Case Reports in Dermatology

Case Rep Dermatol 2011;3:175–180
DOI: 10.1159/000331427

Published online:
August 26, 2011

ISSN 1662–6567
www.karger.com/cde

Complete Healing of a Giant Wart in a Severely Immune-Compromised Patient with HIV Infection Treated with Acupuncture

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Key Words
HIV · Papillomavirus giant warts · Acupuncture

Abstract
Giant warts are infrequent dermatological viral infections caused by Papillomavirus (HPV) in immune-compromised patients. Treatment may often be difficult and unsatisfactory, either by surgery or cytotoxic agents, because of poor immune control of viral activity in such hosts. Here we report on the case of a patient with advanced and persistent immune suppression caused by HIV disease, who developed a monstrous wart covering the entirety of the radial district of his right hand. He was completely healed after a long treatment with traditional Chinese acupuncture, in spite of minimal immune recovery induced by efficacious antiretroviral therapy. To the best of our knowledge, therefore, the present report may be the first direct clinical evidence that acupuncture may be effective in the treatment of cutaneous warts also in HIV-infected patients.

Introduction

Human papillomavirus (HPV) infections manifest as both cutaneous and anogenital diseases in HIV-infected patients [1, 2], with a variety of skin lesions, both benign and malignant, including common warts, epidermodysplasia verruciformis-like lesions, non-melanoma skin cancers, and the giant condyloma of Buschke and Löwenstein (GCBL) [1]. The prevalence of HPV infections is significantly increased in HIV-infected patients, and unusual HPV types are frequently detected in this population [1, 3, 4]. Warts are often

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larger (giant wart), more numerous, more aggressive and more recalcitrant to therapy than those presenting in HIV-uninfected patients [1]. They represent a formidable therapeutic challenge, as treatment by either surgery or cytotoxic agents may be difficult and unsatisfactory because of poor immune control of viral activity in these patients [5–8]. The use of traditional Chinese acupuncture has been reported in the general population for the treatment of several kinds of skin lesions, including warts, with variable success rates, although the precise mechanism of action has not been elucidated [9, 10]. As far as we know, this approach has never been reported for the treatment of warts in the context of HIV infection.

Here we report on the case of a patient with advanced immune suppression caused by long-lasting HIV disease, who developed a monstrous wart covering the entirety of the radial district of his right hand. He was treated with an acupuncture-based approach for approximately 19 months, reaching complete healing of the lesions in spite of minimal immune recovery by antiretroviral therapy for HIV infection during the same period.

Case Report

A 37-year-old male drug addict was diagnosed with HIV and HCV infections in 1996; antiretroviral therapy was started in 1997, when his CD4 T-cell counts were 236 cells/mm^3 and his viral load was 23,104 copies/ml. His adherence to antiretrovirals was suboptimal until 2005. He carried on a dual therapy with Zidovudine and Didanosine at standard doses until 1998, when he started his first Highly Active Antiretroviral Therapy (HAART) regimen including Stavudine, Lamivudine, Nevirapine and Nelfinavir. He remained with persistently low CD4 T-lymphocytes under different sequential HAART regimens. In June 2006, he was hospitalized in our ward due to seizures, dermatological diffuse lesions involving his face and neck, caused by *Microsporum gypseum*, and a giant wart on his right hand. He was first treated with i.v. liposomal Amphotericine B for his mycosis. He developed nephrotic syndrome with secondary anemia, which resolved after interruption of Amphotericine B. His CD4 T-cell counts were 72 cells/mm^3, HIV-RNA was 351,000 copies/ml. A salvage HAART regimen including Enfuvirtide, Tenofovir, Zidovudine, Lamivudine and Tipranavir/r was started, based on his Genotype Resistance Testing (GRT; RT: M41L, E44D, T67N, Y181C, L210V, T215Y; Pr: M36I, M46I, L90M, L10I, K20I, A71V, L63P), yielding incomplete viro-immunonological improvement; his diffuse dermatophytosis resolved after successful treatment with i.v. Itraconazole.

The giant wart appeared a couple of years in advance of his hospitalization on his right hand. At the time of hospitalization for seizures, it had slowly and progressively covered the entire surface of the radial district of his right hand (**fig. 1**). Bleeding had been frequent in recent months, even caused by minimal traumas, and the patient felt this condition to be troubling and quite disabling. Approximately 6 months in advance of hospitalization, cryotherapy had failed to reduce the extension of the lesion; a radical surgical approach was discarded by our consultant dermatologist because of persistent immune suppression by HIV. When CD4 T-cell counts were 120 cells/mm^3, a treatment based on traditional Chinese acupuncture was attempted, lasting for 19 months through 58 treatment sessions. For the first 2 months, these were delivered twice weekly; in the following 4 months, they were weekly and in the remaining 13 months, the patient was treated once every 2 weeks. Each treatment session lasted approximately 30 min. According to the therapeutic principles of traditional Chinese medicine, needles were set at the auricle of the left ear, on the abdomen and the upper and lower limbs (**table 1**); further needles were placed at the roots of major wart elements (**fig. 2**). At the end of treatment, the surface of the right hand was completely healed, with only minimal dyschromic spots remaining over a smooth and fresh skin surface. CD4 T-cell count at the end of treatment was 180 cells/mm^3 (**fig. 3**).

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Discussion

Giant manifestations are rare but well-recognized clinical expressions of human papillomaviruses. The GCBL, described by Buschke and Löwenstein in 1925, is a slow-growing verrucous lesion affecting the penis and other districts of the anogenital region [11, 12]. The viral origin of these tumors led to the use of local or systemic interferon with moderate success, intralesional administration producing complete responses in a remarkable proportion of cases. The treatment of choice for GCBL and other giant lesions, however, is wide surgical excision, resulting in disease cure in almost half of patients [13–15]. Oral and topical chemotherapeutic agents were also used with variable success, as well as topical cidofovir in cases refractory to other conventional treatments [11, 12, 16, 17].

It is well known that subjects with persistent cell-mediated immune defects, including those with HIV infection, are at increased risk of persistence of both infection with and disease caused by Papillomaviruses, but the specific mechanisms whereby HIV-infected subjects develop severe cutaneous warts, including giant lesions, remain unknown [18]. Different explanations have been proposed [1]: first of all, a HIV-mediated direct or local role in HPV transcription, as well as an impaired HPV antigen presentation by depleted cutaneous Langerhans cells in HIV-infected patients [19, 20]. Furthermore, HIV-induced immune deficiency may alter the cellular immunity normally required to control HPV replication [1]. Recent studies focused on the different roles played by humoral and cell-mediated immunity [18, 21]. Humoral immunity to the viral capsid of HPV has been shown to be sufficient for the protection against infection, while innate and adaptive cell-mediated immunity appear important for the eradication of HPV [18]. Therefore, cell mediated immunity impairment caused by HIV may have a pivotal role in causing the spreading and difficult eradication of the wart, especially in its giant variants [18]. In the present case, the development of a monstrous wart covering the entirety of the radial district of the patient's hand, a very different district in comparison with classical GCBL, took place while CD4 T-cell counts were persistently low and unresponsive to HAART.

Our patient, with poor clinical and immune status (CD4 T-cells persistently <200 cells/mm^3), was ineffectively treated with cryotherapy; this approach was indeed discontinued after a few sessions, in the evidence of inter-session overgrowth; similarly, invasive surgery was a priori considered inappropriate because of the size and site of his lesions. As a consequence, acupuncture was elected for a further trial, to help our patient with his serious disability, as a plausible alternative to other chemical or pharmacological methods for second-line treatment. Acupuncture appeared attractive at the time of its choice because of its potentially immune-modulating action. A number of clinical studies indicate its potential role in the treatment of immune-related diseases, including allergic disorders, and infections [22]. In our patient, however, the minimal residual T-cell resources seemed unlikely to support a prompt response at the extensive site of the lesions. Unexpectedly, acupuncture turned out to be slowly but completely efficacious, leaving a healthy skin surface in the end. To the best of our knowledge, therefore, the present report may be the first direct clinical evidence that acupuncture may be effective in the treatment of cutaneous warts also in HIV-infected patients, even in the extreme expression of giant warts in patients with severe immune depletion [10].

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Acknowledgements

We are indebted to Mr. Vincenzo Massei, Mrs. Loredana Puglielli and Angela Pisciella for their invaluable contribution in the clinical management of the patient.

Disclosure Statement

None of the authors has any conflict of interest to declare. T.U. and E.P. were funded by a grant from the Fondazione Camillo de Lellis per l'Innovazione e la Ricerca in Medicina, Pescara, Italy.

Table 1. Relevant ear and body acupoints used in patient

Acupoints		Indications according to traditional Chinese medicine
Ear acupoints	Ear Shenmen	Mental disorders, insomnia, pain
	Kidney	Asthenia, immune deficits
	Liver	Acute and chronic liver diseases, skin diseases
	Fingers (right ear)	Pain and dysfunction at corresponding areas of the hand, skin diseases of the hand
Body acupoints	CV12 – Zhong Wan	Pain, epigastric pain, abdominal distension, nausea, vomiting, insomnia
	CV10 – Xia Wan	Abdominal pain, borborygma, diarrhea
	CV6 – Qi Hai	Abdominal pain, diarrhea, oedema
	CV4 – Guan Yuan	Immune deficits, mental disorders
	PC6 – Nei Guan	Hand affections, mental disorders, febrile diseases, nausea, vomiting
	ST36 – Zu San Li	Epigastric pain, abdominal distension, nausea, vomiting, immune deficits
	LR3 – Tai Chong	Pain, itching, psychosomatic symptoms such as stress and restlessness, muscular tension

Fig. 1. Giant wart covering the radial district of the patient's right hand.

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Fig. 2. Needles placed in the wart elements at the patient's hand.

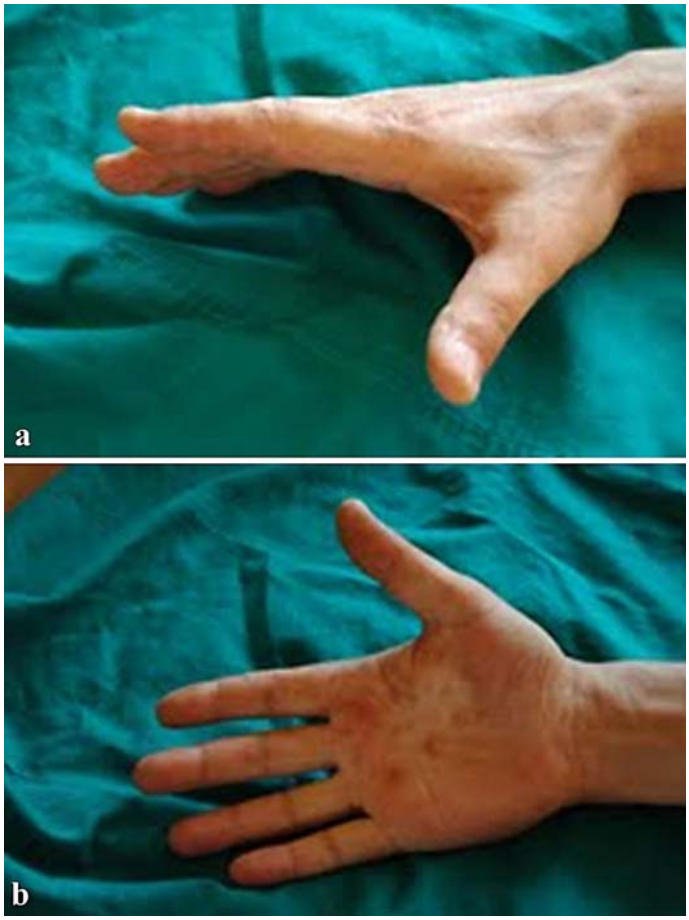

Fig. 3. **a** Patient's hand back at the end of treatment. **b** Patient's hand palm at the end of treatment.

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