A case of Acquired Epidermodysplasia verruciformis in a renal transplant recipient clearing with multimodal treatment including Gardasil vaccination.

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Epidermodysplasia verruciformis (EV) is an uncommon autosomal recessive inherited skin condition (1) characterised by susceptibility to infection with beta genus of cutaneous human papillomaviruses (HPV), which are associated with an increased risk of malignant transformation into squamous cell carcinoma (2).

Acquired epidermodysplasia verruciformis (AEV) describes EV developing usually in immunocompromised patients such as organ transplant recipients (OTR) (2, 3). Reports of AEV in renal transplanted patients are rare with only a few cases described in the literature worldwide.

We describe a case of AEV occurring in a 50-year-old female renal transplant recipient and discuss her response to multimodal therapy including Gardasil (recombinant vaccine to HPV types 6, 11, 16, 18).

This patient was referred to our specialised transplant dermatology clinic in 2014 with a two-year history of numerous papules scattered bilaterally in the inguinal region (Fig. 1). She had undergone renal transplantation in 2002 due to renal failure secondary to Alport's syndrome. At presentation her immunosuppressive medications were tacrolimus 1mg twice daily, mycophenolate 500mg twice daily and prednisolone 3mg daily.

Examination revealed multiple, erythematous, flat-topped papules on the inguinal folds extending to the upper thighs, but not extending to the vulva. There was neither associated pain nor pruritus, however it posed a cosmetic concern for the patient.

Skin biopsy confirmed the diagnosis of AEV with enlarged keratinocytes demonstrating blue-grey cytoplasm, vacuolated cells in the upper epidermis and coarse keratohyaline granules (Figure 2).

HPV genotyping by polymerase chain reaction (PCR) on the biopsy specimen and swab detected HPV-5, a beta-papilloma virus associated with SCCs (4).

The patient was initially treated with topical Tretinoin 0.05% on alternating days coupled with oral Acitretin 10mg daily. There was local skin irritation initially, which improved with treatment breaks. A few months later, she was commenced on topical Imiquimod 5% cream, initially applied once weekly, gradually increasing to three times weekly. There was no improvement and the papules had spread.

Twenty-seven months after initial presentation, the patient was prescribed the first of three Gardasil vaccinations, which were completed six months later. The patient remained on topical imiquimod 5% twice weekly, topical tretinoin 0.05% and oral acitretin at 10mg daily.

On examination one month after completion of the three doses of Gardasil vaccine, the lesions were found to be completely flattened with a small amount of remaining erythema (Fig 3.). PCR on skin swab was negative for HPV.

We report the first case of AEV responding to multimodal therapy, including Gardasil vaccination. We were also able to demonstrate clearance of HPV 5 by PCR.

HPV types associated with EV include the common genotypes 3 and 10 in addition to genotypes 5 and 8, which are rarer (5). Gardasil vaccine is indicated for the prevention of HPV-associated cervical, vulvovaginal and anal cancers.

AEV is often difficult to treat. The treatments such as cryotherapy, topical retinoid, imiquimod, 5-fluorouracil, podophyllotoxin, and topical cidofovir can produce improvement, but usually not clearance of the lesions (5). Gardasil seemed to be effective in our patient when used in combination with other therapies.

With advancements in immunosuppression, the incidence of AEV is likely to continue to rise. The main objective of AEV management is treatment to prevent malignant transformation, especially given the already increased risk of skin cancers in immunosuppressed patients.

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Figure Legend:

Figure 1: Patient at initial presentation: Numerous papules scattered bilaterally around her groin.

Figure 2: A skin biopsy from the patients' inguinal region shows enlarged cells in the granular layer. These cells have a distinctive blue-grey swollen cytoplasm, which reflects HPV infection and is consistent with epidermodysplasia verruciformis. (Original magnification: X20)

Figure 3: Lesions had flattened and become less erythematous after completion of 3 Gardasil vaccinations.

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