



Overview of Plantar Warts: Causes; Classification and Differential Diagnosis

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ABSTRACT

Viral warts or verruca pedis (plantar warts) are common skin conditions seen in both children and adults. Plantar warts are common cutaneous lesions of the plantar aspect of the foot that are caused by the human papillomavirus (HPV), a DNA virus, is responsible for plantar verrucae. It needs an epidermal abrasion and a transiently impaired immune system to inoculate a keratinocyte. Warts are scaly, rough, spiny papules or nodules. Once a plantar wart is established, it sheds HPV via desquamated epithelial cells. The viral particles can subsequently infect other sites and hosts. Plantar warts tend to develop at areas of increased pressure on the sole of the foot, including the heel and metatarsal heads. This article is aimed to review the cause and types of plantar warts; and how to differentiate it from other skin lesions.

Keywords: Plantar Warts; Causes; Classification and Differential Diagnosis

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INTRODUCTION

Warts are caused by human papillomaviruses (HPVs) which infect keratinocytes. Warts are the most common viral infection of the skin, affecting 7-10% of the general population (1). Plantar warts appear on the sole of the foot and typically resemble a cauliflower, with tiny black petechiae in the center. Pinpoint bleeding may occur when these are scratched. Plantar warts may be painful when standing or walking (2).

Ubiquitous in our environment, asymptomatic infection with HPV occurs frequently, with most infections controlled or cleared by cellular and humoral immune responses. However, certain populations have been observed to manifest plantar warts at higher rates compared with the general population, placing them at increased risk for wart-induced pain and complications (3,4).

Plantar warts exhibit an annual incidence of 14%. The majority of cases occur in children and adolescents (5). However, other populations, such as immunocompromised patients, are at increased risk for acquiring plantar warts, which can lead to pain, embarrassment, and, in rare cases, cancer (6,7).

Causes of Plantar Warts

The cause of plantar warts, HPV, is not a single virus but rather a group of nonenveloped DNA viruses that are categorized into more than 150 types according to similarities within their DNA sequences. These types are then further classified into species. Species are categorized into 1 of 5 genera, including α , β , γ , μ , and ν . The species of HPV can also be broadly categorized according to whether they preferentially cause cutaneous or mucosal lesions or both (8,9).

The types of HPV that have been isolated from plantar warts include HPV-1, -2, -3, -4, -27, -29, -57, -60, -63, -65, -66, and -69. In one randomized controlled trial, 88% of plantar warts were caused by HPV-1, -2, -27, or -57. Most plantar warts are attributed to HPV-1, however, the most plantar wart-causing HPV types belong to the categories of cutaneous or mucosal/cutaneous lesions, and there are rare instances, such as in immunocompromised persons, in which a mucosal HPV type can cause cutaneous lesions, including plantar warts. Human papillomavirus is species specific to human hosts, and humans are the primary reservoir of the virus. The virus is transmitted via contact with HPV particles (10,11).

Human papilloma virus can stay a live months to years on surfaces without a host. Infection can occur via direct contact, autoinoculation, or indirect contact with fomites, towels, socks, shoes, flooring, and sports equipment (12). There is no systemic dissemination of HPV infection. So, the contact with body fluids, except those from the wart itself, does not transmit HPV (13).

Pre-existent microtrauma or abrasion of the epidermal barrier permits entry of the virus on contact (14). The cellular differentiation strategy of the host cell affects the HPV's life cycle. The virus invades epithelial basal cells with the capacity to differentiate (15). When the basal cell divides, a new basal cell forms along with a daughter cell that separates from the basement membrane and begins to differentiate (Fig. 1). The daughter cells leave the cell cycle, alter their gene expression pattern, go through terminal differentiation, and eventually desquamate from the epithelium (16).

The amount of viral particles varies depending on the lesion's type and rate of growth. Plantar warts contain a larger viral load than common warts, while younger warts have a higher viral load compared to older warts. The center of the lesion is the main site of viral concentration (12).

The factors that influence rate of clearance are viral type, host immune status, extent and duration of warts (4). About 70% of HPV infections naturally disappear after a year and 90% in two years, whereas the remaining 20% develop HPV persistence (10).

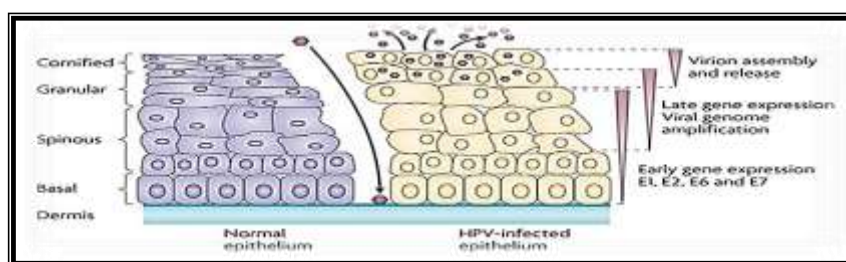


Figure (1): Life Cycle of Human Papillomaviruses (16).

In the development of the viral infection, the viral capsid is crucial. The proteinaceous coat of non-enveloped viruses, such as HPVs, encloses and shields the viral nucleic acid and serves as the virus's first point of contact (17).

Viral binding to epithelial cells appears to depend on the L1 and cell surface heparan sulphate. The early HPV genes E1 and E2 facilitate viral DNA segregation and replication, allowing infected cells to remain in the lesion for an extended length of time. As High-level amplification of the viral genome occurs when infected daughter cells move toward the epithelial surface and create viral late gene products to start the vegetative phase of the HPV life cycle (14).

The epithelium's granular layer and the layers above show signs of viral particles. The virus is thought to be shed together with the cornified layer (9). In addition, E6 functions

upregulate telomerase activity and downregulate immunological response, epithelial differentiation, cell proliferation, and survival signalling pathways (12).

When E7 attaches to pRb, pRb is degraded, functionally rendered inactive, and cells are propelled towards the S-phase. Additionally, E7 increases chromosomal defects and genomic instability (18). A significant number of cellular proteins necessary for DNA replication, including DNA polymerase and thymidine kinase, are then transactivated by E2 (12). Through the inactivation of E2 expression, the primary inhibitor of E6 and E7, and the disruption of host genes as a result of the viral sequence insertion, HPV integration can also promote the development of cancer (11).

The regulation of E6 and E7 is handled differently in the LR HPV strains. The impacts on p53 and Rb are handled differently, and it is not obvious how much each contributes to immune evasion. Except in cases of persistently dysregulated viral gene expression, LR HPVs very infrequently result in neoplasia and malignancy (19).

Plantar Warts Types

The usual appearance of a plantar wart is that of a strongly defined, spherical lesion with a rough, keratotic surface encircled by a smooth collar of thickened horn. A plantar wart first appears as a small, shiny "sago-grain" papule. Plantar warts are visible as rough, thick, brown or yellow growths with black pinpoint centres, which are the microscopic thrombosed capillaries that provide the growth with blood (18).

Similar in structure to an iceberg, a plantar wart typically has a component under the skin that is at least twice as large as the area that is visible on the skin. Plantar warts can expand into clusters and become mosaic warts if they are not treated, growing up to two inches in circumference (20).

The abrupt separation between the wart tissue and the protective horny ring becomes more visible if the surface is gently pared with a scalpel. Small bleeding points at the tips of the elongated dermal papillae become visible if the paring is sustained (16).

A typical but variable symptom is pain. Many warts are only found during routine inspections and can range from severe and disabling to missing. Mosaic warts are frequently painless, while myrmecia, which appear on the bottom of the foot, are typically painful (11).

They are seen in three different manifestations (**Fig. 2**): exophytic (mosaic), myrmecia, and endophytic (21).

Endophytic plantar warts often take the form of a circumscribed keratinous plaque with a central depression and a thick, whitish keratinous ring with slightly sloping borders and a black, pointed core area (thrombosed capillaries). Typically, they are sharp, intense, and painful (21,22).

Myrmecia or inclusion wart is the deep variant that resembles an anthill. Myrmecia warts feature huge inclusions that have been mostly associated with HPV-1 and seldom with HPV-2 or HPV-60 virologically. Myrmecia warts can appear on the sides and tips of toes in addition to the palms and soles (23).

Exophytic plantar verrucae is a large plaques combine in a tile-like pattern to create mosaic plantar verrucae. They are superficial and are typically found on the heels. They are typically brought on by HPV 2 and either don't hurt or hurt just a little (24).

Epidermodysplasia Verruciform (EV) (Levan-dowsky-Lutz) is an uncommon autosomal recessive genetic disorder. Extensive beta HPV replication is caused by the classic, inherited type EV (IEV), which first appears in childhood or adolescence and is caused by Trans Membrane Channel (TMC) - 6 and 7 (EVER-1 and 2) gene mutations (75%) (25).

In the immunocompromised host, acquired-type EV (AEV) is a non-hereditary clinical entity of EV (26). AEV can start at any age as a result of an "exogenous" cause of T-cell ID, such as immunosuppressive medications, cancer, or HIV infection (27).

On the face and neck, EV are flat, scaly, reddish hypo- and hyperpigmented macules that are indistinguishable from plane warts; however, on the trunk and limbs, they tend to be larger and come in two primary types: Hypo- and hyperpigmented lesions resembling pityriasis versicolor or seborrheic keratosis (24).



Figure (2): Types of Plantar Warts; (a) Endophytic plantar wart,(b) Myrmecia or inclusion wart, and (c) Mosaic (Exophytic) plantar warts (21).

Differential Diagnosis

It's important to distinguish plantar warts from calluses and neurovascular corns. The hyperkeratotic callus and corn are waxy, yellowish, ill-defined thickenings that are typically observed over areas of intense friction or pressure. Tenderness is triggered in the bony prominences beneath them rather than in the lesion itself. Since they don't contain any blood vessels, they don't bleed when cut. The characteristic appearance of structureless white-yellow patches and numerous small linear brown to red spots and streaks (splinter haemorrhages) on dermoscopy can also aid to distinguish a plantar wart from a corn or a callosity (28).

Rarely can plantar warts mistaken for the discrete horny papules of punctate hereditary palmoplantar keratoderma, which occur in irregular clusters during adolescence or early adulthood and are frequently greatest in pressure points (29).

Verrucous carcinoma of the foot is a rare, locally invasive, well-differentiated low-grade squamous cell carcinoma that may develop from the human papilloma virus, making it vital to distinguish VC from plantar wart. Clinically, a straightforward 3 mm punch biopsy should be performed when soft tissue lesions are difficult to distinguish to avoid harmful destructive pedal events (18).

Dermoscopy

Dermoscopy is an easy, quick, non-invasive, yet, precise diagnostic method for identifying surface and subsurface morphological traits that are not visible to the naked eye. Therefore, it can be viewed as a link between a clinical examination and a histological evaluation (30).

Plantar warts are characterized by the presence of verrucous, yellowish papilliform surface with multiple irregularly distributed red - brown to black dots or linear streaks due to hemorrhages. Skin lines are typically interrupted in plantar warts (Fig. 3). Furthermore, different dermoscopic patterns can occur in a single wart (31).

Plantar Warts can occasionally be difficult to distinguish from calluses and corns however dermoscopy can differentiate between them (Table 1) (32).

Different kinds of cutaneous warts share some common features under Dermoscopy, such as papillomatous growth, dotted vessels, linear vessels, bleeding; however, flat warts differ in background colors (18,33).

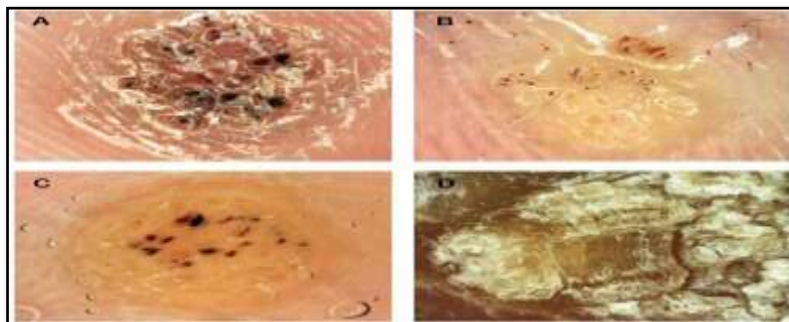


Figure (3): Different patterns of plantar warts under the dermoscope. (A) frogspawn pattern. (B) scaly yellowish structureless with bleeding streaks and spots, (C) yellow-gray structureless with bleeding streaks and spots, (D) raised papilliform scaly yellowish wart (31).

TABLE 1: Dermoscopic differentiation of warts, corns, and calluses (30).

Variables	Wart	Corn	Callus
Homogenous black/red dots	Present	No	No
Papilliform surface	Present	No	No
Interrupted skin lines	Present	No	No
Translucent central core	No	Present	No
Homogenous opacity	No	No	Present

Dermoscopy of corn revealed a yellow region, a whitish annular ring, and a translucent central core. Dermatoglyphics had been preserved. There were no red dots or a yellow or white halo (31).

Callus, under dermoscopy, demonstrated a prominent opaque yellow area with preservation of dermatoglyphics. Focal white areas were found. Unlike plantar warts, vascular elements were absent (33).

Summary and Conclusion

Planter warts are caused by human papillomaviruses (HPVs) which infect keratinocytes. Because all currently available plantar wart management modalities address the lesion itself, none adequately manage the risk of transmission, which is intrinsic to the pathophysiologic mechanism by which the plantar wart develops and sheds viral particles. Dermoscopy can improve the accuracy of diagnosing different types of clinically nonclassical cutaneous warts, as well as help in distinguishing them from other similar skin lesions.

No Conflict of interest.

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