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Papillomavirus-negative Verrucous Lesions in a Diabetic Patient with Neuropathy

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Abstract A 47-year-old diabetic Japanese female presented with verrucous lesions over the both first metatarsal heads. A neurological examination showed neuropathy with both sensory and motor loss on the feet, and distal lower legs. Although a histological analysis revealed hyperkeratosis, acanthopapillomatosis, and vacuolated keratinocytes in the epidermis as verruca vulgaris, we were not able to detect papillomaviruses by means of immunohistochemical staining and polymerase chain reaction (PCR). The pathogenesis of these verrucous lesions might be related to chronic pressure or friction in an area of neuropathy.

Introduction

Although there have been numerous reports about skin changes in association with diabetes mellitus, none is specific to the disease. We describe a diabetic Japanese female with symmetrical verrucous lesions over metatarsal heads. A neurological examination showed neuropathy with both sensory and motor loss on the feet, and distal lower legs.

Case Report

A 47-year-old Japanese female was admitted to the Dermatology Clinic of Yamaguchi University Hospital in October, 1995 for evaluation of one-year history of verrucous lesions over metatarsal heads. In 1994, the results of biopsy examinations performed at another hospital had been interpreted as a giant wart and the lesions were treated with cryosurgery. The treatment was unsuccessful, and the lesions continued to be enlarged gradually. Thus she was finally referred to our outpatient clinic. She had two daughters with normal pregnancies, but the weights of them at the birth were over 4,000g. There is no to be described in particular in her family history.

On physical examination, there were oval, well-demarcated verrucous lesions about 4 cm in diameter over metatarsal heads with central ulcerations (Fig.1). A neurological examination showed neuropathy with both sensory and motor loss on the feet and distal lower legs.

Abnormal laboratory findings included WBC 11,700/μl↑, Hb 10.1g/dl↓, Alb 2.9 g/dl↓, Glu 315mg/dl↑, TG 144mg/dl↑, HbA 1c 13.8%↑. Hematochemical and immunological examination of thyroid, hypophyseal and adrenal hormones did not reveal any alterations.

The lesions were excised with a 0.5cm margin to the underlying fascia and the wounds were covered by skin grafts.

The surgically removed specimens showed

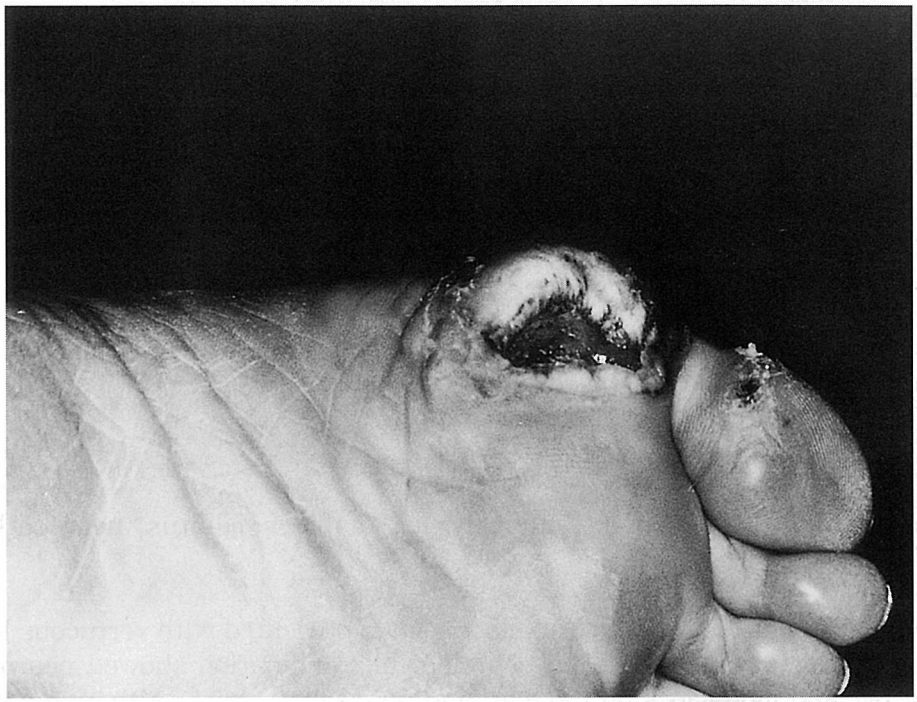

Fig 1. Verrucous lesions with central ulceration over the right metatarsal head.

hyperkeratosis, acanthopapillomatosis, and vacuolated keratinocytes in the epidermis with no cellular atypia with hematoxylin-eosin staining (Fig.2). Though detection of antigens of papillomaviruses was attempted with an LSAB kit (Dako, Carpinteria, USA) and a monoclonal antibody against human papillomavirus (YLEM, Rome, Italy), we were not able to detect any antigens of human papillomaviruses. Then, using PCR, we analyzed DNA extracted from paraffin sections with primers to the highly conserved HPV L1 gene, as previously described by Resnick et al[1]. But we could not detect the PCR products of human papillomavirus. Positive control specimen was obtained from a 23-year-old male with verruca vulgaris on the sole. We could detect the exist of human papillomavirus by means of both immunohistochemical examination and PCR.

Discussion

There are numerous complications of diabetes mellitus on the feet, which are occasionally called the diabetic foot[2]. It includes infections, neuropathy, vasculopathy, and poor wound healing.

Especially neuropathy and vaculopathy make the patients more susceptible to

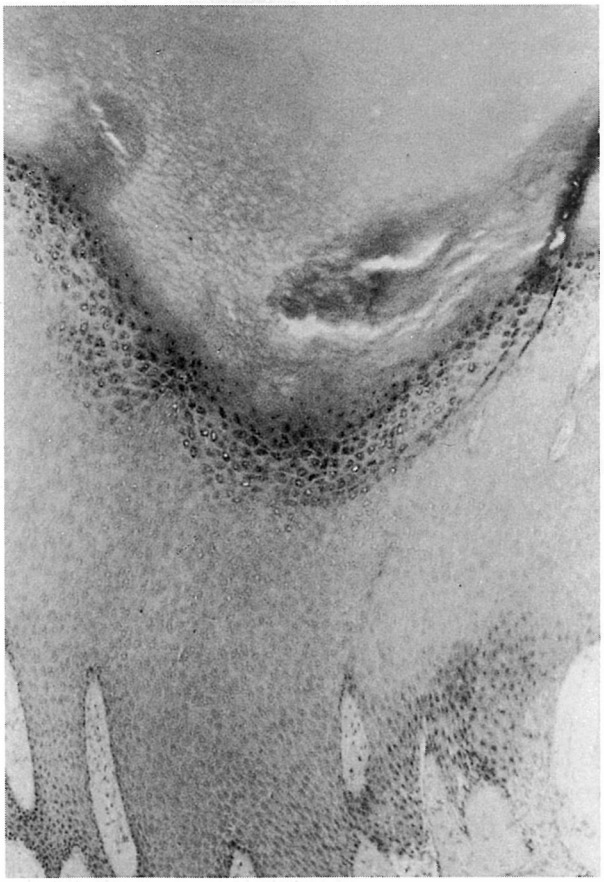

Fig. 2. A biopsy from the right verrucous lesion showing hyperkeratosis, acanthopapillomatosis, and vacuolated keratinocytes with no cellular atypia.

microbial invasion.

Verrucous lesions on the feet needs to be differentiated from squamous cell carcinoma, verrucous carcinoma, and wart. Recently, verrucous carcinoma has been reported to be associated with human papillomavirus infection [3]. Gerbig and Hunziker reported verrucous skin lesions in a diabetic patient with neuropathy with a partial sensory loss on the feet and the distal lower legs[4]. They described an entity similar to the verrucous skin lesions on the legs of leprosy patients and had been unable to detect antigens of human papillomaviruses by means of immunohistochemical staining. Therefore they suggested that the etiology of verrucous skin lesions in diabetic neuropathy might be related to chronic pressure or friction in an area of sensory loss. In our case, the patient suffered diabtes mellitus and neuropathy with both sensory and motor loss on the feet and distal lower legs, and cutaneous examinations showed verrucous lesions over metatarsal heads with central ulcerations. Histopathological finding showed hyperkeratosis, acanthopapillomatosis, and vacuolated keratinocytes with no cellular atypia and papillomaviruses could not be detected by means of immunohistochemical examination and PCR. These findings were suggested to be consistent with that of Gerbigs' patient. Srinivasan and Desikan reported cauliflower growths in neuropathic plantar ulcers in leprosy patients[5]. The etiology of verrucous skin lesions remains to be unclear, although we suggested neuropathy might be a possible factor for the lesions.

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