Linear Arrangement of Multiple Seborrheic Keratosis: Absence of Human Papillomavirus

Yong-Hyun Jang, M.D., Gyu Young Jeong, M.D.*, Hee Young Kang, M.D.

*Department of Dermatology, Ajou University School of Medicine, Suwon, Korea, *Seoul Clinical Laboratories, Seoul, Korea*

We report an 81-year-old obese female patient with multiple verrucous lesions arranged in a linear pattern on both inner thighs. Histopathological examination showed characteristic features of seborrheic keratosis. Because the linear distribution of lesions observed in this case may reflect a role for human papillomavirus, we investigated the presence of human papillomavirus utilizing a polymerase chain reaction and DNA microarray but our results were negative. Other possible mechanisms for the pathogenesis of a linear arrangement of seborrheic keratosis are discussed. (Ann Dermatol 16(3) 138~140, 2004)

Key Words: DNA microarray, Human paillomavirus, Linear seborrheic keratosis, Polymerase chain reaction

Seborrheic keratosis (SK) is a benign hyperplasia of localized groups of keratinocytes. UV irradiation, immunoreactive growth hormones in association with malignancies and a senescent condition have been suggested as possible causes of SK[1-3]. When the SK presents in a linear pattern, human papillomavirus (HPV) may be implicated in this configuration[4]. We report a case of multiple SK in a unique linear distribution. We investigated the potential role of the human papillomavirus.

CASE REPORT

An 81-year-old woman presented with a 20-year history of multiple, asymptomatic brownish verrucous lesions in the bilateral inguinal area. The patient stated lesions appeared gradually over several years. She was obese, even potbellied, which obscured the lesions. Her medical history included diabetes mellitus, hypertension and chronic renal insufficiency. Physical examination revealed multiple brownish verrucous papuloplaques in a linear distribution on both inguinal areas (Fig. 1). On the face, neck and abdomen, widespread brownish, flat warty lesions of different sizes were observed. A skin biopsy was taken from the right inguinal area and the pathologic findings showed typical histologic features of hyperkeratotic SK: marked laminated hyperkeratosis, epidermal hyperplasia, a proliferation of

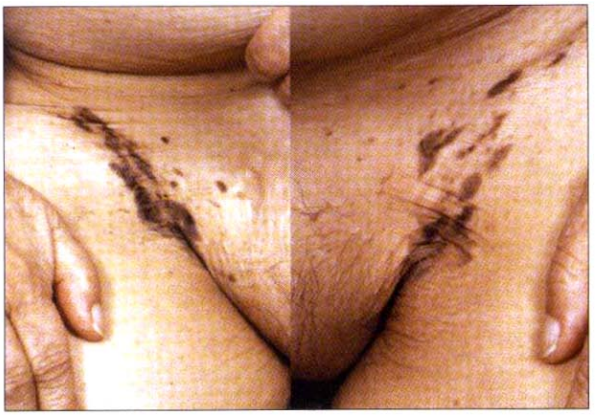

Fig. 1. Multiple brownish verrucous papuloplaques with a linear distribution on both inguinal areas of an 81-year-old obese woman.

Received May 11, 2004
Accepted for publication July 24, 2004

Reprint request to: Hee Young Kang, M.D., Department of Dermatology, Ajou University School of Medicine, 5 Wonchon-dong, Yeongtong-gu, Suwon 443-721, Korea.
Tel. 82-31-219-5190, Fax: 82-31-219-5189
E-mail. hykang@ajou.ac.kr

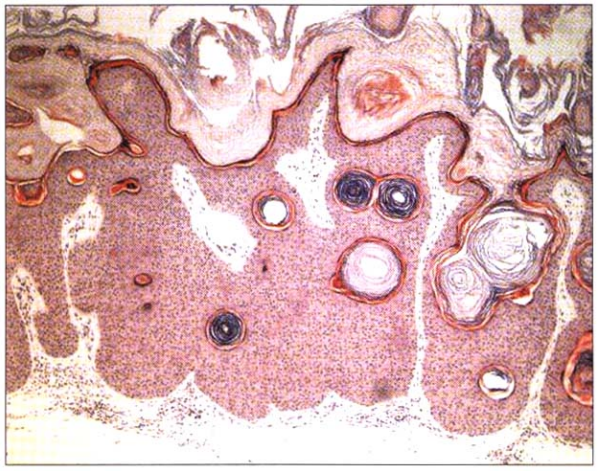

Fig. 2. Proliferation of basaloid cells with hyperkeratosis, papillomatosis, and several horn pseudocysts (H&E, × 100).

basaloid cells and several horn pseudocysts (Fig. 2). We used type 6, 18 specific polymerase chain reaction (PCR) and DNA chip microarray to detect HPV DNA. The HPV DNA chip is an oligonucleotide chip that enables the rapid and easy detection and genotyping of 18 high risk HPV types (16/ 18/ 26/ 31/ 33/ 35/ 39/ 45/ 51/ 52/ 56/ 58/ 59/ 66/ 68/ 69/ 70/ 71), 14 low risk HPV types (6/ 11/ 32/ 34/ 40/ 42/ 43/ 44/ 53/ 54/ 55/ 57/ 61/ 62) and other types of HPV DNA (a positive result in all HPV types, but type is not specified). In our analysis, PCR was negative for types 6 and 18 HPV DNA. DNA chip microarray also showed the absence of HPV DNA.

DISCUSSION

Although the relationship between HPV and genital SK has been well documented, the role of HPV in non-genital SK is still controversial. Two reports suggest a possible role of HPV in non-genital SK. Tsambaos et al[5]. found HPV DNA in 34 of 179 cases (Type 6, 31, 33 and/or 35) using in situ hybridization. Gushi et al[6]. used in situ hybridization, PCR and southern blot hybridization to reveal HPV DNA in 30 of 104 SK samples (Type 18, 6, 18, 1, 2). However, Zhu et al[7]. detected HPV type 6 DNA in only one of 29 non-genital SK cases using PCR. Also, Lee et al[8]. used in situ PCR, but could not demonstrate HPV genomes type 6, 11, 31, or 33 in the 40 non-genital SK cases. In our investigation, we used DNA microarray, which is based on the PCR method and has the advantage of high sensitivity and the ability to detect single and multiple infection of 32 types of HPV at once[9]. We could not detect any types of HPV DNA in our sample.

The cause of the unique distribution of SK in this case is currently unclear. One possible explanation is that repetitive traumatic stimuli may determine the linear appearance of SK, as suggested in other linear benign neoplasms including melanocytic tumors[10]. The linear distribution is a clinical manifestation of the Koebner phenomenon[11]. Accordingly, we hypothesize that constant friction, especially in obese individuals may give rise to a proliferative condition of keratinocytes that is responsible for the development of SK. Pariser and Bluemink[10] described linear dermal melanocytosis developing after blunt trauma. They suggested that trauma could have induced a reactive neurotrophic response resulting in dermal melanocytosis. Heng et al[12]. suggested that an epidermal growth factor secreted by the underlying tumor is a possible cause of the SK. They reported five cases of linear eruptive SK associated with colonic malignancy, in which resolution of the cutaneous lesions was observed after removal of the colonic tumors. Our patient had no apparent malignancies or other epidermal hyperplastic phenomenons. Nevertheless, certain elevated immunoreactive growth hormones (for example, insulin like growth factor) in diabetes patients could be a possible cause of SK.

Linear seborrheic keratosis should be differentiated from other linear hyperkeratotic or verrucous lesions, namely, linear epidermal nevus, lichen striatus, linear porokeratosis, linear Darier's disease, linear lichen planus, and linear psoriasis. But, it is easily distinguished from other diseases by the typical histology of SK such as horn pseudocysts and the proliferation of basaloid cells.

Future molecular studies involving SK are needed to confirm these concepts and determine the origin of SK.

REFERENCES

1. Kwon OS, Hwang EJ, Bae JH, et al.: Seborrheic keratosis in the Korean males: causative role of

sunlight. Photodermatol Photoimmunol Photomed 2003;19:73-80.
2. Groves RW, Allen MH, MacDonald DM: Abnormal expression of epidermal growth factor receptor in cutaneous epithelial tumours. J Cutan Pathol 1992;10:66-72.
3. Nakamura S, Nishioka K: Enhanced expression of p16 in seborrhoeic keratosis; a lesion of accumulated senescent epidermal cells in G1 arrest. Br J Dermatol 2003;149:560-565.
4. Somach S, Morgan M: Benign keratosis with a spectrum of follicular differentiation: a case series and investigation of a potential role of human papilloma virus. J Cutan Pathol 2001;28:156-159.
5. Tsambaos D, Monastirli A, Kapranos N, et al.: Detection of human papillomavirus DNA in nongenital seborrhoeic keratoses. Arch Dermatol Res 1995;287:612-615.
6. Gushi A, Kanekura T, Kanzaki T, Eizuru Y: Detection and sequences of human papillomavirus DNA in nongenital seborrhoeic keratosis of immunopotent individuals. J Dermatol Sci 2003;31: 43-49.
7. Zhu WY, Leonardi C, Penneys NS: Detection of human papillomavirus DNA in seborrhoeic keratosis by polymerase chain reaction. J Dermatol Sci 1992;4:166-171.
8. Lee ES, Whang MR,. Kang WH: Absence of human papillomavirus DNA in nongenital seborrheic keratosis. J Korean Med Sci 2001;16:619-622.
9. Hwang TS, Jeong JK, Park M, Han HS, Choi HK, Park TS: Detection and typing of HPV genotypes in various cervical lesions by HPV oligonucleotide microarray. Gynecol Oncol 2003;90:51-56.
10. Pariser RJ, Bluemink GG: Acquired linear dermal melanocytosis. Nerve course distribution. Arch Dermatol 1982;118:125-128.
11. Weiss G, Shemer A, Trau H: The Koebner phenomenon: review of the literature. J Eur Acad Dermatol Venereol 2002;16:241-248.
12. Heng MC, Soo-Hoo K, Levine S, Petresek D: Linear seborrheic keratoses associated with underlying malignancy. J Am Acad Dermatol 1998;18: 1316-1321.