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Case Report

Epidermodysplasia verruciformis Associated with Mental Retardation and Seizure Disorder

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Abstract

Epidermodysplasia verruciformis (EV) is a rare inherited disorder characterized by disseminated infection by human papillomavirus (HPV), associated with development of cutaneous malignancies and immunological disturbances. Associated mental retardation has been reported in a few patients. We report a case of 23 year old male with plane wart and Pityriasis versicolor-like lesions since the age of 3 years with associated mental retardation and seizure disorder. The case is reported to highlight the association of mental retardation and seizure with a rare dermatological disorder (German J Psychiatry 2010; 13(4): 185-187).

Keywords: Epidermodysplasia verruciformis, mental retardation, seizure disorder

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Introduction

Epidermodysplasia verruciformis (EV) is a rare genodermatosis, characterized by susceptibility to widespread and persistent infection by distinct types of human papillomavirus (HPV) (Androphy et al., 1985; Astori et al., 1988) The disease begins in infancy and is manifested by multiple flat wart-like lesions and/or pityriasis versicolor-like macules (PV) (Boxman et al., 1997; Glisnki et al., 1976; Haftek et al., 1985). After the third decade of life, roughly 30 to 50% of patients may develop skin cancer, which is frequently multiple and most commonly found in the areas of intense sun-exposure (Haftek et al., 1985; Haftek et al., 1987) Bowen's disease may also be seen on sun exposed sites (Harris et al., 1997). The disease shows immunological alterations especially of cell-mediated immunity (Jablonska et al., 1972).

Case Report

A 23 year old male presented to the department of dermatology with complaint of erythematous macules and plaques. The lesions started from face and upper chest when the patient was about 3 years old. The lesions gradually extended to involve trunk and limbs as well. The lesions were asymptomatic in nature. Similar lesions were not seen in any of the family members. The patient had difficulty in understanding the questions and a history of subnormal intelligence and generalized tonic clonic movements, hence was sent for psychiatric evaluation.

Psychiatric evaluation of the patient revealed a history of full term normal delivery at home. There was no history of parental consanguinity. Regular vaccination was carried out as per the schedule. Milestones were slightly delayed as compared to the elder sibling; unassisted sitting at 10 months, started walking at 18 months. Language was also delayed, started speaking first word by the age of around 18 months. As per the parents he was friendly. He started going to

school at around the age of 5 years. He had below average performance and had to be promoted without even passing the exams. However he was pulled out of the school after the same performance continued for the 3 consecutive years. Patient used to go to field with his father and carry out small amount of work for which he was to be supervised regularly. He was unable to take decisions in the field or at home. However, he used to make his wants and needs known.

Patient started developing generalized tonic-clonic movements since the age of 6 years, associated with frothing, incontinence of urine, uprolling of eyeballs and loss of consciousness lasting for about 15 minutes. Treated with phenytoin 300 mg per day, the seizures decreased in frequency but the patient was never seizure free. Patient discontinued the treatment after around 2 years. There after till the time of presentation patient was never on any antiepileptic drugs. Last seizure episode was about a four days before the presentation to the OPD.

A diagnosis of seizure disorder and mild to moderate mental retardation was considered on clinical basis.

Examination: The patient was moderately built. The cardiovascular; respiratory and the gastrointestinal system were normal. Examination of the skin lesions revealed erythematous macules and plaques over face, chest, abdomen, back and limbs. Few crusts were seen over the forehead. Most of the lesions on trunk were confluent whereas those on limbs were discrete.

Investigations: Routine blood investigations including Hb, TLC, DLC, liver function tests, kidney function tests and urine examination were normal. The EEG showed generalized slow waves (hyperventilation could not be done). Detailed IQ assessment could not be done (as the patient was uncooperative). Skin biopsy revealed changes in the epidermis. The epidermis showed hyperkeratosis and slight acanthosis. Vacuolated cells were present in the upper stratum Malpighi and granular layer. The affected keratinocytes had abundant slightly basophilic cytoplasm and round, basophilic keratohyaline granules with occasional enlarged, hyperchromatic, atypical nuclei. The dermis was normal. A diagnosis of *Epidermodysplasia verruciformis* was made.

Final diagnosis: Keeping in view the above mentioned history and investigations a final diagnosis of *Epidermodysplasia verruciformis* associated with seizure disorder and mental retardation (mild to moderate) was made.

Discussion

EV is usually considered as an autosomal recessive condition (Boxman et al., 1997). X-linked recessive (Jablonska et al., 1979) or autosomal dominant (Jablonska et al., 1991) modes of inheritance, however, have been postulated in single families, pointing to a possible genetic heterogeneity of the disease. EV results from an abnormal susceptibility to specific related human papillomavirus (HPV) genotypes. Whereas EV-associated HPV (EV-HPV) genotypes cause widespread inapparent infections in the general population (Jablonska, 1993; Lutzner et al., 1978), infection leads to the early development of disseminated flat wart-like and *pityriasis versicolor*-like lesions in EV patients. Patients are unable to reject their lesions and cutaneous Bowen's carcinomas in situ and invasive squamous cell carcinomas develop in about half of them, mainly on sun-exposed areas (Androphy et al., 1985; Majewski et al., 1995; Majewski et al., 1997).

The disease was often initiated during infancy, though cases have been described of earlier onset (after birth) and later (third and fourth decade). The most frequent initial lesion is of the flat wart-like type, located mainly on the dorsa of the hand. *Pityriasis versicolor*-type macules, characteristic of the disease, develop a few years after the first lesion. They are initially erythematous, but hypochromic in later stages of the disease (McKusick, 1998).

In benign lesions, the viral cytopathic effect was only observed in the upper layers of the epithelium, granted the aspect of "bird eyes", characteristic of this kind of disease (Haftek et al., 1985; Orth et al., 1979).

EV is accepted as a pre-malignant condition. The malignant transformation occurs in about 30 to 50% of cases and is associated with oncogenic HPVEVs, genetic factors of the host cell, and actions of the extrinsic co-carcinogens, mainly UVB and radiotherapy (Androphy et al., 1985, Haftek et al., 1985; Haftek et al., 1987; Orth, 1987; Ostrow et al., 1982). Patients can prematurely show solar elastosis and numerous actinic keratosis-like lesions in the areas of greatest photoexhibition. Haftek et al., 1985; Ramoz et al., 2004; Rueda and Rodriguez, 1976).

Most malignant tumors (roughly 50%) developed on the forehead of patients, which may be justified by the joint or isolated action of the following factors: (1) greater area exposed to ultra-violet rays, (2) presence of long-life cells, stem cells, hair follicles, probable reserves of HPVEV, and (3) synergic action of chemical carcinogens (squalus and fatty acids in sebum). Haftek et al., 1985; Ramoz et al., 2004) Cancers are usually associated with HPV5 and occasionally with HPV types 8, 14, 17, 20, or 47 (Ruiter et al., 1970).

In a review of 147 EV patients from 125 families, mental retardation was reported in 8% of the EV patients (Boxman et al., 1997). In three out of thirteen siblings (23%), variable degrees of mental retardation were observed (McKusick, 1998). Walmar et al. (2002) reported severe mental retardation in one of their Colombian families.

A very few cases have been reported regarding the comorbidity of EV and seizure disorder (Gutiérrez et al., 1987).

We report this case to highlight the association of the three conditions viz. *Epidermodysplasia verruciformis*, mental retardation, and seizure disorder.

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