

Case Report

A case of extensive verrucosis in 45-year-old women and CD4 lymphopenia treated with electrodesiccation using general anesthesia and isoprinosine

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Abstract

The human papilloma virus (HPV) is a viral infection that has a broad variety of clinical manifestation. The clinical manifestation really depends on the type of HPV virus and the immunity status of the host, particularly the cell-mediated immunity. Extensive verrucosis is one of the significant clinical manifestation of a disseminated HPV infection that is related with a severe immunodeficiency status. Electrodesiccation or laser surgery is a method of treatment that could directly destroy the lesion in one time. We described a case of a 45 years-old woman with extensive verrucosis. The patient complained multiple warts lesion on the hands, face, neck, lower arms and lower extremities since eight years ago. Physical examination revealed on the dorsum and palmar hands, both of finger nails (I, II, III, and IV), face (forehead and cheeks), anterior of neck, lower arms and 2/3 distal of lower extremities part anterior, there were single and groups of flesh coloured papules and flesh coloured plaques, skin colour papules with flat topped, greyish papules and greyish plaques with verrucous surfaces and brownish crusts. The CD4 count of the patient was 91 cells/ μ L. Skin biopsy and histopathology examinations showed hyperkeratosis, papillomatosis, and acanthosis with vacuole cell (koilocytes). The patient was treated with electrodesiccation using general anaesthesia and isoprinosine 3x500 mg. The result after two weeks post-treatment showed that there were no new lesions appeared on post electro surgery site. This case highlights the importance of the treatment for the success of extensive verrucosis with CD4 lymphopenia.

Keywords: HPV, extensive verrucosis, CD4, lymphopenia, laser surgery

Introduction

Extensive verrucosis is characterized as a progressive cutaneous of the human papilloma virus (HPV) infection with a clinical manifestation of an appearance of more than 20 lesions in the body, usually even hundreds to thousands of lesions. The distribution of the lesions is generally in more than one region of the body, if it's limited then it would be in the acral distribution, involving the digits or altering the daily living of the patient. Histopathological examination of extensive verrucosis revealed the thickening of the stratum corneum (hyperkeratosis), papillary dermal hyperplasia and koilocytosis. Extensive verrucosis includes inherited genetic diseases like epidermodysplasia verruciformis, congenital immunodeficiency syndrome such as WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis), idiopathic CD4 lymphocytopenia, GATA2 deficiency, X-linked immunodeficiency with hyper-immunoglobulin M, Wiskott-Aldrich syndrome and the acquired immunodeficiency disease such as HIV/AIDS (Cheng et al., 2021; Sri et al., 2012; Starling, 2010).

Assessment for underlying disease is crucial at the time the initial examination of the extensive verrucosis patient is made. The patients with an immunodeficiency status (HIV/AIDS or any immunosuppression diseases that are related with organ transplantation) or hereditary diseases such as epidermodysplasia verruciformis is

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usually found with extensive verrucosis (Kirnbauer et al., 2008; Starling, 2010). Extensive verrucosis could manifest as verrucous papules and plaques that spread all over the body. When the first lesion begins to appear, relatively 78% of the lesions usually would regress spontaneously in two years in healthy individuals. However, most of the lesions tend to spread to other parts of the body and persist for several years (Leerunyakul et al., 2022; Satolli et al., 2019).

The treatment of warts depends on size and distribution of lesions, duration since the lesions first appeared, the scale of physical and emotional discomfort, the immunity status and the patient's willingness to receive the therapy. The treatment includes topical therapy such as 5-fluorouracil, cidofovir, bleomycin, cautery, cryotherapy, curettage, granulocyte-macrophage colony stimulating factor (GM-CSF), imiquimod, interferon, laser therapy, and surgical excision. In addition, systemic therapy such as cidofovir, interferon and radiation therapy are also available. Topical therapy could be used as a series for localized treatment in the body (Androphy and Lowy, 2008; Sri et al., 2012). This case study we describe described a case of extensive verrucosis in a 45 years-old woman with CD4 lymphopenia.

Case

A 45-years old woman presented with asymptomatic lesion, warty lesions on hands, face, neck, lower arms, and legs since eight years ago. Some of the warts were flesh-coloured, some had greyish coloured and smooth surfaces, while the other warts were rough, raised and had irregular surfaces. The wart lesions were spread out solitarily or in group and never ever healed completely. The patient admitted that there were no other skin diseases on the affected area before the lesion appeared and no history of a long term medications (such as allergy, chemotherapy or other chronic diseases). No history of a significant weight gain in a short time since the disease started, no history of recurrent upper respiratory infection such as cough for a long time and no complaint of gastrointestinal disease such as diarrhoea. There was also no lesion on genitalia or mouth or other parts of the body and no history of recurrent skin disease of the mouth such as sprue. There was no history of organ transplantation or blood transfusion. There were no family members or friends that had suffered from the same disease or warts. Physical examination for general state was within normal range. Cutaneous examination revealed multiple, extensive, solitary and confluent skin-coloured verrucous papules on both hands, face, neck, lower arms, and legs.

Blood examination results were in normal range. CD4 and CD8 examinations showed that CD4 absolute: 91 cells/ μ L (normal ranges 410-1590 cells/ μ L), CD4%: 5% (31-60%) suggesting decreased T-helper lymphocytes. CD8 absolute: 209 cells/ μ L (190-1140 cells/ μ L), CD8%: 11% (11-41%) suggesting normal lymphocyte T-suppressor. CD4/CD8 ratio was 0.44 (0.9-2.3). HIV rapid test was negative and Internal Medicine Department's consultation affirmed that there was no evidence of an opportunistic infection.



Figure 1. Multiple warts located on both hands of the patient

Histopathological examination of skin biopsy demonstrated basket weave hyperkeratosis, papillomatosis, acanthosis with vacuole cell (koilocytes). There was thickness of granulosum layer and fibro collagen with mild lymphocytes perivascular. Based on the anamnesis, physical examination, laboratory tests and histopathological examination the patient was diagnosed with verrucae vulgaris, verrucae plana and verrucae periungual. The patient was treated with electrosurgery (electrodessication and curettage using general anaesthesia) and isoprinosine 3x500 mg.

After 2 weeks of treatment there was an improvement. It was planned treat the patient using a serial electrosurgery (electrodessication and curettage) using local anesthesia and isoprinosine tab 3x500 mg.

Discussion

We reported a 45-year-old woman presented with extensive verrucosis (verrucae vulgaris, verrucae plana and verrucae periungual) with CD4 lymphocytopenia. The patient was diagnosed based on anamnesis, physical examination, laboratory finding and histopathological examination. The patient was treated with electrosurgery (electrodessication and curettage) using general anaesthesia. Extensive verrucosis is one of the significant clinical manifestation of a disseminated HPV infection that is related with a severe immunodeficiency status (Reid et al., 1976; Sri et al., 2012). However, different of diseases are associated with extensive verrucosis (Table 1). In our case, extensive verrucosis seemed to be associated with low CD4 count which was only 91 cells/ μ L since no abnormality from physical examinations and other laboratory tests.

Table 1. Diseases that are related with generalized verrucosis (Henrickson, 2020; Sri et al., 2012)

Diseases	Characteristics	Immune defect	Gene defect
Epidermodysplasia verruciformis	Several flat warts or lesions similar to tinea versicolor warts, tends to be malignant Location: trunk, neck, and extremities	Cell-mediated immunity defect	EVER1, EVER2 (transmembrane channel-like gene family)
WHIM Syndrome	A syndrome with hypogammaglobulinemia and neutropenia. The patient tends to be vulnerable to warts and bacterial infections	CXCR4 (chemokine receptor)	Unknown
GATA2 Deficiency	GATA2 is an important transcription factor in hematopoiesis.	Monocytopenia, decreased CD4, decreased NK	GATA2 gene mutation
X-linked immunodeficiency with hyper-immunoglobulin M	A disease that's characterized by a disorder of abnormal T cell and B cell function	Decreased IgG, IgA, and IgE Increased IgM	CD40 ligand gene
Wiskott-Aldrich syndrome	A syndrome that's characterized by immune deficiency, eczema and could potentially damage the ability to form blood clot	Reduced B and T cells Decreased NK	WAS/WASp
HIV	Vulnerable to opportunistic infections	Decreased CD4 None	NA
Idiopathic CD4 T lymphocytopenia	Vulnerable to opportunistic infections	Decreased CD4 but no HIV detected	Unknown

Some case reports of extensive verrucosis have been published previously with different underlying diseases and treatments. Alisjahbana et al. (2010) reported a 39-year-old man with extensive verrucosis associated with a HPV2 infection, pulmonary infection and hepatitis B infection. Laboratory result was a chronic CD4 lymphocytopenia (CD4 cell count 314 cells/ μ L). The treatment included a series of surgical procedure and 40% of salicylic acid lotion to inhibit the growing of massive hyperkeratosis. The intravenous cidofovir's also used for the therapy (300 mg per infusion in normal saline solution), but the renal function of the patient was deteriorated and therefore it was stopped after two intravenous infusions in one month period. Surgical procedure was used to treat the remaining warts (Alisjahbana et al., 2010). Antoniali et al. (2021) reported a 12-year-old boy presented with multiple cutaneous warts that's resistant to conventional treatments. The patient admitted that the warts first appeared on the hands, knees and foot at the age of four years old. At that time, the treatment with cryotherapy and electrocauterization were unsuccessful. The patient was also diagnosed with myelodysplastic syndrome (MDS) when turned 11 years old and the mother was also diagnosed with MDS when was 30 years old. MDS was known as a disease related to GATA2 mutation that's caused monocytopenia, bone marrow failure and immunodeficiency. Because the lesions were extensive, the systemic treatment consisted of 10 mg acitretin daily and topical 60% trichloroacetic acid (TCA) twice a week were used. In three months, the lesions were resolved and the therapy was stopped. There was no recurrence of warts over one year of follow up (Antoniali et al., 2021).

A case report reported 42-year-old Caucasian man a more than 20 years history of an intractable, extensive verrucae associated with HPV-57 (Marquart et al., 2006). The past treatments that were ineffective included electrocautery, topical salicylic acid 17%, topical cantharidin 0.7%, topical fluorouracil 5% and intralesional bleomycin. The improvement was shown when the patient's treated with etretinate (Marquart et al., 2006). Another case report reported a 31-years-old Caucasian man with idiopathic CD4 T lymphocytopenia (ICL), lymphocytopenia of 250/ μ L, that's associated with numerous warts on the face, head and hands of eight years responding to interferon alfa (Fischer et al., 2008). The patient was unsuccessfully treated with 5% topical imiquimod and interferon gamma-1b. Later, the patient was treated with interferon alfa-2b, 5 MU three times a week and reduced to 4 MU once a week and there was a significant regression of the warts yet there was no significant changes in T-cell subsets (Fischer et al., 2008). Other case-reports also have been published with different underlying diseases and treatments (Berth-Jones and Hutchinson, 1992; Fernandes et al., 2019; Kosumi et al., 2020; Paul et al., 2017; Sri et al., 2012; Yarmohammadi and Cunningham-Rundles, 2005).

Our patient had CD4+ lymphocytopenia with non-specific cause. Idiopathic CD4+ T cell lymphocytopenia (ICL) is a syndrome that was first established as a disease in 1992 by the Centers for Disease Control (CDC). The criteria of ICL are the decreased numbers of circulating T lymphocytes (fewer than 300 cells/ μ L or less 20% of peripheral lymphocytes) on more than one laboratory check up, no evidence of HIV infection, no history of other immunodeficiency or immunosuppressive medications and no immunity defect ever since the individual was born. This disease always linked to low CD4+ T cells but low CD8+ T cell counts were also reported in some ICL cases (Campos et al., 2020). The primary causes and pathogenesis of ICL are still remain poorly understood (Campos et al., 2020).

Viral warts have been reported in ICL in a rare case. The polymerase chain reaction (PCR) could be used to detect the evidence of HPV infection, including novel types. HPV DNA is often presented in an extremely low level in normal skin and hairs follicles of immunocompetent individuals. In this case we did not find the source of infection.

We were unable to determine the exact cause of lymphopenia, but there was a possibility to suspect an idiopathic CD4 T lymphopenia. WHO criteria on idiopathic CD4 T lymphopenia are (1) absolute CD4 T-cell level 300 cells/ μ L or 20% in more than on at least two laboratory tests; (2) no evidence of HIV infection (including HIV serology and PCR); (3) no history of any defined immunodeficiency disorder or therapy associated with T-cell depletion; and (4) no immunity defect since the individual was born. Re-examination for complete blood cells count, CD4 and CD8 count, serum protein electrophoresis and HIV rapid plasma three months later.

The treatment of extensive verrucosis and CD4 lymphopenia was more difficult and it has a high chance for recurrence in the future. Combination therapy, especially with electrosurgery with immunotherapies such as cidofovir or interferon will provide higher clearance rate. However, the drug is difficult to obtain and rather expensive, which was also a limitation of the treatment for this patient. There was also no standard therapy for ICL, except for the management of the associated conditions, in this case the generalized warts. We treated the patient with isoprinosine 3x500 mg and a serial of electrosurgery (electrodessication and curettage) using general anesthesia. In two weeks post-treatment, there was an improvement.

Conclusion

We reported an extensive verrucosis patient with decreased T-helper lymphocytes. We were unable to determine the exact cause of lymphopenia, but there was a possibility to suspect an idiopathic CD4 T lymphopenia. The patient was treated with electrosurgery using general anesthesia with isoprinosine resulting improvement after two weeks post-treatment. Due to inconclusive result, re-evaluation of underlying disease associated with lymphopenia are planned.

Authors' contributions

Conceptualization: WL; Data Curation: SL; Formal Analysis: WL and SL; Investigation: WL; Project Administration: WL; Supervision: SL; Validation: WL and SL; Writing – Original Draft Preparation: WL; Writing – Review & Editing: WL and SL.

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Conflict of interest

There are no competing interests that exist.

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