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LETTERS TO THE EDITOR

Infiltration of mast cells in pachydermia of pachydermoperiostosis

Dear Editor,

Pachydermoperiostosis (PDP; Online Mendelian Inheritance in Man #614441) is a rare hereditary disease characterized by distinctive digital clubbing, periostosis and pachydermia.[1] Patients with PDP harbor homozygous mutations in the solute carrier organic anion transporter family member 2A1 gene (*SLCO2A1*) or the 15-hydroxyprostaglandin dehydrogenase gene (*HPGD*), resulting in elevated prostaglandin E2 (PGE2) levels.[1]

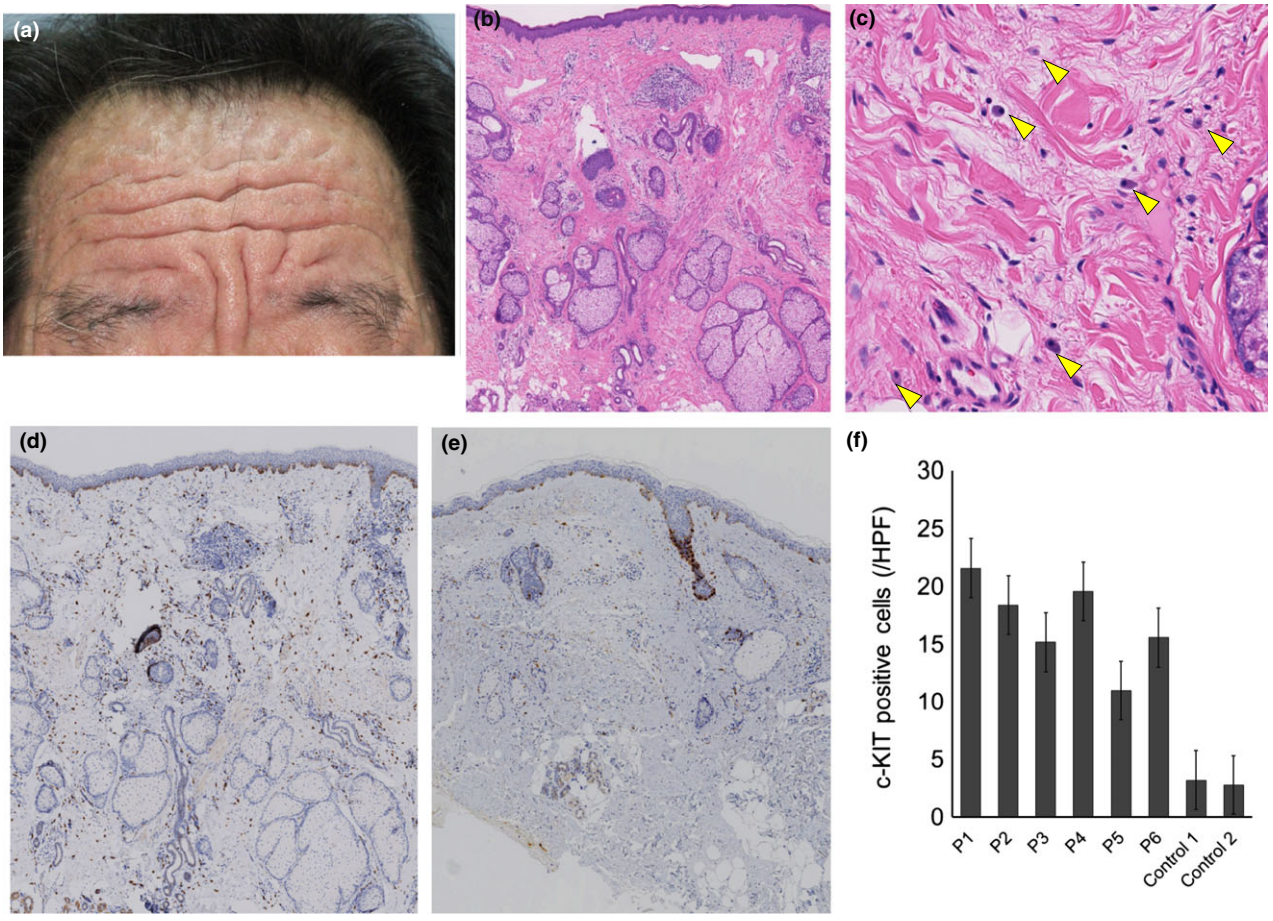

Figure 1. (a) Representative clinical features of the forehead. Moderate pachydermia was noted in the forehead of patient 1. (b) Representative histopathological features of pachydermia (hematoxylin–eosin, original magnification ×4). This specimen was obtained from the forehead of patient 1. Dermal edema, fibrosis and sebaceous hyperplasia were noted. (c) High-powered view at ×200. Infiltration of mast cells was noted (yellow arrowheads). (d) Immunohistochemical analysis of pachydermia sample for c-Kit staining (×4). The sample was obtained from the forehead of patient 1. Prominent infiltration of c-Kit-positive cells was noted in the dermis. (e) Immunohistochemical analysis of normal forehead skin with c-Kit staining (×4). This specimen was obtained from the area surrounding a benign tumor and used as a control. (f) Score of the c-Kit-positive cells in the dermis. Dermal c-Kit-positive cells from five different randomly selected areas in the dermis were counted using a high-powered field (HPF, ×400), and the average of the five sums was calculated. The number of c-Kit-positive cells in the dermis was increased in the pachydermia samples approximately three- to eightfold compared with controls.

Correspondence: Hironori Niizeki, M.D., Ph.D., Department of Dermatology, National Center for Child Health and Development, 2-10-1 Okura, Setagaya-ku, Tokyo 157-8535, Japan. Email: niizeki-h@ncchd.go.jp

Pachydermia shows the histopathological findings of dermal edema, mucin deposition, elastic fiber loss, dermal fibrosis and sebaceous gland hyperplasia. Previously, we reported that the degree of these findings is correlated with pachydermia severity.[2] Upon further observation, we found that mast cells were notably infiltrated in the dermis of pachydermia samples.

In this study, pachydermia specimens obtained from six patients with PDP were analyzed. Diagnosis was made according to established clinical and radiological criteria.[3] The study was approved by the ethics committee of the National Center for Child Health and Development and Keio University School of Medicine. Participants provided written informed consent. Patient characteristics are summarized in Table S1. All participants were male (age range, 19–51 years). No participant had a family history of PDP. Samples were obtained from the forehead (Fig. 1a) and stained with hematoxylin–eosin (Figs 1b,c, S1), immunohistochemical staining for c-Kit (Figs 1d,e,S1) and toluidine blue (Fig. S1). The number of infiltrated mast cells was calculated by counting and averaging the number of dermal c-Kit-positive cells or toluidine blue metachromatic staining cells in five randomly selected areas using ×400 magnification (Fig. S2). Two samples of normal skin from the forehead of a healthy individual were used as a control (Figs 1e,S1). The slides were independently interpreted by two investigators (K. T. and A. I.) without any knowledge of the clinical data. Any discrepancies in the findings were reconciled by a third investigator (H. N.). The number of dermal c-Kit-positive cells was three- to eightfold higher in pachydermia samples than in controls (Fig. 1f). Increased dermal mast cells were also confirmed by toluidine blue staining, as c-Kit-positive cells may include dermal melanocytes (Fig. S2).

Mast cells are filled with secretory granules containing histamine, protease, cytokines, chemokines and proteoglycans.[4] These granules are released into the extracellular environment by a variety of mechanisms such as immunoglobulin E cross-linking, complement activation and neuropeptide stimulation.[4] A recent report showed that PGE2 can directly activate mast cells to secrete histamine, mediating PGE2-induced vascular permeability.[5] Mast cell degranulation may cause not only dermal edema but also proteoglycan deposition positive for Alcian blue staining; these findings are typically noted in pachydermia.[2] However, the mechanisms of increased mast cells are yet to be clarified, including the role of upregulated PGE2. Nevertheless, we speculate that mast cells are closely associated with the pathobiology of PDP. Further analysis is necessary to reveal the role of mast cells not only in the skin, but also in the other organs of PDP patients.

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CONFLICT OF INTEREST: None declared.

Keiji TANESE,[1] Hironori NIIZEKI,[2] Atsuhito SEKI,[3] Kazuhiko NAKABAYASHI,[4] Shinsuke NAKAZAWA,[5] Yoshiki TOKURA,[5] Yuhei KAWASHIMA,[1] Akiharu KUBO,[1] Akira ISHIKO[6]

[1]Department of Dermatology, Keio University School of Medicine, Departments of [2]Dermatology, [3]Orthopedics, National Center for Child Health and Development, [4]Department of Maternal-Fetal Biology, National Research Institute for Child Health and Development, Tokyo, [5]Department of Dermatology, Hamamatsu University School of Medicine, Shizuoka, and [6]Department of Dermatology, Toho University School of Medicine, Tokyo, Japan

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Figures show the histological features of six pachydermia samples and two normal control samples stained with hematoxylin–eosin staining (original magnification ×40), c-KIT (×100) and toluidine blue (×100).

Figure S2. (a) Representative high-powered field (original magnification ×400) microscopic feature of pachydermia sample stained for c-Kit.

Table S1. Summary of the patients analyzed in this study.

