occurring on the neck and major flexors of elder people. Skin tags are histologically composed of loose collagen fibers and dilated capillaries enclosed in a hyperplastic epidermis. **Objectives:** The aim of this study is to perform quantitation of mast cells and collagen fibers in skin tags and normal skin in diabetics and non diabetics, in order to find the the possible correlation between mast cells and collagen fibers in the pathogenesis of skin tags. **Participants and Methods:** Thirty participants with skin tags were divided into two groups (15 diabetic and 15 non diabetic).3 biopsies were obtained from each one : a large skin tag, a small skin tag and adjacent normal skin. Mast cell count was done in 10 fields and the average count was correlated with mean collagen area % in 5 fields done by the Image analyzer. **Results:** A statistically significant correlation between mast cell count and collagen mean area % was detected in both studied groups (except in large lesions of the non diabetic group, but it was near to be significant ;Pvalue = 0.052). In our study mast cell count in skin tags and normal control was statistically higher in the diabetics than the non diabetics. **Conclusion:** Both mast cell mediators and hyperinsulinaemia are involved in the pathogenesis of skin tags.

Key words: Skin tags, mast cells, hyperinsulinaemia.

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List of abbreviations

AIDS	Acquired immune deficiency syndrome
BMI	Body mass index
CD34	Cluster differentiation 34
cDNA	Complementary deoxyribonucleic acid
CNS	Central nervous system
DNA	Deoxyribonucleic acid
DM	Diabetes mellitus
ECCL	Encephalo-cranio-cutaneous-lipomatosus
ECF-A	Eosinophil chemotactic factor of anaphylaxis
GAGs	Glycosaminoglycans
GIT	Gastro-intestinal tract
GM-CSF	Granulocyte monocyte-colony stimulating factor
GS	Glodenhar syndrome
GVHD	Graft versus host disease
HDL	High density lipoproteins
H&E	Haematoxylin and eosin
HMC-1	Human mast cell line-1
HPV	Human papilloma virus
HRT	Hormone replacement therapy
ICAM-1	Intercellular adhesion molecule-1
Ig-E	Immunoglobulin-E
IGF-1	Insulin –like growth factor -1
IGF-BP3	Insulin –like growth factor-binding protein 3
IL	Interleukin
IRS	Insulin resistance syndrome
MCP-1	Monocyte chemoattractant protein -1
MC_T	Mast cell tryptase
MC_{Tc}	Mast cell tryptase chymase
ml	Milli liter
µm	Micro meter
m RNA	Messenger ribonucleic acid
µ u	Micro unit
OAFNS	Oculo- auriculo- frontonasal syndrome
OAVD	Oculo-auriculo-vertebral dysplasia
OSD	Occult spinal dysraphism
PAF	Platelet activating factor

PS	Pai syndrome
RELM-β	Resistin like molecule - beta
SCF	Stem cell factor
SHBG	Sex hormone binding globulin
ST	Skin tag
Th-2	T helper - 2
TNF-α	Tumour necrosis factor alpha
VIP	Vasoactive intestinal peptide
VLDL	Very low density lipoprotein

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Introduction and aim of the work

Introduction:

Skin tags are small flesh coloured to dark brown sessile or pedunculated papillomas commonly occur on the neck frequently seen in axilla and eyelids less often on the trunk and groin. Both sexes have the same incidence which tends to increase with age and obesity (**Chiritescu and Maloney, 2001).**

Skin tags are histologically composed of loose collagen fibers and dilated capillaries (**Almeida et al., 2007)**.

Mast cell count was found to be significantly higher in small and large skin tags than normal skin (**Zaher et al.,2007)**.

The mapping techniques indicate that the greatest density of mast cells occur in the most superficial dermal zone,just below the dermo- epidermal junction (**Cowen et al., 1979).**

Mast cells participate in the pathogenesis of fibrotic diseases,they are found to stimulate fibroblast proliferation and collagen synthesis through some fibrotic mediators such as histamine and tryptase (**Williams and Wilkins, 2003) .**

Mast cells are intimately associated with fibroblasts in tissues. Fibroblasts maintain mast cells in vivo. After co-culture with fibroblasts immature mast cells changed to mature mast cells capable of synthesizing heparin and proteoglycans as well as changing their phenotype to resemble connective tissue type mast cells(**Rothenberg and Austen, 1989).**

Aim of the work:

The aim of this study is to perform quantitation of mast cells and collagen fibers in skin tags and normal skin in diabetics and non diabetics, in order to find the possible correlation between mast cells and collagen fibers in pathogenesis of skin tags.

Skin tags

Introduction:

Skin tags are small flesh coloured to dark brown sessile or pedunculated papillomas commonly occur on the neck frequently seen in axilla and eyelids less often on the trunk and groin.

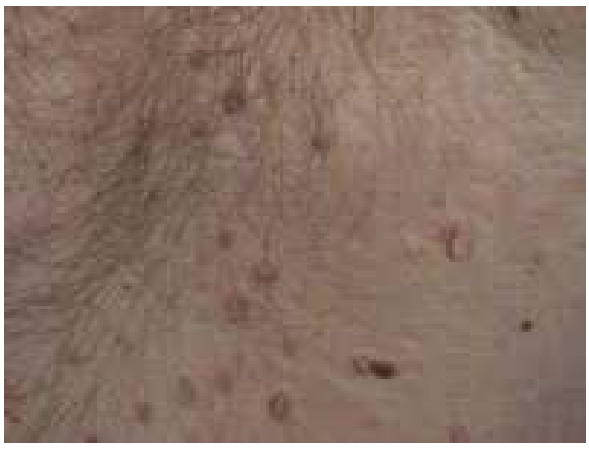
Both sexes have the same incidence which tends to increase with age and obesity(**Chiritescu and Maloney, 2001).**

Many synonyms were described for skin tags such as acrochordons, cutaneous tags, fibroma pendulum, eruptive lipofibroma and cutaneous papilloma (**Huntley, 1983).**

Clinical types of skin tags:

Skin tags occur as three types:

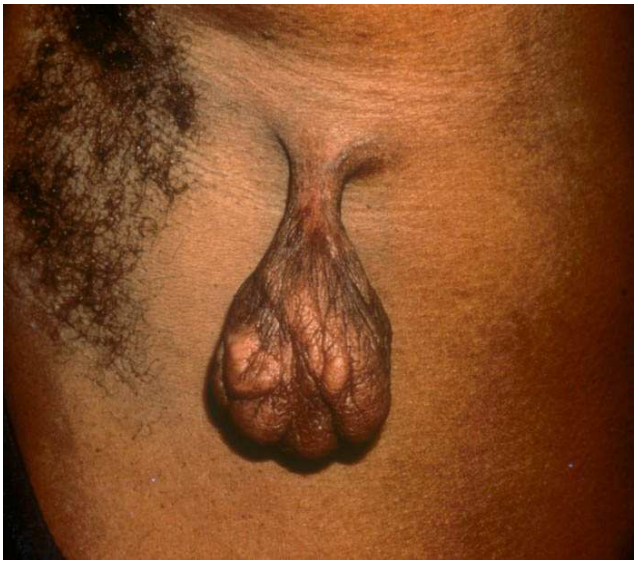
a) Multiple, small, furrowed papules, especially on the neck and axilla, generally 1 to 2 mm long as seen in figure 1.



Figure(1):Multiple axillary skin tags.

b) Single or multiple filiform smooth growths in varying locations, about 2mm wide and 5 mm long.

c) Solitary bag-like pedunculated growths, usually about 1 cm in diameter but occasionally much larger, as seen in figure 2 most commonly occur on the lower trunk (**Elder et al., 1999)**.



Figure(2): Solitary pedunculated skin tag in the axilla.

Histopathology of skin tags:

Skin tags are histologically composed of loose collagen fibers and dilated capillaries (**Almeida et al., 2007)**.

a) The multiple small furrowed papules usually show papillomatosis, regular acanthosis and hyperkeratosis and occasionally horn cysts within their acanthotic epidermis.
b) The filiform smooth growths show slight to moderate acanthosis and occasionally mild papillomatosis. The connective tissue stalk is composed of loose collagen fibers and often contain numerous dilated capillaries.
c) The bag-like soft fibromas generally show a flattened epidermis overlying loosely arranged collagen fibers and mature fat cells in the center. In some instances, the dermis is quite thin, so that the fat cells compose a significant portion of the tumour, which may then be regarded as a lipofibroma(**Elder et al., 1999).**

Diseases associated with skin tags:

Skin tags may be associated with several diseases:

Diabetes mellitus:

In 1987, kahana et al., found that skin tags are associated with impaired carbohydrate metabolism and may serve as a means for identifying patients at increasing risk of having non-insulin dependant diabetes mellitus. They found no association between the localization, size, colour and number of the skin tags and the presence of diabetes mellitus.

Skin tags were reported to have a probable association with diabetes mellitus. **In 2002, Demir et al.,** evaluated 120 patients with the skin tags for the presence of impaired carbohydrate metabolism and they found 88 patients with overt diabetes, 6 patients with glucose intolerance and 4 patients with reactive hypoglycemia. So concluded that patients with skin tags should be evaluated for the presence of diabetes mellitus.

In 2005, Erdogan et al., evaluated atherogenic risk factors : insulin resistance, impaired carbohydrate metabolism, impaired lipid metabolism and obesity; in patients with skin tags in a case-control study by performing: oral glucose tolerance test, serum insulin, total cholesterol, high density lipoproteins (HDL), very low density lipoproteins (VLDL), triglycerides and body mass index (BMI). The BMI and total cholesterol were significantly higher in skin tag patients than in controls. They advised that follow up of skin tag patients with regard to the development of diseases associated with atherosclerosis may be beneficial.

In a case control study **in 2007, Rasi et al.,** found that patients with skin tags had higher frequency of diabetes mellitus than the control

group. Patients with multiple (more than 30) skin tags were particularly at an increased risk of diabetes mellitus. No correlation was found between number of skin tags and BMI. No correlation between the anatomical localization of skin tags and impaired carbohydrate metabolism except for skin tags under the breast in women**.**

Obesity:

Obesity is associated with a number of dermatosis and increases the incidence of cutaneous infections. Acanthosis nigricans is the most common dermatological manifestation of obesity. Skin tags are more commonly associated with diabetes than with obesity(**Scheinfield, 2004).**

In a study of 156 obese patients, the percentage of skin tags increased with the severity of obesity (**Garcia-Hidalgo et al., 1999).**

Insulin sensitivity improves with weight loss, therefore the increased incidence of skin tags seen at higher BMI may be due to greater insulin resistance (**Muscelli et al., 2005).**

Acromegaly:

Cutaneous changes in acromegaly result from excess growth hormone and insulin like growth factor -1 (IGF-1) on skin cells and adnexae. Common features include: skin puffiness, oily skin with large pores, hypertrichosis and excessive sweating. Also pigmented skin tags, acanthosis nigricans and psoriasis may be encountered in acromegaly (**Ben-Shlomo and Melmed, 2006).**

Crohn's disease:

Perianal Crohn's disease can manifest as skin tags, ulcers, fissures, abcesses, fistulas or stenosis (**Singh et al., 2004).**

Crohn's disease can be diagnosed by biopsy of a perianal skin tag, it will show the pathology of dermal granuloma (**Taylor et al., 1989).**

Aging:

Skin changes after forty are of minor medical importance but wrinkles, skin dryness and hair loss are often regarded as major problems to people. Skin changes also include: seborrheic keratosis, skin tags, hyperplastic sebaceous glands and angiomas (**Turner, 1984).**

Skin tags in children:

- **Child abuse:**

Anal and perianal findings studied in 310 prepubertal children who were determined to be victims of sexual abuse were as follows: 66% of cases had normal perinea and 34% had abnormal findings including anal gapping, skin tags, rectal tears and perineal scarring (**Muram, 1989)**.

- **Organ transplants:**

Skin tags are one of the reported skin disorders occurring in children with organ transplants(**Euvrard et al., 2001)**.

Colonic polyps:

Several reports suggested that skin tags may indicate the presence of colonic polyps in symptomatic patients referred for colonoscopy (**Leavitt et al.,1983, Kune et al., 1985, Chobanian et al .,1985, Beitler et al.,1986, Vinel et al., 1987).**

However, other several studies failed to find any association (**Deschamps et al., 1985, Dalton and Coghill, 1985, Anciaux et al., 1986, Luk et al., 1988, Gould et al.,1988, Brendler et al., 1989, Akhtar and Zhuo,2003).**