e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 89-93

Original Research Article

The Role of Differentiation of Bowen's Disease of the Nail Apparatus from it's Mimickers and it's Association with Human Papilloma Virus

Mehak Jindal[1], Amandeep Rathi[2], Vivek Singh[3], Sanjeev Kumar[4]

[1]Senior Resident, Pathology, Maharishi Markandeshwar College of Medical Sciences and Research, Ambala
[2]Junior Resident, Internal Medicine, Philadelphia Hospital, Ambala
[3]Senior Resident, DVL, Maharishi Markandeshwar College of Medical Sciences and Research, Ambala
[4]Senior Resident, Pathology, Maharishi Markandeshwar College of Medical Sciences and Research, Ambala

Received: 02-04-2024 / Revised: 23-04-2024 / Accepted: 06-05-2024
Corresponding Author: Dr. Sanjeev Kumar
Conflict of interest: Nil

Abstract:

Background: The aim of the study is to study the mimickers of bowen's disease of the nail apparatus and it's association with human papilloma virus. Bowen's disease is the most frequent malignant condition of nail unit and presents as a verrucous plaque predominantly involving men.

Material and Methods: We reviewed 30 cases of various conditions involving the nail apparatus at our institute to study the positive cases of bowen's disease for the presence of human papilloma virus (HPV) DNA. We used specimens fixed in 10% neutralized buffered formalin, embedded in paraffin wax to study their histopathology as well as for HPV DNA testing via PCR.

Results: In our study we found maximum cases of bowen's disease (33.3%). The chi-square statistic is 0.9184. The *p*-value is 0.037904. The result is significant at $p < 0.05$. Our study demonstrated 63.4% of cases in the duration of 01-02 years. In addition, we found 60% cases of bowen's disease to be associated with HPV. The chi-square statistic is 2.48365. The *p*-value is 0.317798. The result is not statistically significant at $p < 0.05$.

Conclusion: Biopsy and histopathological examination are required for diagnosis and differentiation of bowen's disease from other ungula and periungual diseases. The strong association of high-risk HPV infection and BD of the nail unit as reviewed in various literatures and described in our original study supports a causative role of the virus in digital BD, and should prompt the early follow-ups and biopsy of digital associated lesions in patients and partners.

Keywords: Occurrence, HPV, Bowen's disease, Nail apparatus.
Study Design: Observational Study.

Introduction

Bowen's disease (BD) is a squamous cell carcinoma (SCC) in situ of the skin. In 3–5% of cases, it progresses to invasive carcinoma with the capability to develop metastasis. BD of the nail apparatus differs from BD of the skin since it may mimic various benign conditions such as chronic eczema, verruca vulgaris, paronychia or onychomycosis.

Therefore, it has been frequently misdiagnosed for many years. Furthermore, it appears to be associated with human papillomavirus (HPV) infections in genital areas whereas this is a rather rare event in BD of the exposed skin [1,2]. However, the precise aetiology of BD of the nail unit is unclear. Chronic traumatization, exposure to arsenic or ultraviolet and ionizing radiation have been discussed. In addition, HPV infection is now thought to be a causative factor [3-5].

Material and Methods

Biopsy specimens from 30 patients treated in our facility for 01 Year at Maharishi Markandeshwar College of Medical Sciences and Research, Ambala with various diseases of the nail apparatus were used for this investigation and the specimen positive for the presence of bowen's disease were analysed for the presence of HPV DNA. These tissue specimens fixed in 10% neutralized buffered formalin and embedded in paraffin wax were subjected to routine histopathological examination. we also focused on the distribution of gender, age at onset of disease as well as the frequency of digit involvement. Informed consent was obtained from all subjects. HPV DNA testing was done on formalin fixed paraffin embedded tissue using polymerized chain reaction (PCR) which was outsourced.

Inclusion Criteria: Lesions involving the nail apparatus, clinical history availability, no concomitant history of immunocompromised state or previous treatment

Exclusion Criteria: Cases affecting the digits outside the nail apparatus

Result

Table 1: Age distribution

			P Value
Age	**No**	**Percentage**	
30-40	**04**	**13.3**	
41-50	**09**	**30**	0.030287
51-60	**12**	**40**	
61-70	**05**	**16.7**	

In our study we found maximum cases in age group of 51-60 (40%). The chi-square statistic is 4.693. The *p*-value is 0.030287. The result is significant at $p < 0.05$.

Table 2: Distribution of Males Polydactylous

Digit	Males		Total	P Value
	Left Hand	Right Hand		
1	**03**	**05**	**08/26.6**	
2	**03**	**03**	**06/20**	
3	**04**	**04**	**08/26.6**	0.560732
4	**05**	**02**	**07/23.3**	
5	**00**	**01**	**01/3.3**	
Total	**15**	**15**	**30/100**	

In our study we found maximum cases in 1 &3 digit (26.6%). The chi-square statistic is 0.0024. The *p*-value is 0.560732. The result is *not* significant at $p < 0.05$.

Table 3: Distribution of Females Polydactylous

Digit	Females		Total	P Value
	Left Hand	Right Hand		
1	**03**	**04**	**07/23.3**	
2	**07**	**06**	**13/43.3**	
3	**02**	**03**	**05/16.6**	0.049703
4	**02**	**02**	**04/13.3**	
5	**01**	**00**	**01/3.3**	
Total	**15**	**15**	**30/100**	

In our study we found maximum cases in 2 digit (43.3%). The chi-square statistic is 1.6968. The *p*-value is 0.049703. The result is significant at $p < 0.05$.

Table 4: Disease

	Disease		P Value
	No	**Percentage**	
Bowen's disease	**10**	**33.3**	
Chronic eczema	**06**	**20**	0.037904
Verruca vulgaris	**05**	**16.7**	
Paronychia	**03**	**10**	
Onychomycosis	**06**	**20**	

In our study we found maximum cases in Bowen's disease (33.3%). The chi-square statistic is 0.9184. The *p*-value is .037904. The result is significant at $p < 0.05$.

Table 5: Sun Exposure

Sun Exposure	No	Percentage	P Value
Yes	**13**	**43.3**	
No	**17**	**56.7**	.297365

In our study we found 43.3% Sun Exposure. The chi-square statistic is 1.086. The *p*-value is 0.297365. The result is *not* significant at $p < 0.05$.

Table 6: Duration

Duration	No	Percentage
Less than 01 Year	06	20
01-02	19	63.4
02-03	04	13.3
More than 03 Years	01	3.3

In our study we found 63.4% in duration of 01-02 years.

Table 7: Association of positive cases of bowen's disease with HPV DNA positivity

Bowen's disease	Total (10)	Percentage	P Value
HPV DNA positive	06	60	
HPV DNA negative	04	40	.317798

In our study we found 60% of cases of bowen's disease to be associated with HPV.
The chi-square statistic is 2.48365. The *p*-value is .317798. The result is not significant at $p < 0.05$.

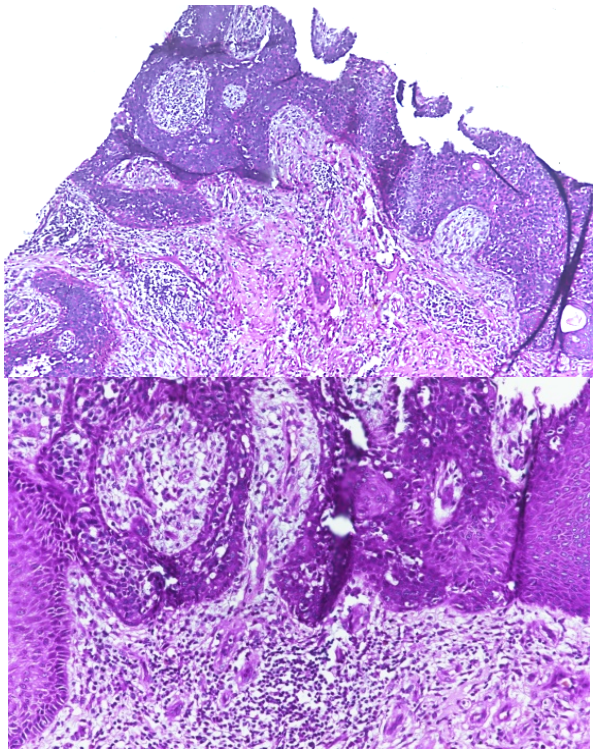

Figure 1 & 2: Section examined shows epidermis showing acanthosis with elongation and thickening of rete ridges. The cells in the epidermis are disorderly arranged, with most of the cells exhibiting moderate atypia in the form of large, atypical cells showing keratinization. These tumor cells are seen extending into follicular infundibulum. The upper dermis shows a band of dense chronic lymphoplasmacytic infiltrate. The horny layer is thickened and consists of parakeratotic cells. (The radial margins included in specimen were free of tumor)

Figure 3: A scaly, verrucous and crusted lesion with periungual swelling

Discussion

The present study adds to a growing literature of reported cases on extragenital manifestations of genital HPV disease. Maximum cases were found in the age group of 51-60 (40%) with maximum cases involving the first and third digits in males, whereas in females second digit was the most commonly involved site. Out of the total specimens biopsied, 33% cases turned out to be bowen's disease and out of these, 60% were found to be associated with HPV DNA. However, this result was statistically insignificant due to presence of confounding etiological factors such as sun exposure. Five clinical cases mis-diagnosed as benign conditions were histologically diagnosed as BD and thus later re-evaluated.

While BD is commonly found on the trunk, face, fingers and genitalia, the occurrence in the nail apparatus is rare. In this location, involvement of the nail fold typically presents as either an erythematous plaque or as a scaly, verrucous or crusted lesion with periungual swelling. Nail bed involvement may cause onycholysis, Verruca vulgaris, Paronychia and chronic eczema, whereas nail matrix involvement may lead to longitudinal erythronychia or melanonychia [6]. However, this rare occurrence is now being supported by various literatures.

Various studies have attributed an aetiological role of HPV in the development of bowen's disease of genital regions such as cervix, penile or anal, however the role of HPV in causation of BD of the nail unit, is still being studied [7]. There is convincing evidence that α-HPV type 16 and related mucosal types play a crucial role in the development of cervical and anogenital carcinomas [8]. The role of HPV in skin cancer was first demonstrated in patients with the rare hereditary skin disease epidermodysplasia verruciformis. However, involvement of HPV in the development of SCC in non-genital skin is frequently missed [9,10]. As shown here by analysis of the literature, BD of the nail unit is highly associated with high-risk α -HPV infection. Therefore, initiation or progression of ungual BD by HPV to SCC is very likely.

It appears that periungual skin is predisposed to HPV infection due to microtrauma. This idea is supported by the notion that BD usually arises at the lateral or proximal nail fold or hyponychium and invades the nail unit by extension. In support of this idea, the right thumb of men, which is predominantly exposed to traumata or abrasion, followed by the second, third and fourth fingers in either gender are affected. Furthermore, cases of polydactylous disease have been reported, supporting a role of an infectious agent in periungual BD [11].

Detection of the same HPV types in anogenital lesions and BD of the nail unit suggests the possibility of auto-inoculation of the finger from the genital area to the finger or vice versa as it has been exemplified by several cases showing the same HPV genotype found in lesions of BD of the nail and genital epithelial dysplasia/ neoplasia. In line, one interesting paper described an 80-year-old gynaecologist who developed periungual BD on the left index finger, which was positive for α -HPV type 18 DNA by PCR typing. Since α -HPV type 18 DNA is usually not detected in BD of the nail unit, it is very likely that infection occurred during carrying out his professional work [12].

Conclusion

Biopsy and histopathological examination are required for diagnosis and differentiation of bowen's disease of nail apparatus from other benign ungual and periungual diseases. The strong association of high-risk HPV infection and BD of the nail unit as reviewed in various literatures as well as described in our original study supports the causative role of the virus in digital BD, and should prompt the early follow-ups and biopsy of such digital lesions in patients and partners.

References

1. McBride AA. Human papillomaviruses: diversity, infection and host interactions. Nat Rev Microbiol. 2022; 20:95-108.
2. Kombe Kombe AJ, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y, et al. Epidemiology and burden of human papillomavirus and related diseases, molecular pathogenesis, and vaccine evaluation. Front Pub Healt. 2021; 8:55 2028.
3. Bradbury M, Xercavins N, Garc´ıa-Jim´enez ´A, et al. Vaginal intraepithelial neoplasia: clinical presentation, management, and outcomes in relation to HIV infection status. J Low Genit Tract Dis 2019; 23: 7–12.
4. Kelly H, Chikandiwa A, Alemany Vilches L, et al. Association of antiretroviral therapy with anal high-risk human papillomavirus, anal intraepithelial neoplasia, and anal cancer in people living with HIV: a systematic review and meta-analysis. Lancet HIV 2020; 7: e262–78.
5. Kravvas G, Ge L, Ng J, et al. The management of penile intraepithelial neoplasia (PeIN): clinical and histological features and treatment of 345 patients and a review of the literature. J Dermatol Treat 2022; 33: 1047–62.
6. Wikstr ¨om A, Hedblad MA and Syrj¨anen S. Penile intraepithelial neoplasia: histopathological evaluation, HPV typing, clinical presentation and treatment. J Eur Acad Dermatol Venereol 2012; 26: 325–30.
7. D'Hauwers KW, Depuydt CE, Bogers JJ, et al. Human papillomavirus, lichen sclerosus and

penile cancer: a study in Belgium. Vaccine. 2012; 30:6573–77.
8. McGrae JD, Jr., Greer CE and Manos MM. Multiple Bowen's disease of the fingers associated with human papilloma virus type 16. Int J Dermatol 1993; 32: 104–107.
9. Shimizu A, Kuriyama Y, Hasegawa M. Nail squamous cell carcinoma: a hidden high-risk human papillomavirus reservoir for sexually transmitted infections. J Am Acad Dermatol 2019; 81: 1358–70.
10. Turowski CB, Ross AS, Cusack CA. Human papillomavirus-associated squamous cell carcinoma of the nail bed in African American patients. Int J Dermatol 2009; 48: 117–20.
11. Namgoong S, Kim J, Jeong KM, et al. Association of human papillomavirus and extragenital Bowen disease (squamous cell carcinoma in situ): a systematic review. J Am Acad Dermatol 2021; 84: 822–5.
12. Montesu MA, Onnis G, Lissia A, et al. Extragenital human papillomavirus 16-associated Bowen's disease. Indian J Dermatol 2017; 62: 97–8.
13. 12. Kechagias KS, Kalliala I, Bowden SJ, Athanasiou A, Paraskevaidi M, Paraskevaidis E et al. Role of human papillomavirus (HPV) vaccination on HPV infection and recurrence of HPV related disease after local surgical treatment: systematic review and meta-analysis. BMJ. 2022; 3: 378-84.