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Histopathological Study of Warts in Egyptian Patients

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ABSTRACT

Background: Cutaneous warts are regarded as the primary manifestation of human papillomavirus (HPV) types. The cell-mediated immune response is believed to be essential for the clearance of HPV.

Aim: To study histopathological changes in warts of Egyptian.

Patients and Methods: The research involved 25 cases with warts. Histopathologic ally, Skin specimens from lesions have been collected, fixed, sectioned, and stained with H&E for examination under light microscopy and subsequent photography.

Results: Biopsies demonstrated variable degrees of papillomatosis, hyperkeratosis, and acanthosis. Also, perinuclear space (koilocyte) and pyknotic nucleus have been discovered. They also showed that most of the patients (56%) have grade 3 hyperkeratosis and parakeratosis while 64% of the patients have grade 2 acanthosis. It also showed that most of the patients (44%) have grade 3 papillomatosis, while 55% of the patients have grade 0 dermal infiltrate.

Conclusion: It was concluded that HPV caused mainly the same histopathological changes with different grades.

Keywords: Cutaneous warts; Histopathological; Biopsies.

INTRODUCTION

Warts are viral cutaneous infections induced by human papillomavirus, characterized by verrucous growth on skin surface. It can impact the skin and mucous membranes. HPV infection obtained through direct contact with an infected individual or the environment. Over 100 different types of HPV have been discovered [(1,2)]. Warts may appear at any location. HPV infection is categorized into mucosal or anogenital, Non-genital (Cutaneous), and Epidermodysplasia verruciformis (EV) [(3,4)].

Warts are predominant globally and impact around ten percent of the people. The incidence in school-aged kids is 10% to 20% [(5,6)].

HPV is transmitted primarily through skin-to-mucosa or skin-to-skin contact. Sexual transmission is the most common way of transmission, but studies also suggest non-sexual courses like the horizontal transfer of HPV, which involves mouth, fomites, fingers, and skin contact. Self-inoculation is another route of transmission [(7)].

Human papillomavirus penetrates epithelial tissues through minor injuries, and its life cycle is closely correlated with keratinocyte differentiation process. For example, keratinocytes advance to the spinous layer, there is an enhancement expression of gene accompanying viral DNA replication [(8,9)].

The histopathologic characteristics of different types of warts shows variable degrees of “acanthosis, digitated epidermal hyperplasia, papillomatosis, compact orthokeratosis, hypergranulosis, tortuous capillaries within the dermal papillae, and vertical tiers of parakeratotic cells with red blood cells” hide above digitations tips. Extended rete ridges can extend radially towards the lesion's center. In the granular layer, HPV-infected cells show rough keratohyalin granules and adjacent vacuoles near wrinkled-appearing nuclei. Koilocytic cells are indicative of a specific pathology [(10)].

The aim of this words was to study histopathological changes in warts of Egyptian.

PATIENTS AND METHODOLOGY

Twenty-five patients with warts participated in this research. Cases have been carefully chosen from the Dermatology Outpatient Clinic at Suez Canal University Hospital in Ismailia, Egypt, between January 2023 and August 2023.

Ethical Considerations:

The Research Ethics Committee of the Faculty of Medicine at Suez Canal University accepted the research protocol. Informed consent has been obtained from all adult patients and the caregiver of any child who took part in the study. Then samples were processed and examined in the pathology lab, Suez Canal University Hospital. The Helsinki Declaration was followed throughout the study's conduct.

Inclusion criteria were patients of both sexes, older than 8 years old and with warts of different size and clinical

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types. We excluded patients with acute febrile illness, patients who received any systemic or topical treatment for wart during the previous month, patients with autoimmune diseases, patients with a previous history of cancers, those with past history of allergic skin disorders and pregnant or lactating patients.

This study included a single group of patients diagnosed with warts. All eligible patients were recruited from the Dermatology Outpatient Clinic at Suez Canal University Hospital, Ismailia. Each patient underwent history taking, medical investigations, and a thorough dermatological examination, which included lesion assessment (site, size, number, and distribution) under proper lighting, along with dermoscopic evaluation for diagnostic confirmation.

Then samples were processed and examined in the pathology lab, Suez Canal University Hospital. Punch biopsy was taken from the lesion using a sterile skin punch (5 mm) from sterilized skin after local anesthesia. After taking the sample, the sample was fixed in 10% neutral buffered formalin (NBF). Then the sample was stained with Hematoxylin and Eosin and subsequently analyzed using a light microscope for histopathological modifications.

Statistical analysis

The data have been examined utilizing SPSS software. Quantitative data have been expressed as mean ± standard deviation and categorical data were expressed as frequency and percentage.

RESULTS

This research involved 25 patients with warts, they have been carefully chosen from Dermatology outpatient clinic, Suez Canal university hospital. Cases age ranged between 8 and 55 years old. Patients were 13 males and 12 females. 21 patients (84%) warts were in single site including the scalp, lower limb and upper limb while 4 patients (16%) were in multiple sites. The mean number of lesions was 3.50 ± 2.50 with minimum number of one and the maximum number was 10 lesions.

Additionally, the mean duration of the lesions was 7.50 ± 6.50 months with a minimum duration of 15 days and a maximum of 2 years. 1 patient (4%) had filiform warts, 3 patients (12%) had plane wart, 3 patients (12%) had multiple types, 7 patients (28%) had palmoplantar while 11 patients (44%) had common warts.

We found most of the patients (56%) had grade 3 hyperkeratosis and parakeratosis while 64% of the patients had grade 2 acanthosis. We also found that most of the patients (44%) had grade 3 papillomatosis while 55% of the patients had grade 0 dermal infiltrate as showed in **Table (1).**

Table 1: Histopathological changes in patients with warts (n = 25)

Histopathological changes	No.	%
Hyperkeratosis, Parakeratosis		
1	4	16.0
2	7	28.0
3	14	56.0
Acanthosis		
1	3	12.0
2	16	64.0
3	6	24.0
Papillomatosis		
1	7	28.0
2	7	28.0
3	11	44.0
Dermal infiltrate		
0	13	52.0
1	9	36.0
2	1	4.0
3	2	8.0

Hyperkeratosis, acanthosis and papillomatosis were found in all biopsies as showed in **Figure (1) and (2).** They also showed koilocytosis and perinuclear halo as showed in **Figure (3) and (4).**

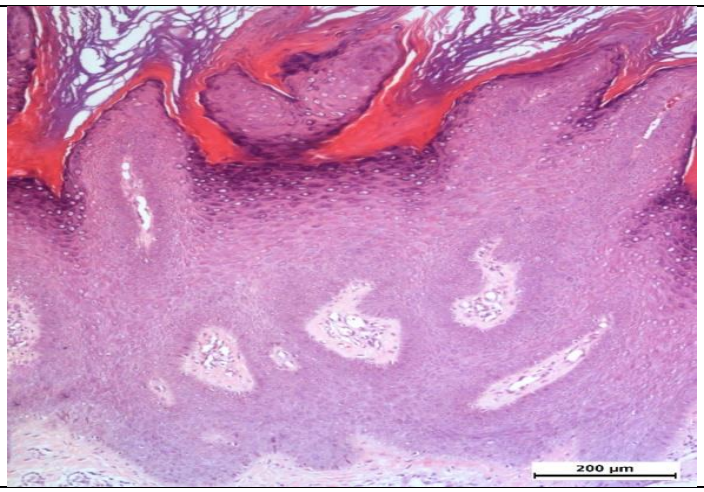

Figure 1: Histopathology of wart by H&E showing hyperkeratosis, acanthosis and papillomatosis (x 200 um)

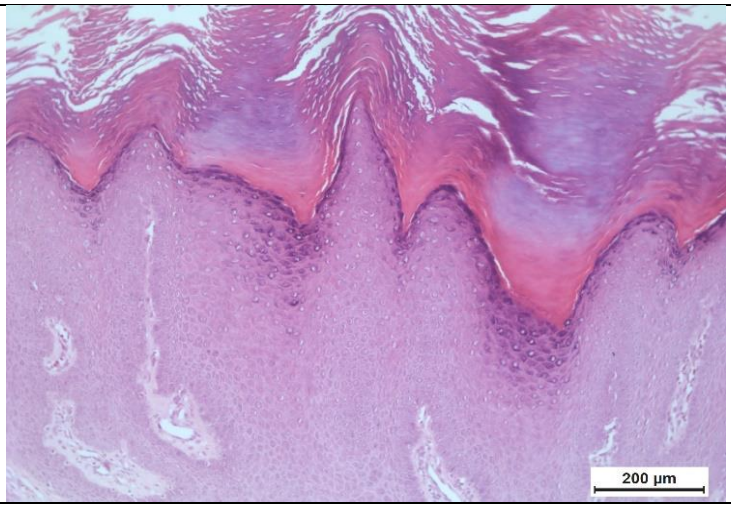

Figure 2: Histopathology of wart by H&E showing hyperkeratosis, acanthosis and papillomatosis (x 200 um)

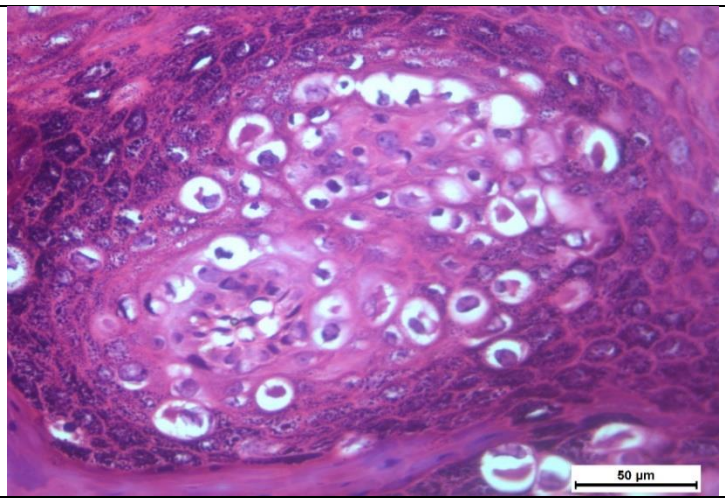

Figure 3: Histopathology of wart by H&E showing koilocytosis and perinuclear halo (x50 um)

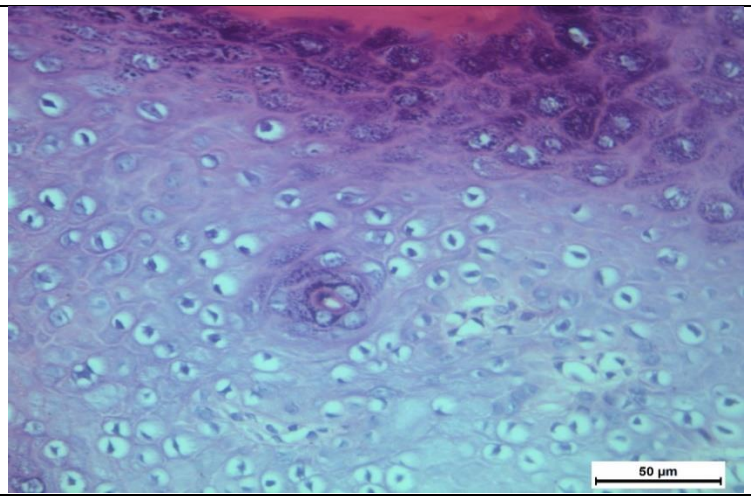

Figure 4: Histopathology of wart by H&E showing koilocytosis and perinuclear halo (x50 um)

DISCUSSION

Warts are viral cutaneous infections induced by human papillomavirus, characterized by verrucous proliferation on the skin surface [(11)].

The majority of HPV infections are efficiently cleared by the host's immune response. Nevertheless, in certain people, the HPV may cause a chronic infection. The persistent presence of high-risk HPV is the primary risk factor for tumor progress [(12)].

Following infection, the host basal keratinocyte divides and replicates viral deoxyribonucleic acid to produce several stem cells that each contain twenty to one hundred copies of the viral DNA. Cellular replication causes viral genome intensification that leads to a hyper-keratinized papule. The virus is released without lysing the cells; instead, it is shed along with the cornified layer as cells are slough from the epithelial surface [(13)].

Our biopsies showed variable degrees of hyperkeratosis, papillomatosis and acanthosis. Also, perinuclear space (koilocyte) and pyknotic nucleus have been discovered. Most of the patients (56%) have grade 3 hyperkeratosis and parakeratosis while 64% of patients have grade 2 acanthosis. It also showed that most of patients (44%) have grade 3 papillomatosis while 55% of patients have grade 0 dermal infiltrate.

In comparison of our results to **Cubie** [(14)]; She found that histologically, warts are benign lesions characterized by hypertrophy of all dermal layers, leading to papillomatosis (folding), hyperkeratosis (increase in the horny layer) and acanthosis (thickening), frequently accompanied by abnormal keratohyaline granules, which were observed in all wart tissues.

Al-Malak *et al.* [(15)] discovered that human papillomavirus may cause verrucous, papillomatous, and hyperplastic lesions in squamous cells of various mucosal locations and the skin. Abnormal keratin and koilocytes in the superficial epidermal layers, along with the elongation of dermal papillae, are additional diagnostic characteristics characterizing this infection, indicating that the virus primarily affects keratinocytes and the epithelial layers of the epidermis, specifically the granulosum and spinosum layers. These results align with our investigation's outcomes.

Also, **Al-Malak *et al.*** [(15)] demonstrated cellular infiltrates of inflammatory cells and the destruction of the smooth surface beneath HPV colonies, which indicated that infection can induce skin damage and a histological response against virus, characterized by the infiltration of phagocytes and lymphocytes. Other investigations have demonstrated that the cellular infiltrates in regressing warts predominantly consist of mononuclear phagocytes and lymphocytes, that are located in the areas of damaged epidermis and keratinocytes. We additionally identified dermal infiltrate in several wart biopsies.

Warts are histologically defined by hyperkeratosis and papillomatosis, with parakeratosis observed on upper surface. This phenomenon can be attributed to the influence of the virus and keratinocytes function in stratum corneum. These findings are consistent with research indicating that parakeratosis overlying the tips of papillomatous projections, alternating with orthokeratosis overlying the cavities [(16)].

Human papillomavirus infections are typically regulated by humoral immune responses and functional cell-mediated. Regression is primarily influenced by cytotoxic T cells and natural killer cells, whereas protection against infection with the same human papillomavirus type arises from the activation of the production of antibodies and the adaptive immune response. Nonetheless, the sequestration of human papillomavirus within epithelial cells protects virus, leading to poor priming of the adaptive response,

infection persistence and inefficient activation of innate immunity [17].

CONCLUSION

It was concluded that HPV caused mainly the same histopathological changes with different grades.

DECLARATIONS

- **Consent for publication:** I certify that each author has granted permission for the work to be submitted.
- **Funding:** No fund
- **Availability of data and material:** Available
- **Conflicts of interest:** None
- **Competing interests:** None

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