# Bowen's Disease Associated With Two Human Papilloma Virus Types

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***Received: 16 May 2016; Accepted: 26 Mar. 2017***

**Abstract**- Bowen's disease (BD) is an epidermal in-situ squamous cell carcinoma (SCC). Most *Human Papilloma Viruses* (HPV)-positive lesions in Bowen's disease are localized to the genital region or distal extremities (periungual sites) in which HPV type-16 is frequently detected. Patient was a 64-year-old construction worker for whom we detected 2 erythematous psoriasiform reticular scaly plaques on peri-umbilical and medial knee. Biopsy established the diagnosis of Bowen's disease and polymerase chain reaction assay showed HPV-6, -18 co-infection. Patient was referred for surgical excision.



*Acta Med Iran* 2017;55(9):594-596.

**Keywords:** Bowen's disease; Human papilloma virus; Squamous cell carcinoma

## Introduction

Bowen's disease (BD) is an epidermal in-situ squamous cell carcinoma (SCC), originally described in 1912 by Bowen on sun protected areas possibly related to arsenic (1). Human papilloma viruses (HPV) are a heterogeneous group of small non-enveloped epitheliotropic DNA viruses replicating in the basal cells of stratified epithelia at either mucosal or cutaneous sites (2) HPV has been associated with genital and non-genital BD since 1990 (3,4).

Most HPV-positive lesions in Bowen disease are localized to the genital region or distal extremities, in which HPV type-16 is frequently detected (5).

Different types of virus can be present in a single lesion or patient especially if genetically susceptible (6). Here we report a case of multiple BD associated with HPV types -6, -18.

## Case Report

The patient is a 64-year-old fair-skinned Iranian male, construction worker who presented with chief complaint of pruritic exudative lesions of dorsal feet since 20 days ago following unprotected contact with cement. Personal history was not significant for contact with arsenic, radiation, tar or other potentially carcinogenic compounds. There were no known cases of skin malignancies in his family members. However, his brother died of lung cancer 5 years ago at the age of 58. On Physical examination apart from contact dermatitis of dorsal feet, 2 erythematous psoriasiform reticular scaly plaques on peri-umbilical and medial knee measuring 10×10 cm and 10×7 cm, respectively were detected. Upon questioning, it became clear that they were present since 5 years ago with gradual enlargement; and nodules developed on the thigh lesion from 7-8 months ago (Figure 1). The lesions were asymptomatic; hence, the patient sought no medical attention.

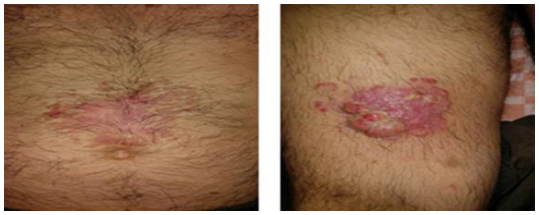

**Figure 1.** Lesions on the abdomen (left) and medial thigh (right)

Our patient was exposed to arsenic contact neither by ingestion drinking water or foods nor by direct contact with colemanit. Our patient didn't have weakness, fatigue, and loss of weight, palmar and plantar keratoses and no gastrointestinal complaints. CT-scan and ultrasonography of the abdomen were both normal. The laboratory findings consist of mild anemia with normal white blood cells without eosinophilia. Liver function tests were in normal range. In urinary examination and

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cystoscopy, no abnormalities were found.

Serum arsenic level was normal however we couldn't determine the arsenic levels in tissue and urine.

His wife's Pap smear (liquid-based thin preparation) was negative for intraepithelial lesion or malignancy.

Incisional biopsy of the lesions showed irregularly thickened epidermis with markedly disordered maturation pattern and full thickness dysplasia in the form of marked nuclear enlargement and hyperchromasia, cytoplasmic vacuolization, individual cell dyskeratosis and increased mitotic activity including atypical mitoses. Underlying dermis shows chronic inflammatory infiltration largely composed of plasma cells. There were no obvious dermal invasions even in the biopsy of the nodular part (Figure 2). Polymerase chain reaction (PCR) and DNA sequencing of the medial knee lesion was positive for HPV-6, -18 but the peri-umbilical lesion was negative for HPV DNA.

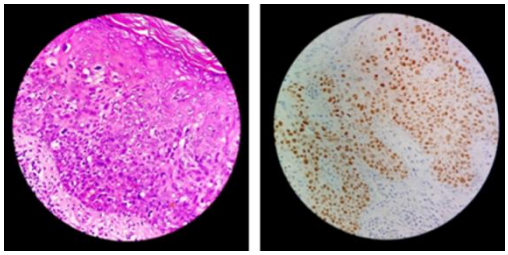

**Figure 2.** Patient's tissue sample of medial thigh, showing full-thickness atypia (H and E (left)) and proliferation (p53 (right))

## Discussion

Bowen's disease is an intraepidermal SCC of the skin which follows a slow course with horizontal or intraepidermal growth over a period of years; however, it may progress to invasive SCC by vertical growth (7).

BD commonly develops on sun-exposed areas of the body. It is more prevalent among fair-skinned elderly patients. It typically presents as a well-demarcated, erythematous scaly plaque with an irregular border, characterized by full-thickness epidermal atypia on histology. An annual incidence of 15 per 100 000 had been suggested in the U.K (8). Etiologies suggested for BD include irradiation: ultraviolet irradiation (solar, iatrogenic and sun beds), radiotherapy and photochemotherapy, carcinogens (eg, arsenic; especially for lesions of sun protected areas), immunosuppression (after organ transplantation, AIDS and therapeutic), viral (strong association of perianal and genital lesions with HPV; especially HPV16 genome) as well as chronic injury or dermatoses (eg. chronic lupus erythematosus) (5,8,9).

Murao and colleagues showed that HPV DNA could be detected in almost 12% of BD lesions and the most commonly detected types were HPV type 16 and 33 although other types (e.g., 6, 52, 56, 58 ,59) were also detected with less frequency (2).

It is generally accepted that BD of the fingers and genital areas is associated with high-risk types of HPV infection, and there have recently been several case reports of HPV-associated BD on other extragenital locations, although the extent of involvement in pathogenesis is not clear yet (1-8).

In Bowen's disease, lesions usually are found in areas of the skin and mucous membranes including the nail beds, palms, and soles. Individual lesions of Bowen's disease have a tendency to persist for many years without progression to invasive carcinoma. However, 5-15% of BD will progress to invasive SCC or metastasis, if untreated although studies do not support a relationship between Bowen's disease and internal cancers (7). In our patient, no focus of internal malignancy was detected.

Ikenberg *et al.*, identified HPV in six of 10 cases of BD and proposed the involvement of HPV in its formation. Hama *e al.*, reported only one of 21 cases with BD showed HPV DNA, which was positive for HPV 31. This type of HPV is categorized in the mucosal high-risk group and considered to be a sex-transmitted or auto inoculated kind (10).

In HPV 16, E6 protein combines with p53, and E7 protein binds to Rb protein. The suppression of these tumor suppressor genes provokes oncogenesis (10).

HPV can contribute to the progression of extragenital BD. The prevalence of HPV in extragenital BD ranges 0-83%. Murao *et al.*, reported one out of 142 patients with BD lesions for the mucous-type HPV (HPV 6). In total, 8.3% of extragenital BD lesions harbored HPV DNA. The HPV-associated Mucous-type HPV are usually distinguished in lesions involving the cervix and external genitalia. The exact mechanism by which mucous-type HPV is spread to regions outside of the external genitalia is unclear, but the autoinoculation is suspected to occur by fingers (2).

Our patient showed no anogenital lesions related to HPV infection, although he had HPV-related Bowen's disease on his thigh.

In summary, our report demonstrated tumor cells with high copy numbers of viral genome regarded as two type of mucosal HPV (type 6 and 18) found in Bowen's disease of the thigh. This data proposed that HPV-associated Bowen's disease is not confined to the genitalia or fingers.

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