

Pathogenesis of Plantar Epidermal Cyst: Three-Dimensional Reconstruction Analysis

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Dear Editor:

Epidermal cysts are common benign subcutaneous lesions known to result from progressive cystic ectasia of the infundibular portion of hair follicles¹. Occasionally, epidermal cysts are known to occur in hairless skin such as in soles and palms. In such cases, a different pathogenesis is proposed. These cysts are considered to develop as a result of blunt penetrating injury implanting epidermal fragments into the dermis. Since the year 1986, there is increasing evidence implicating a close association between human papillomavirus (HPV), especially HPV type 57 and 60, and plantar epidermal cysts²⁻⁴. More recently, some authors reported that plantar epidermal cysts are located near or connected to dermal eccrine ducts, suggesting an eccrine ductal origin⁵. Moreover, there are reports of concomitant HPV isolation from the cyst wall and the adjacent eccrine duct⁶. Clearly, the pathogenesis of plantar epidermal cyst is controversial. The aim of this study was to assess the anatomical relationship between plantar epidermal cyst and surrounding structures including eccrine ducts by using three-dimensional (3D) reconstruction analysis as an attempt to understanding its etiology.

The patient studied was a 19-year-old healthy woman with a palpable solitary tender subcutaneous nodule on her left sole. She also had several warts on her sole, which were previously treated with multiple sessions of cryotherapy. She noticed the nodule 2 years ago while receiving treatment for plantar warts but the nodule had turned

painful only for the 2 months preceding the current consultation. The location of the palpable nodule was close to a treated wart and the patient could not recollect whether the nodule appeared in the same position as a treated wart (Fig. 1). Informed consent was obtained and excision of the subcutaneous nodule was performed under local anesthesia. The excised tissue was fixed in 10% neutral formalin and embedded in paraffin. The paraffin block was sliced into 5- μ m-thick serial sections and stained with hematoxylin and eosin. Slides were subjected to digital photomicrography at 40 \times magnification (Olympus BX51; Olympus Co., Ltd, Tokyo, Japan). 3D reconstruction analysis was performed by using reconstruction software (Reconstruct ver.1.1.0.0, 1996~2007, Hohn C. Fiala). Digital photomicrographs were imported by the software and the main structures on the images were targeted and traced to perform 3D reconstruction.

Histopathological findings on examination of the excised specimen were consistent with epidermal cyst. In addi-



Fig. 1. A solitary tender subcutaneous nodule (arrow) and multiple warts on the patient's sole.

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tion, on serial sections, a bulge like a pit was observed on the epidermal side of the cyst wall along with marked fibrosis around the cyst wall (Fig. 2A). A total of 300 serial sections were utilized in reconstructing a 3D image (Fig. 2B, C). The reconstructed image demonstrated the cyst as located in the deep dermal layer surrounded by abundant sweat glands. A number of eccrine dermal ducts were identified, most of which appeared to drain the sweat glands. While it was possible that the ducts not draining the sweat glands were connected to the cyst, an exact point of connection between the cyst and eccrine duct(s) could not be demonstrated (Fig. 2D).

In this study, we performed 3D reconstruction analysis to demonstrate a structural relationship between plantar epi-

dermal cyst and its adjacent eccrine ducts. The cyst appeared to be compressed by an abundance of sweat glands and had a bulge, characteristic of a connection to another structure, on its epidermal side. While most ductal structures were draining the sweat glands on either side of the cyst, some of them appeared to be directed towards the bulge over the cyst wall. This finding favors the possible relationship of plantar epidermal cysts to eccrine ducts in explaining their pathogenesis.

HPV may have a role in the pathogenesis of plantar cyst via eccrine ducts as it was concomitantly identified in plantar cysts and adjacent eccrine ducts²⁻⁵. HPV may have a high affinity for eccrine duct epithelium, infect the distal portion of the eccrine duct, and then migrate into its der-

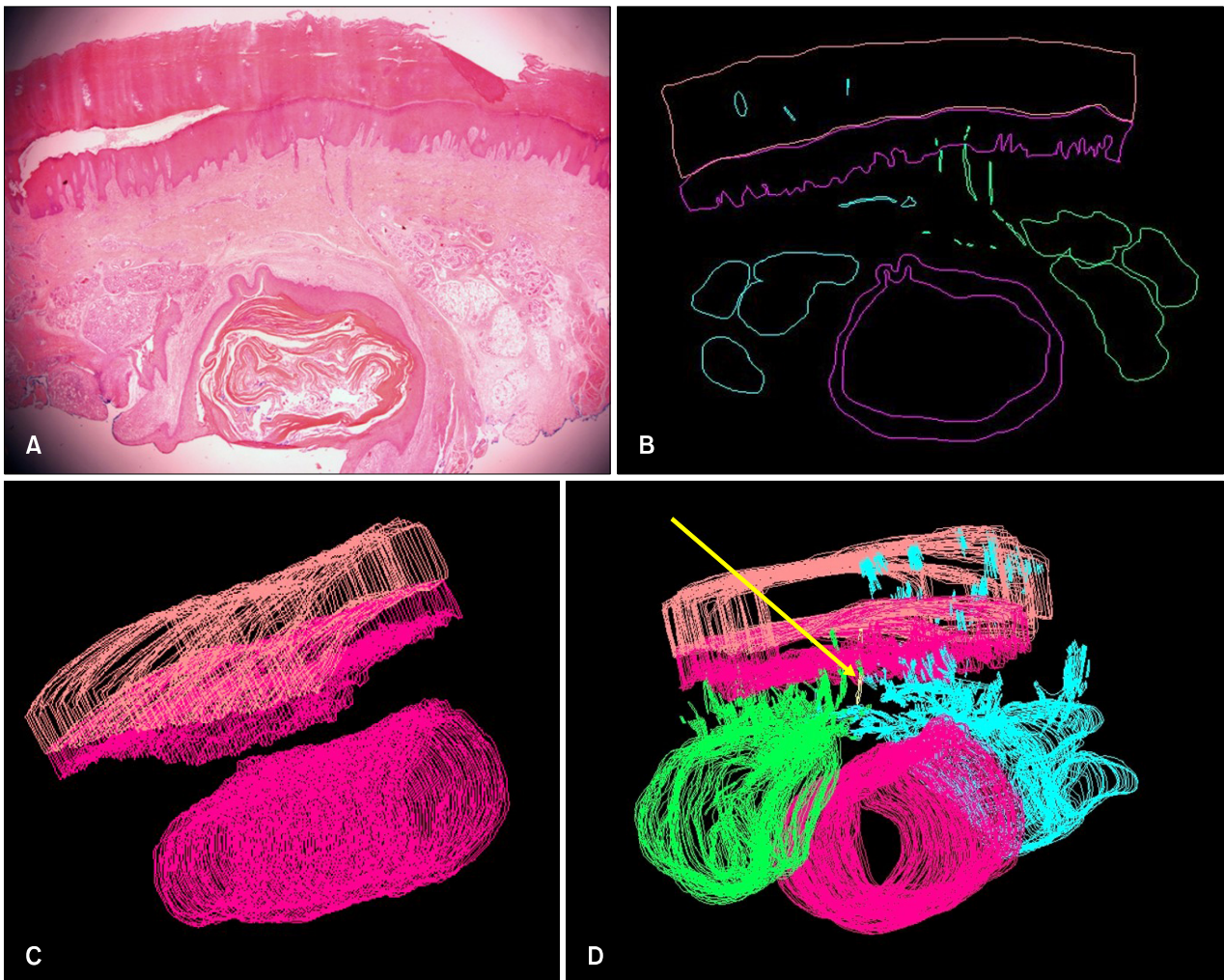


Fig. 2. (A) Histology showed a characteristic bulge on the epidermal side of the cyst wall, fibrosis surrounding the cyst, and abundant eccrine glands and ducts (H&E, $\times 40$). (B~D) Process of three-dimensional reconstruction analysis. (B) Tracing of the outline of the cyst wall, ductal structure and overlying epidermis. (C) A wire frame of the cyst wall and the overlying epidermis generated by three-dimensional reconstruction software by using a montage of tracings of a major part of the serial sections. (D) A wire frame of all the traced structures. Apricot color: keratin layer, pink: epidermis and cyst wall, green and blue: sweat glands and ductal structures on either side of the cyst, yellow: suspicious duct, which might be connected to the cyst wall.

mal portion, finally leading to the formation of an epidermal cyst⁶.

Some authors oppose the hypothesis of eccrine ductal origin of epidermal cyst because the expression of cytokeratin, involucrin, and carcinoembryonic antigen (CEA) as seen on immunohistochemistry of epidermal cysts, is identical to the suprabasal layers of the epidermis but not to eccrine dermal ducts^{4,7,8}. However, the findings of Egawa et al.⁵ that the connected portion of the eccrine duct was hypertrophied with stratified squamous epithelium expressing CEA and involucrin suggests epidermoid metaplasia of eccrine duct epithelium and supports eccrine ductal origin of epidermal cysts. Magnetic resonance imaging and ultrasonography findings of two cases of HPV-associated plantar epidermal cyst were reported recently as demonstrating a linear arrangement of several globular cysts placed adjacent to each other and referred to as the 'linear globular pattern'⁹. The authors suggested that this pattern may have resulted from HPV-associated eccrine duct metaplasia leading to cyst formation and subsequently traumatic rupture, eventually resulting in multiple cystic components placed linearly.

The 3D reconstruction analysis software used by us provides professional quality reconstruction and is available for download, free of charge. A drawback of this software is that the target structures in each of the serial sections requires to be aligned and traced individually and may be time-consuming. Despite that, it is an easily accessible and useful tool to assess and understand 3D images of the skin and its structures¹⁰. Our failure to demonstrate the exact connecting point between the cyst wall and the eccrine duct could be owing to fibrotic changes around the cyst wall, possibly caused by recent inflammation as suspected on account of recent onset tenderness over the cyst. It is also possible that the critically important parts of the paraffin block were lost during the histologic examination performed to confirm diagnosis before 3D reconstruction.

The use of 3D reconstruction analysis was effective in demonstrating the structural relationship of the plantar epidermal cyst with the surrounding eccrine ducts. These findings suggest that the plantar epidermal cyst may be connected to eccrine dermal ducts, supporting the hypothesis that certain plantar epidermal cysts develop from epi-

dermoid metaplasia of eccrine duct.

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