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An unusual case of oral warty dyskeratoma associated with human papilloma virus

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Abstract

Warty Dyskeratoma (WD), also known as isolated Darier's disease or focal acantholytic dyskeratosis, is a rare mucocutaneous anomaly and is known as a benign solitary tumor of the skin, vulva, oral cavity. The size of many oral lesions associated with the virus is smaller than 1 cm. An example of such a lesion might be given as squamous papilloma. In such situations, the presence of viral particles will be a distinguishing factor in the case of squamous papilloma lesions. The histological examinations and Polymerase Chain Reaction (PCR) techniques were employed to investigate the potential involvement of Human Papilloma Virus (HPV) infection in the development of Oral Warty Dyskeratoma (OWD). Degenerate primers were utilized for this purpose. The diagnosis of OWD was verified through histopathological investigation, and the presence of HPV DNA was detected through PCR. Currently, the only study found in the literature that has demonstrated the existence of HPV DNA in a case of OWD is by special techniques like PCR. For future research, it would be advantageous to employ sequencing to determine the HPV-DNA.

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Introduction

Warty Dyskeratoma (WD), alternatively is referred to as isolated Darier disease or focal acantholytic dyskeratosis, is an infrequent mucocutaneous anomaly [1]. Generally, it appears as a solitary, asymptomatic umbilicated papule, commonly observed in the head and neck area of individuals in the middle to older age group [2]. There has been a slight predisposition towards males that has been identified. Occasional reports have indicated the presence of involvement in the oral and vaginal mucosa [3,4]. When observed within the oral cavity, WD is predominantly observed on the hard palate and alveolar ridge [5]. The etiology of Oral Warty Dyskeratoma (OWD) remains unknown, although a majority of cases have demonstrated a correlation with tobacco smoking/chewing, local chronic trauma/irritation caused by a sharp tooth, or an improperly fitted denture [6]. A disease known as warty dyskeratoma exhibits morphologic traits that resemble those of the typical viral wart, potentially indicating a connection to Human Papillomavirus (HPV) infection as an underlying cause.

Currently, there is a lack of comprehensive research investigating the possible role of HPV infection in the development of these lesions. Recently, there have been notable instances of

WD that have histological similarities to HPV-induced verrucous lesions. This observation indicates a broader range of morphological variations in this lesion than previously acknowledged, and suggests a potential association with HPV infection as an etiological factor [7]. Currently, there is no evidence of HPV-associated oral warty dyskeratomas in the existing literature, and none of the documented cases have experienced a recurrence [8].

This study thoroughly analyses a case of oral warty dyskeratoma occurring in the same patient at distinct locations and at different times. This is the first report of warty dyskeratoma thought to be linked with HPV in a current collection of literature.

Case presentation and result

Patient 68-year-old male patient first presented to Gazi University Faculty of Dentistry, Department of Oral and Maxillofacial Surgery in 2018 for evaluation of a white lesion in the left retromolar region. The patient reported that he did not have any systemic disease, did not take any medication regularly, and did not have any skin lesions. In the anamnesis, it was discovered that the patient had been smoking around 30 cigarettes per day for a period of 40 years. No abnormalities were observed during the assessment of the extraoral examination. Intraoral examination revealed a white lesion in the left retromolar region, which was white, erythematous in some areas and did not go away with scraping. The preliminary diagnosis of the lesions were oral papilloma, oral leukoplakia, and oral squamous cell carcinoma. The lesion was surgically excised. To obtain a conclusive diagnosis, the sample was preserved in a solution of 10% buffered formalin and then transported to the Oral Pathology Department at Gazi University for histologic investigation. Macroscopically, the lesion was observed as an off-white mucosal tissue with an irregular surface measuring 1.5x1.3x1 cm in size. Histopathologically, invaginations and verrucous extensions on the surface of orthokeratinized epithelium as well as suprabasilar separation and keratin plug were observed. Small groups of individual keratinocytes were seen in the areas of basilar separation in the lesions. The final diagnosis reported by the pathology department was oral warty dyskeratoma (Figure 1).

Although no recurrence was expected after total excision, the same patient presented to Gazi University Oral, Dental and Maxillofacial Surgery in 2022 for examination of a white lesion on the right palatinal mucosa. Upon intraoral examination, a firm and white plaque was observed on the right hard palate, which was resistant to removal with scraping. The histopathologic analysis showed a halo appearance in the cytoplasm of keratinocytes in the spinous layer of the epithelium, along with the results of the lesion in the retromolar region in the second biopsy. Therefore, the presence of HPV was suspected in second biopsy, and PCR analysis was performed to investigate the presence of HPV.

The potential presence of HPV was hypothesised based on histochemical staining, and further molecular tests were conducted to determine the presence of HPV-DNA. Formalin-Fixed Paraffin Embedded (FFPE) tissue samples were cut into 5 sections of 10-micron thickness and taken into ependorf tubes. After deparaffinization, DNA extraction was performed using FFPE DNA isolation kit (Qiagen, Germany), following the manufacturer's instructions. PCR was conducted after isolating the sample, utilising the MY09/MY11 primer combination to amplify the HPV location. PCR studies were conducted with a negative control containing a PCR mixture without DNA, and the patient material with known HPV presence was used as a positive control. Ten microliters of the PCR product were loaded onto a 2% agarose gel for gel electrophoresis. The gel was then stained with ethidium bromide at a concentration of 500 ng/ml in 1x TBE buffer solution. A GeneRuler DNA ladder (Thermo Scientific in Vilnius, Lithuania) was utilised as a molecular weight standard. The analysis yielded a band indicative of the presence of HPV, which was observed at the 450bp region (Figure 2). With the molecular data and histopathologic data observed in this study, the final diagnosis reported by the pathology department was HPV-associated warty dyskeratoma.

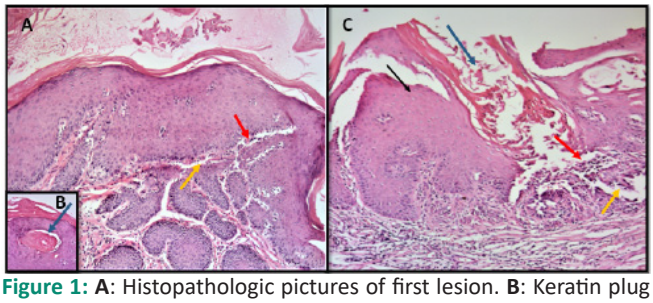

Figure 1: **A**: Histopathologic pictures of first lesion. **B**: Keratin plug in first lesion. **C**: Histopathologic pictures of second lesion (Red arrow: suprabasiler separation; Yellow arrow: Small groups of individual keratinocytes; Blue arrow: keratin plug; Black arrow: halo appearance in the cytoplasm of keratinocytes)

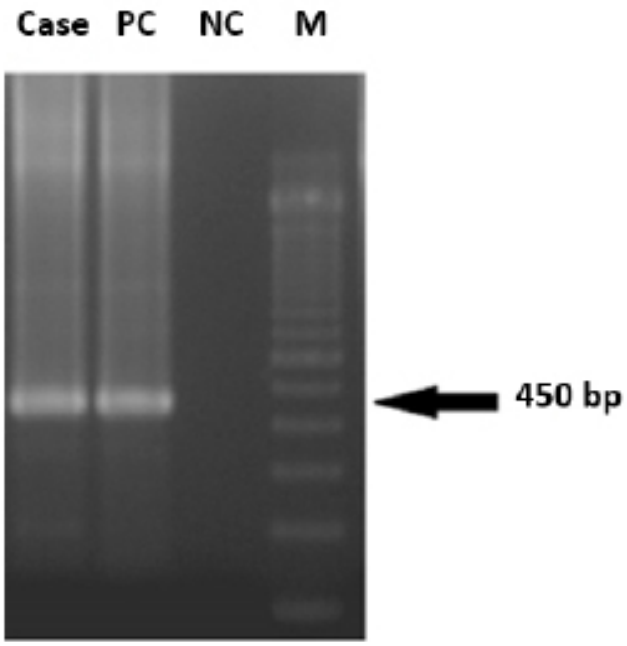

Figure 2: The identification of HPV positive by the utilisation of MY09/11 primers. (PC: Positive control; NC: Negative control; M: Marker).

Discussion

WD is considered to be a skin lesion of relatively low prevalence. OWD is commonly encountered on keratinized mucosa, such as the maxillary and mandibular alveolar ridges and the hard palate [1]. Tobacco and alcohol intake have been identified as the most prevalent risk factors connected with OWD [8]. This study documented a case of OWD occurring in the retromolar region and on the right side of the hard palate, with a time gap of 4 years in the same patient. It was noticed that the patient had a longstanding habit of smoking.

OWD can be categorized as a verruco-papillary lesion based on its clinical appearance. In some cases, a relatively smooth surface in the form of papules or patches was seen. It was observed that in certain instances, the surface was rather smooth and took the appearance of papules or patches. The lesion appears white because to the hyper-keratinization of the surface epithelium. When a white patch is present, the color white and the related tobacco habits frequently result in a provisional diagnosis of leukoplakia. In the case of a rough surface, it may indicate verrucous carcinoma/verrucous hyperplasia or Oral Squamous Cell Cancer (OSCC) [8].

Despite being a non-progressive minor lesion, it often needs further investigation due to its clinical and histopathologic similarities With Oral Potentially Malignant Diseases (OPMDs) and OSCC [9]. During the diagnostic process, it is essential to do histopathologic examination in order to distinguish OWD from other lesions that may have similar characteristics. Leukoplakia is a term used to describe a lesion that appears as a white patch, particularly when there is a history of tobacco use. In instances of this nature, the lack of epithelial dysplasia, the existence of suprabasal clefting, the presence of keratin-filled crypts, and the occurrence of acantholytic dyskeratotic cells (known as corps ronds and grains) would serve as the differentiating characteristics from tobacco-induced possibly malignant leukoplakic lesions [9]. Warty dyskeratoma can be differentiated from Squamous Cell Carcinoma (SCC) based on its histological characteristics, despite its similar verruciform appearance and chronic ulceration. Notably, warty dyskeratoma lacks atypia or mitotic activity [10]. In contrast to OSCC, the OWD is characterized by its inherent self-limiting nature and absence of malignant progression. In instances of this sort, the disparity in size may serve as a significant signal of the characteristics of the lesion. The majority of instances of OWD are smaller than 1 cm in size and exhibit a distinct and clearly defined boundary [11]. The term “wart” suggests that the lesion typically has a surface that is rough and bumpy, resembling warts. Thus, the typical clinical differential diagnosis includes Verrucous Hyperplasia (VH), Verrucous Carcinoma (VC). Unlike VC and VH, OWD is self-limiting and does not lead to malignant change. OWD is clearly delineated, unlike locally invasive lesions such as VC, VH [8].

The majority of prior descriptions mostly focus on individual case reports or small series. Thus far, there have been only a limited number of comprehensive clinicopathologic studies conducted [12,13]. The etiology and classification of warty dyskeratoma remain uncertain. Numerous writers claim that various external variables or a contagious viral pathogen could potentially play a role in the development of these lesions. However, earlier studies have failed to support these hypotheses or provide any substantiated proof of a viral infection in relation to these lesions [14]. The histopathological characteristics of WD, particularly the striking similarity between cystic lesions and verrucous lesions, led us to investigate the potential association between HPV infection and the development of these lesions [7]. While previous reports have shown that focal oral warty dyskeratomas do not exhibit recurrence, our case study, as documented by Kaugars (1984) [5], presents evidence to the contrary. Specifically, we noticed a recurrence in our instance after a period of 4 years. In order to investigate this particular issue, Kaddu et al. (2002) [7] conducted a polymerase chain reaction analysis to detect the presence of HPV DNA in 13 lesions of WD. The results of their study did not reveal any indication of HPV DNA. However, in our study supported by PCR, we demonstrated the presence of HPV in warty dyskeratoma.

Rushiti et al. (2023) [15] found that HPV-associated oral mucosal lesions exhibited an average recurrence period of 1 year. No cases of recurrent OWD were found in previous studies and the presence of HPV was not detected in any of these studies. Taken together, this may suggest the possibility that the identification of HPV and the observation of multifocal recurrence in our case are related. It is necessary to conduct sequence studies on biopsies taken from patients who have experienced a recurrence in order to confirm this concept. The answer to whether the presence of HPV promotes recurrence or whether the presence of HPV in a multifocal area is connected with HPV can only be found in this circumstance.

Declarations

Data availability statement: The data supporting the findings of this study are available upon request from the corresponding author. The data were not publicly available because of privacy or ethical restrictions.

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