SKIN

BRIEF ARTICLE

Atypical Human Papillomavirus Infection with Secondary Tinea in a Middle-Aged Caucasian Male

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ABSTRACT

We present a case of an atypical diffuse cutaneous eruption due to HPV infection and Tinea in a 51-year-old male patient with a past medical history of mild cytopenia, vasectomy and difficult socio-economic situation. Differential diagnosis at initial visit included Epidermodysplasia Verruciformis vs Pityriasis Rubra Pilaris vs Secondary Syphilis vs Xanthoma Disseminatum vs atypical presentation of Tinea vs less likely other. Through clinical examination, repeat biopsy, tissue culture and extensive HPV testing, it was revealed that the patient had multiple HPV infections type FA52, 96, 16 and 13, with a possible secondary Tinea infection. The patient was treated with antifungal medications first. Topical Cidofovir was recommended but not covered by insurance. The skin eruption improved gradually highlighting the importance of additional samples, tissue culture and extensive HPV testing in such atypical cases. Our case describes the importance of multidisciplinary care to help patients with proper diagnostics and treatment regimens.

INTRODUCTION

Human papillomavirus (HPV) infection is considered as one of the most common sexually transmitted infection (STI) and is caused by a double stranded deoxyribonucleic acid (DNA) virus belonging to family *Papillomaviridae*.[1,2] In Immunocompromised patients, the HPV infection can be persistent which leads to the development of genital warts and even cancers.[3,4]

Tinea corporis is a superficial dermatophyte infection of the skin specially on the trunk and extremities except on the hands, feet, scalp, face and skin folds.[5] Herein we present a case of atypical diffuse cutaneous HPV infection in the setting of secondary Tinea infection.

CASE REPORT

A 51-year-old Caucasian male with a past medical history of mild cytopenia, vasectomy and difficult socio-economic situation presented with chronic diffuse skin eruption for more than 3 years. The skin eruption was present all over the trunk and extremities. He described it as itchy and worse in summer. During the physical exam, we noticed scaly and some waxy pink to tan colored papules

and annular plaques on his shoulders, back, abdomen, genitalia and mucosal lips. The patient had a previous biopsy of the eruption that showed psoriasiform and spongiotic dermatitis with prominent parakeratosis, alternating areas of hypergranulosis, hypogranulosis and superficial perivascular lympho-eosinophilic infiltrate. Periodic acid-Schiff (PAS) stain was negative. Prior treatment included Triamcinolone cream that cured the itch but did not clear the eruption. The differential diagnosis at initial visit included Epidermodysplasia Verruciformis vs Pityriasis Rubra Pilaris vs Secondary Syphilis vs Xanthoma Disseminatum vs atypical presentation of Tinea vs less likely other.

We first had the polymerase chain reaction (PCR)-based high-risk HPV test performed on the prior biopsy for HPV type 6,11,16,18,31,33,51 and it was negative. Two repeat biopsies were conducted which showed mild epidermal hyperplasia with alternating parakeratosis and orthokeratosis, and granules within the stratum corneum with many small oval yeast forms and moderate hyphal elements, and mild superficial mixed dermal inflammation with eosinophils.

Differential diagnosis then included an infectious process, particularly a superficial secondary fungal infection (due to Malassezia or dermatophyte species) with atypical granular parakeratosis (in view of atypical site of involvement). Tissue culture was done that showed the growth of yeast. He was also examined for possible HIV and Syphilis infection where the test results turned out to be negative.

The patient was started on Terbinafine 250 mg daily for 1 week along with Ketoconazole shampoo as a body wash. Adapalene was recommended to help if there was underlying atypical granular parakeratosis. Hematology as well as infectious disease were consulted. Per hematology, his pancytopenia was mild and not likely the cause of his skin eruption. Extensive work up with them was unremarkable for any blood cell dyscrasias and/or malignancies. Infectious disease subsequently treated the patient with Fluconazole 200 mg weekly for 16 weeks, then Itraconazole 200 mg twice daily for 10 days.

There was however minimal to no clinical improvement in his condition and additional extensive HPV PCR testing was suggested on the second set of biopsies. Subsequently, HPV typing by nested PCRs with FAP [6] and PGMY-GP+ [7] primer systems were utilized.

Putative HPV PCR product was detected by FAP primer system in the sample from the abdomen **(Figure 1A,i)**. Presumed HPV PCR bands were visible by PGMY-GP+ primer system in the samples from both the abdomen and the arm **(Figure 1A,ii)**. The putative HPV-PCR products were purified, cloned, and sequenced. The acquired sequencing results were evaluated by computer assisted analysis using NCBI-BLAST program.

In one of the samples from the second set of biopsies, multiple infections with HPV isolate FA52 (closest sequence homology of known HPV type is beta HPV 150) **(Figure 1B)**, HPV type 96 (beta papillomavirus) **(Figure 1C)**, HPV type 16 (alpha papillomavirus) **(Figure 1D),** and HPV type 13 (alpha, papillomavirus) **(Figure 1E)** were detected. In the other sample, infection with HPV type 16 (alpha papillomavirus) **(Figure 1F)** was identified.

Given these findings, we planned on treating the patient with topical Cidofovir. We also recommended he get the HPV vaccine with his primary health care provider. During this time, the patient noticed that his skin eruption was starting to resolve. At a follow up visit it

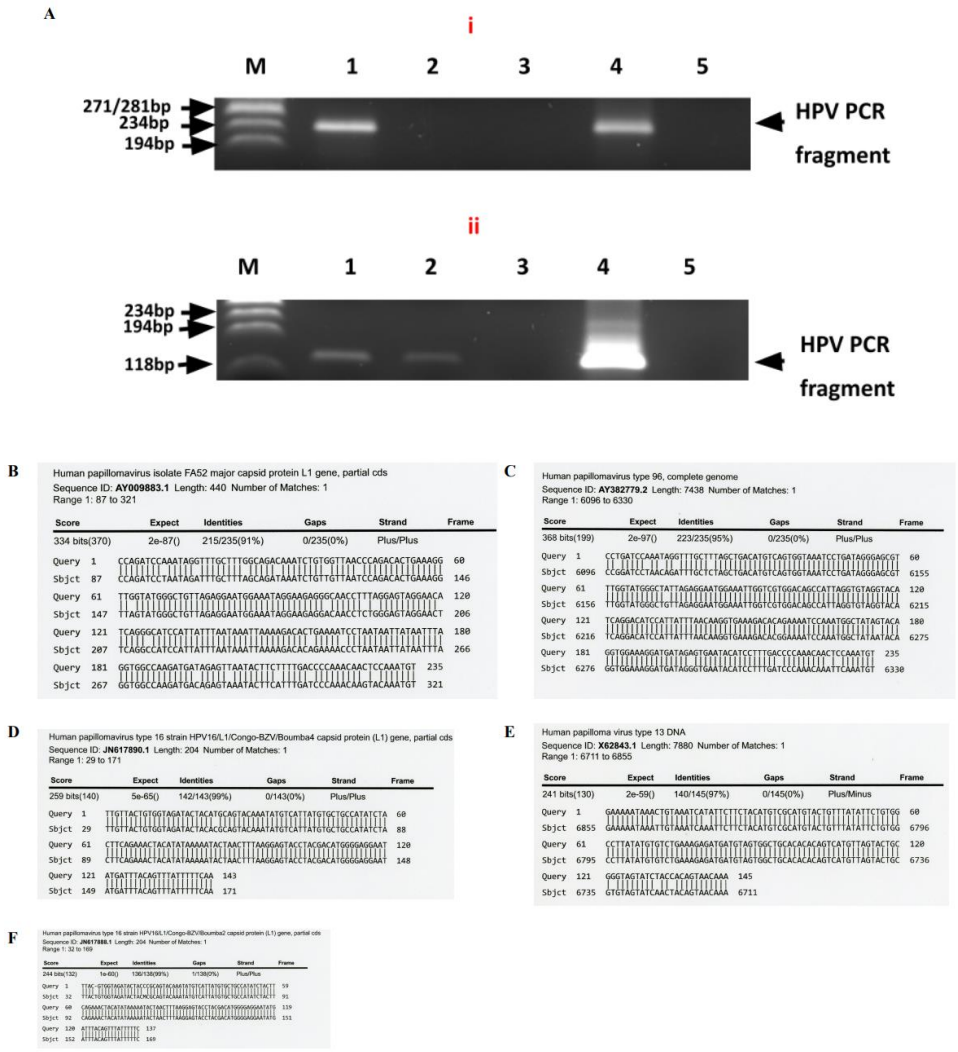
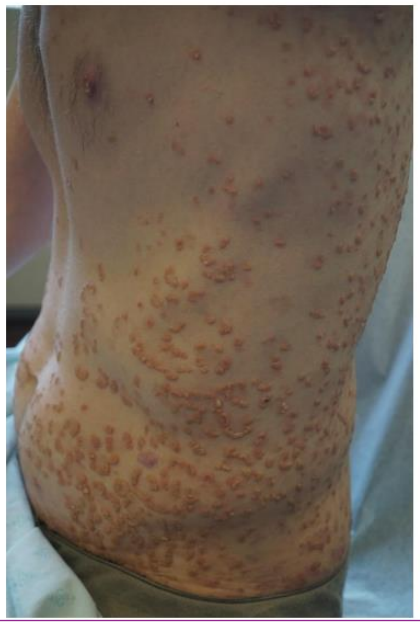


Figure 1. (**A**) i) HPV-PCR fragment obtained by FAP nested PCR system: Lanes M: fx174 RF DNA marker, 1: biopsy from abdomen, 2: biopsy from arm 3: Negative Control DNA, 4: Positive Control, cloned HPV type 5 DNA fragment, 5: Reagent Control ii) HPV-PCR fragments obtained by PGMY-GP+ nested PCR system: Lanes M: fx174 RF DNA marker, 1: biopsy from abdomen, 2: biopsy from arm 3: Negative Control DNA, 4: Positive Control SiHa DNA, 5: Reagent Control (**B**) NCBI-BLAST aligment of sequencing data acquired from the FAP HPV-PCR product (abdominal biopsy). The sequence data attained from clones #1 and #4-6 of patient's HPV PCR DNA fragment (query) showed 91% identities to the isolate HPV FA52 DNA deposited into the NCBI GeneBank (sbjct). (**C**) NCBI-BLAST aligment of sequencing data acquired from the FAP HPV-PCR product (abdominal biopsy). The sequence data attained from the clone #3 of patient's HPV PCR DNA fragment (query) showed 95% identities to the prototype HPV 96 DNA deposited into the NCBI GeneBank (sbjct). (**D**) NCBI-BLAST aligment of sequencing data acquired from the PGMY-GP+ HPV-PCR product (abdominal biopsy). The sequence data attained from the clones #1 , #3 and #4 of patient's HPV PCR DNA fragment (query) showed 99% identities to the HPV type 16 strain DNA deposited into the NCBI GeneBank (sbjct). (**E**) NCBI-BLAST aligment of sequencing data acquired from the PGMY-GP+ HPV-PCR product (abdominal biopsy). The sequence data attained from the clones #2, #5, and #6 of patient's HPV PCR DNA fragment (query) showed 97% identities to the HPV type 13 prototype DNA deposited into the NCBI GeneBank (sbjct). (**F**) NCBI-BLAST aligment of sequencing data acquired from the PGMY-GP+ HPV-PCR product (arm biopsy). The sequence data attained from the clones #1-6 of patient's HPV PCR DNA fragment (query) showed 99% identities to the HPV type 16 strain DNA deposited into the NCBI GeneBank (sbjct)



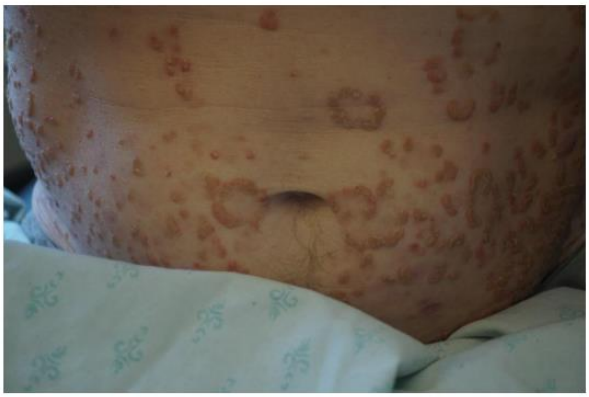


Figure 2. Scaly and some waxy pink to tan colored papules and annular plaques on the **(A)** lower back, flanks, and buttocks and the **(B)** abdomen

was about 70% improved with clear skin on the shoulders, upper back, mid back, and abdomen. Few residual spots were present on lower back, buttocks, and upper extremities. He was still using the ketoconazole shampoo as a wash.

Given the spontaneous resolution and difficulty obtaining topical Cidofovir, we decided to continue ketoconazole shampoo as a wash. A follow up phone call with the patient reported even more improvement in his skin condition.

DISCUSSION

The present case report is a unique case of rare HPV infection phenotype presenting as an atypical cutaneous presentation with possible secondary Tinea infection. It is difficult to explain the improvement in cutaneous eruption. One plausible explanation could be that the antifungals both topical and oral helped clear the secondary Tinea. The HPV was then cleared through him developing immunity.

The first biopsy did not show HPV or Tinea. The present case highlights the importance of additional samples, tissue culture and extensive HPV testing in such atypical cases. It also highlights the importance of multidisciplinary care to help patients with proper diagnostics and treatment regimens.

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