Pathophysiology of Pruritus in Keloids: Site-Specific Analysis of Neuro-Immune Interactions

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Running Title
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BACKGROUND

Keloids not only cause aesthetic concerns but also markedly impair patients' quality of life because of intractable pruritus. We focused on differences in pruritus according to the anatomical site of keloids and investigated the pathogenesis of keloid-associated pruritus through histological and gene expression analyses.

METHODS

Six anterior chest keloids, six ear keloids, and three samples of normal abdominal skin were subjected to histological analyses using hematoxylin-eosin staining and immunohistochemistry for CD45, CD3, CD19, and CD16. In addition, three samples each of anterior chest keloids, ear keloids, and normal abdominal skin were analyzed by immunostaining for PGP9.5 and CD1a, followed by three-dimensional analysis of nerve fibers and Langerhans cells using confocal laser microscopy. Furthermore, gene expression analyses of Th2 cytokines (IL-4, IL-13, and IL-31) and Substance P (SP) were performed.

RESULTS

In anterior chest keloids, destruction of hair follicles accompanied predominantly by CD3-positive T-cell infiltration was observed in the peripheral region. CD1a-positive Langerhans cells were widely distributed throughout the epidermis and were increased in number in both anterior chest and ear keloids. PGP9.5-positive nerve fibers were significantly increased in the peripheral region of anterior chest keloids compared with normal skin and ear keloids, and showed an abnormal distribution

pattern compared with the central region. In contrast, ear keloids exhibited significantly fewer nerve fibers than normal skin and anterior chest keloids. Furthermore, IL-4 and IL-13 expression tended to be higher in the marginal regions than in the central regions of both anterior chest and ear keloids. SP expression was elevated in the peripheral region of anterior chest keloids, whereas only limited detectable expression was observed in ear keloids.

CONCLUSİON

This study demonstrated that the marginal region of pruritic anterior chest keloids exhibited increased numbers of Langerhans cells and nerve fibers, together with upregulated expression of Th2 cytokines and SP. In contrast, although some of these findings were observed in non-pruritic ear keloids, they were not present simultaneously. These findings suggest that neuroimmune interactions may contribute to the pathogenesis of pruritus in keloids.