Research Article

Pathophysiology and Treatment of Fibroepithelial Papillomas

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Abstract
Background: Fibroepithelial papillomas or skin tags (STs) are dermatological lesions commonly found in the general population. The etiology of skin tags (STs) is not fully understood. A relation to diabetes mellitus, obesity, insulin resistance and atherosclerosis was suggested. **Aim of the work:** The aim was to study the pathophysiology of fibroepithelial papillomas, and the efficacy of different lines of treatment of these papillomas. **Patients and Methods:** A total of ٦٠ patients with STs were subjected to clinical examination, estimation of body mass index (BMI), fasting blood glucose (FBG), postprandial blood glucose (PPBG) skin biopsy and finally removal of their skin tags by using scissor excision, electrocautery, cryotherapy or TCA. The obtained skin biopsies were subjected to routine H&E staining and immunohistochemical staining using (CD٣, ٤, ٨, ٢٠, ٦٨ and mast cell tryptase) the stained sections then examined by using both the light and the electron microscopes. **Results:** The examined sections revealed the presence of vacuolated cells in the epidermis and lymphocytic infiltrate in the dermis, positive immunohistochemical staining for the used markers. EM revealed degenerative changes in the vacuolated cells. **Conclusion:** Skin tags are multifactorial in nature and the development of skin tags needs the intrgration of many precipitating factors. The effective line of removal of such skin tags is through the scissor excision.
Key words: Skin tags, Vacuolated keratinocytes, Human papilloma virus and Mast cells.

Introduction
Skin tags (STs), also named soft fibromas, achrocordons or fibroepithelial polyps, are common benign neoplasms of middle-aged and elderly subjects. They usually occur as small, soft, pigmented or skin-colored, filiform, often pedunculated lesions. They grow in the natural folds of the skin such as the neck, axillae, inguinal, thigh, perineal and inframammary regions, in the eyelids and in the intergluteal folds[١].

The etiology of STs is not fully understood. A relation to diabetes mellitus (DM), obesity, friction, atherosclerosis, dyslipidaemia, acromegaly, colonic polyps, and human papilloma virus (HPV) has been suggested[٢].

Although asymptomatic, skin tags constitute the subject of frequent complaints in dermatology clinics for esthetic reasons [٣].

The current medical treatment of skin tags involves clipping or shaving the lesion at the base, cryotherapy, or diathermy[٤].

Patients and Methods
This study was conducted on sixty patients complaining of skin tags. These patients selected from the patients attending the Dermatology Outpatient Clinic of Minya University Hospital.

Each patient was subjected to clinical examination, assessment of fasting and post-prandial blood sugar, skin biopsy and removal of the skin tags.

Two skin biopsies were obtained from each patient. The first biopsy subjected to processing for routine H&E and immunohistochemical staining using (CD ٣, ٤, ٨, ٢٠, ٦٨ and mast cell tryptase) to be examined by the light micro-

scope and the second biopsy subjected to processing to be ready for electron microscopic examination.

The patients were classified according to the technique of skin tags into ٤ groups each group include ١٥ patients:
Group ١: removal of skin tags by scissor excision.
Group ٢: removal of skin tags by electrocautery.
Group ٣: removal of skin tags by cryotherapy.
Group ٤: removal of skin tags by TCA application.

Results

Both sexes were presented where thirty six patients were females (٦٠٪) and twenty four patients were males (٤٠٪). Their ages ranged from ٢١ to ٦٥ years with a mean and SD of ٤١.٥±٩.٧.

There was an increased frequency of skin tags in patients below ٥٠ years and in the female patients. (١٦.٧٪) of the studied patients were of normal body weight while (٨٣.٣٪) of them were either over weight (٢٥٪) or obese (٥٨.٣٪).

In our study we detected (٣٣.٣٪) of our patients with skin tags suffering from NIDDM while the remaining (٦٦.٧٪) were non-diabetic.

There was a strong association between obesity and incidence of developing skin tags, but the association between DM and skin tags was not confirmed.

Table ١: Data of the patients included in the study

		No of patients =٦٠	Percentage
Age in years	< ٥٠ years	٥٤	٩٠٪
	>٥٠ years	٦	١٠٪
Sex	Males	٢٤	٤٠٪
	Females	٣٦	٦٠٪
Weight	Normal	١٠	١٦.٧٪
	Over weight	١٥	٢٥٪
	Obese	٣٥	٥٨.٣٪
DM	Diabdtic	٢٠	٣٣.٣٪
	Non diabetic	٤٠	٦٦.٧٪

Routine H&E examination revealed the presence of vacuolated keratinocytes in the upper and middle epidermis in (٦٠٪) of cases and a moderately dense lymphohistiocytic inflammatory infiltrate in the connective tissue stalk of (٧٠٪) of examined STs (fig ١&٢).

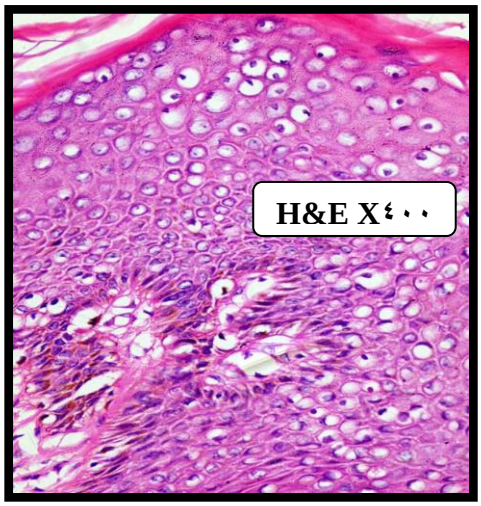


Fig. (١): Vacuolated keratinocytes in the upper and middle epidermis.

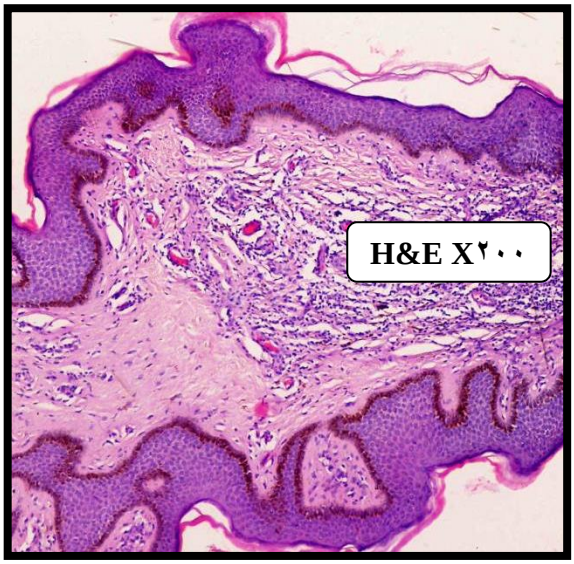


Fig. (٢): A moderately dense inflammatory infiltrate in the connective tissue stalk of a skin tag.

Immunohistochemical staining of the dermal inflammatory infiltrate revealed postive staining for CD٣, CD٤, CD٨, CD٢٠ and CD٦٨ in ٧٠٪ of skin tags and revealed the presence of positively stained mast cells in ٦٠٪ of cases (fig ٣).

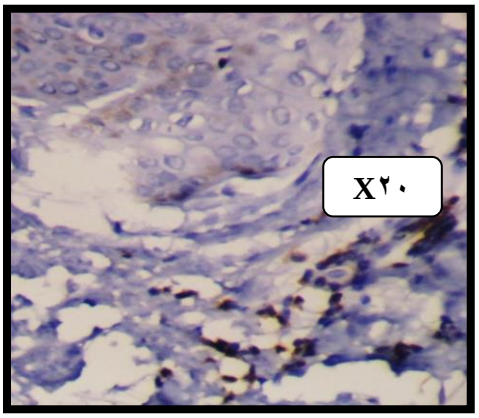
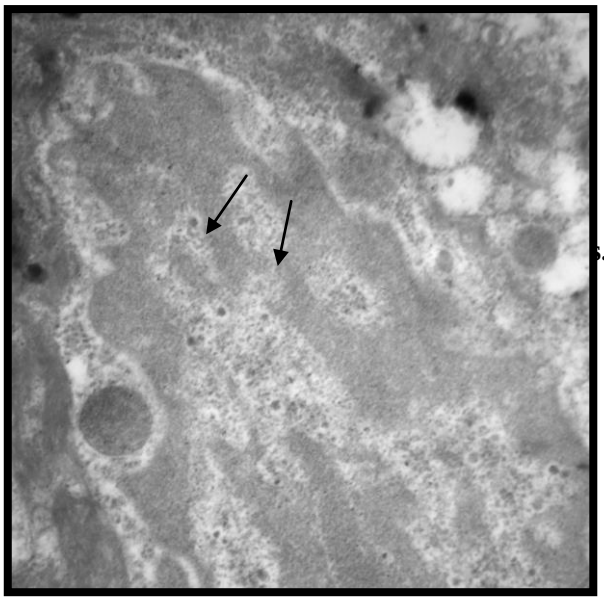
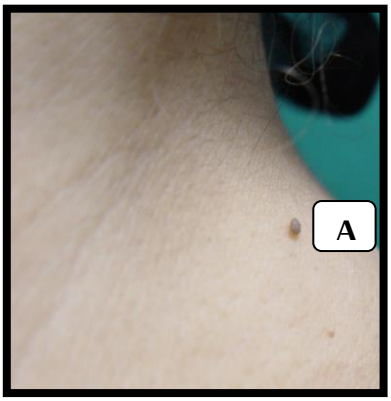


Fig. (٣): Immunohistochemical positive staining in the dermal infiltrate of a skin tag.

Ultrastructural examination of skin tags revealed the presence of Intra nuclear viral particles, swollen and vesiculated rough endoplasmic reticulum, and swollen mitochondria with loss of mitochondrial cristae and intracellular oedema (fig ٤).



The results of the used lines of treatment revealed complete cure in ١٠٠٪ of patients of the scissor excision, electracautery and cryotherapy groups. While in the TCA group the improvement was ٩٠٪. The intra-operative pain and post-operative complications were with the electracautery, cryotherapy and TCA groups but not with the scissor excision group. There was no incidence of recurrence in the used four groups (fig ٥).



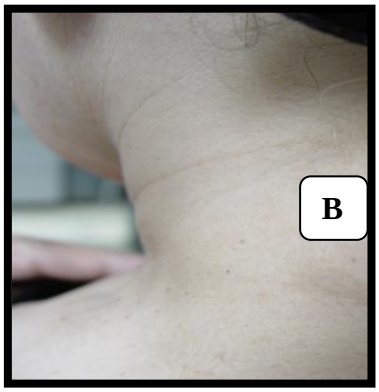


Fig. (٥): (A) before removal of skin tags.
(B) After removal of skin tags.

Table ٤: The comparison between the four modalities of treatment

	G I	G II	G III	G IV	P value					
Pain					<٠.٠٠١					
Yes.	٠ (٠٪)	١٥ (١٠٠٪)	١٥ (١٠٠٪)	١٥ (١٠٠٪)	**G I vs G II**	**G I vs G III**	**G I vs G IV**	**G II vs G III**	**G II vs GIV**	**G III vs GIV**
No.	١٥ (١٠٠٪)	٠ (٠٪)	٠ (٠٪)	٠ (٠٪)	<٠.٠٠١	<٠.٠٠١	<٠.٠٠١	----------	----------	----------
Hypopigmentation:					٠.١٠٢					
Yes.	٠ (٠٪)	٠ (٠٪)	٢ (١٣.٣٪)	٠ (٠٪)	**G I vs G II**	**G I vs G III**	**G I vs G IV**	**G II vs G III**	**G II vs GIV**	**G III vs GIV**
No.	١٥ (١٠٠٪)	١٥ (١٠٠٪)	١٣ (٨٦.٧٪)	١٥ (١٠٠٪)	----------	٠.١٤٣	----------	٠.١٤٣	----------	٠.١٤٣
Tiny scars:					<٠.٠٠١					
Yes.	٠ (٠٪)	١٥ (١٠٠٪)	٠ (٠٪)	٠ (٠٪)	**G I vs G II**	**G I vs G III**	**G I vs G IV**	**G II vs G III**	**G II vs GIV**	**G III vs GIV**
No.	١٥ (١٠٠٪)	٠ (٠٪)	١٥ (١٠٠٪)	١٥ (١٠٠٪)	<٠.٠٠١	----------	----------	<٠.٠٠١	<٠.٠٠١	----------
Erythema:					<٠.٠٠١					
Yes.	٠ (٠٪)	٠ (٠٪)	٠ (٠٪)	١٥ (١٠٠٪)	**G I vs G II**	**G I vs G III**	**G I vs G IV**	**G II vs G III**	**G II vs GIV**	**G III vs GIV**
No.	١٥ (١٠٠٪)	١٥ (١٠٠٪)	١٥ (١٠٠٪)	٠ (٠٪)	----------	----------	<٠.٠٠١	----------	<٠.٠٠١	<٠.٠٠١

Discussion

Skin tags are the most common fibroepithelial skin tumor. They consist of acquired benign polyps that grow in the natural folds of the skin[٣].

ST have received little attention in the dermatological literature and are often considered clinically insignificant cutaneous redundancies that should be removed and destroyed without performing histopathologic study [١].

By measuring the body weight of the patients included in the study, the results revealed that (١٦.٧٪) of the studied patients with skin tags were of normal body weight while (٨٣.٣٪) of them were either over weight (٢٥٪) or obese (٥٨.٣٪). Accordingly, obesity is considered a promoting factor in the development of skin tags. This finding supporting the hypothesis that obesity is a common association with skin tags[٥].

In our study we detected (٣٣.٣٪) of our patients with skin tags suffering from NIDDM while the remaining (٦٦.٧٪) were non-diabetic. Consequently, the association between DM and skin tags could not be confirmed.

These results were in agreement with the results of El-Tahlawy et al. (٢٠٠٠),[٦] where only ٧.٨٩٪ of their patients with skin tags were NIDDM

These results contradicts that of Kahana et al. (١٩٨٧),[٧] who stated that the recognition of skin tags may be an important marker for the presence of impaired carbohydrate metabolism.

In the current study, by the routine H&E stain, we detected the presence of vacuolated keratinocytes in the upper and middle epidermis.

These vacuolated cells were consistent with the koilocytes described in the literature as the hallmark of the cytopathogenic effect of HPV. [٨&٩]

During the histopathological examination of H&E stained sections we observed the presence of a moderately dense lymphohistiocytic inflammatory infiltrate in the connective tissue stalk of (٧٠٪) of examined STs.

This observation was consistent with that of Salem et al. (٢٠١٣),[١٠] who reported the presence of upper dermal inflammatory infiltrate in skin tags. However these findings were not in agreement with the literature, that skin tags show a loose, edematous fibrovascular core with mild chronic inflammation, which is mainly lymphohistiocytic.

In our study immunohistochemical staining of the dermal inflammatory infiltrates revealed postive staining for CD٣, CD٤, CD٨, CD٢٠ and CD٦٨ in ٧٠٪ of skin tags. To the best of our knowledge this is the first time to examine the nature of the dermal infiltrate present in skin tags.

This immunohistochemical staining supports the role of these cells in the local immune response of the skin against a specific antigen, here mostly against the HPV. The presence of such cells confirms the role of cell mediated immunity in the control of HPV infection.

Mast cell tryptase marker staining is a specific marker for mast cells and allows them to be seen even if they have degranulated.[١٠]

The immunohistochemical staining using this marker, revealed the presence of a great number of positively stained mast cells in ٦٠٪ of cases. This is consistent with the results of Salem et al. (٢٠١٣), who reported the presence of a large number of mast cells in STs. this is in agreement also with the results of El Safoury et al., (٢٠٠٩), [١١] they showed the positive correlation between mast cell count in skin tags and percentage of collagen mean area which suggests the critical role of mast cells in the etiogenesis of skin tags.

In the current study ultrastructural examination of skin tags revealed the presence of Intra nuclear viral particles.

The intranuclear viral particles support the role of the HPV in the pathogenesis of skin tags. This is in agreement with both Gupta et al., (٢٠٠٨),[١٢] and Dianzani (١٩٩٨),[١٣] they reported the presence of HPV ٦/١١ DNA by the use of PCR in skin tags.

During the current study by compairing the four modalities of treatment, the removal of skin tags through the scissor excision come in the first line as it is a painless method, the removal of skin tags ends by the end of the session and rare recurrence.

The cryotherapy comes in the second line with less pain, less tissue damage, less post perative complications and no recurrence but the fall of the skin tag take about one week.

The third place is for electrocautery, which showed some intra operative pain, minimal post-operative complications and no recurrence.

The last place is for the TCA, which showed intra-operative burning pain, long time for the skin tag to be removed (about ٢ weeks) but with no recurrence.

Conclusion

As regard the pathophysiology of skin tags we conclude that skin tags are multifactorial in nature. The development of skin tags needs the intrgration of many precipitating factors. These factors include mast cell stimulation by friction or viral infections as HPV, which in turn can localize and start skin tag formation through its interaction with fibroblasts and keratinocytes. These factors are collected together in an obese patient mostly if she is a female below fifty.

If we are talking about the effective line of removal of such skin tags, we put the scissor excision in the first line, followed by the cryotherapy, then the electrau-cautery lastly the use of TCA.

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