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CASE REPORT

Extensive Nevus Comedonicus with Inflammatory Nodules and Cysts Controlled with Adalimumab

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Nevus comedonicus is a very rare skin disorder characterized by the presence of comedo-like dilated pores with keratinous plugs, rarely resulting in painful recurrent inflammatory nodules or cysts. It presents as localized or extensive form. It displays unilaterally or bilaterally segmental distribution. Histopathologically, it is characterized by keratin-filled epidermal invagination with bulbous proliferation of keratinocytes. The condition may be caused by fibroblast growth factor receptor 2 mutation. Although it may be controlled by a variety of therapeutic modalities, it is difficult to achieve complete resolution. We report a case of extensive nevus comedonicus with inflammatory nodules and cysts controlled with adalimumab. **(Ann Dermatol 33(4) 361~364, 2021)**

-Keywords-
Adalimumab, Extensive nevus comedonicus

INTRODUCTION

Nevus comedonicus is a very rare skin disorder first described by Kofmann in 1895. It appears at birth or during childhood and is characterized by the presence of comedo-like dilated pores with keratinous plugs, leading to the development of painful recurrent inflammatory nodules or cysts. It presents as localized or extensive form nevus showing unilaterally or bilaterally segmental distribution. Histopathologically, nevus comedonicus is characterized by keratin-filled epidermal invagination with atrophic sebaceous glands or follicles. It may be caused by fibroblast growth factor receptor 2 mutation[1]. A focal clonal defect in the growth regulation of the infundibular keratinocytes may result in increased expression of proliferating cell nuclear antigen (PCNA), intercellular adhesion molecule 1 (ICAM-1), human leukocyte antigen-DR (HLA-DR), and CD68[2]. In the epidermal nevus syndrome, nevus comedonicus and other epidermal nevi can be associated with anomalies of the central nervous system, skeletal system, and eye. Squamous cell carcinoma and basal cell carcinomas can occur in patients with epidermal nevus syndrome. Inflammatory nodules and cysts in nevus comedonicus may be controlled by topical application of retinoids, tacrolimus and calcipotriene, and by intralesional corticosteroid injection. In addition, surgical interventions, such as extraction, excision, dermabrasion and laser resurfacing, may yield good cosmetic results[3]. However, other therapeutic modalities may be needed to treat recalcitrant nevus comedonicus.

CASE REPORT

A 22-year old male presented with unilateral extensive comedones on the right side of the chest, abdomen, back,

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and pelvis since birth (Fig. 1A). Nodules, cysts, sinus tracts and a lot of scarring developed in the extensive comedones during post-adolescence (Fig. 1B, C). Medical treatment was not effective. He did not have any systemic abnormalities despite the extensive cutaneous involvement. His past history and family history were unremarkable. The results of laboratory testing, including complete blood count, urinalysis, liver function tests and renal function tests, were within normal limits. Histopathologic examination showed a multiplicity of the invagination of the follicular infundibulum with a keratin plug (Fig. 2A). In addition, projecting bulbous proliferation of the infundibular keratinocytes and perifollicular inflammatory infiltrate were seen (Fig. 2B). Immunohistochemical staining showed an increase in the expression of PCNA in the projecting bulbous proliferation of the infundibular keratinocytes and CD68 in the cells of the dermis predominantly near the projecting bulbous proliferation (Fig. 3). However, the expression of HLA-DR and ICAM-1 in the proliferating infundibular keratinocytes was not increased. The patient

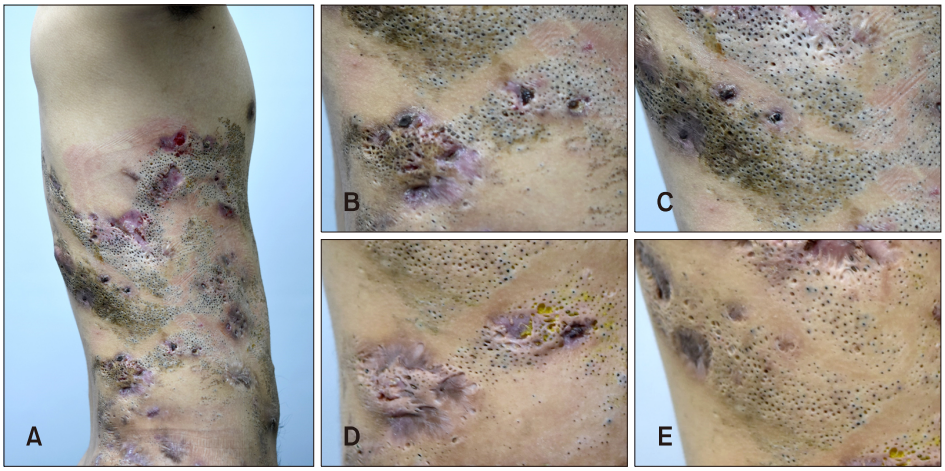

Fig. 1. Clinical appearance of extensive nevus comedonicus. (A～C) Before treatment with adalimumab, the patient presented with extensive comedones, nodules, cysts, sinus tracts and a lot of scarring on the right side of the chest, abdomen, and back. (D, E) The patient's lesions got better 4 months after treatment with adalimumab.

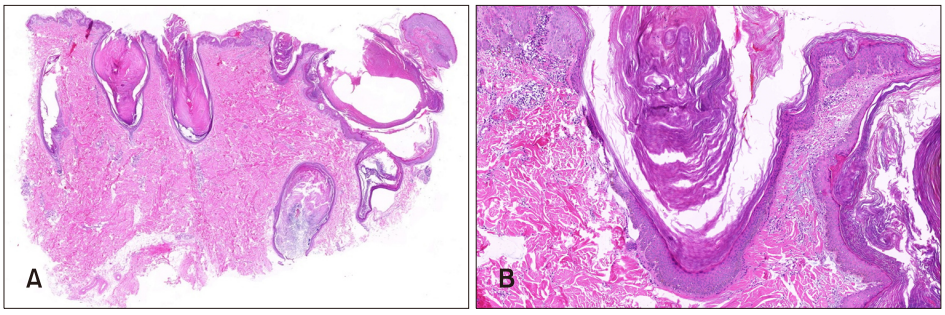

Fig. 2. Histopathological findings of extensive nevus comedonicus. (A) A multiplicity of the invagination of the follicular infundibulum with a keratin plug is shown (H&E, scanning view). (B) Projecting bulbous proliferation of infundibular keratinocytes and perifollicular inflammatory infiltrates are evident (H&E, ×40).

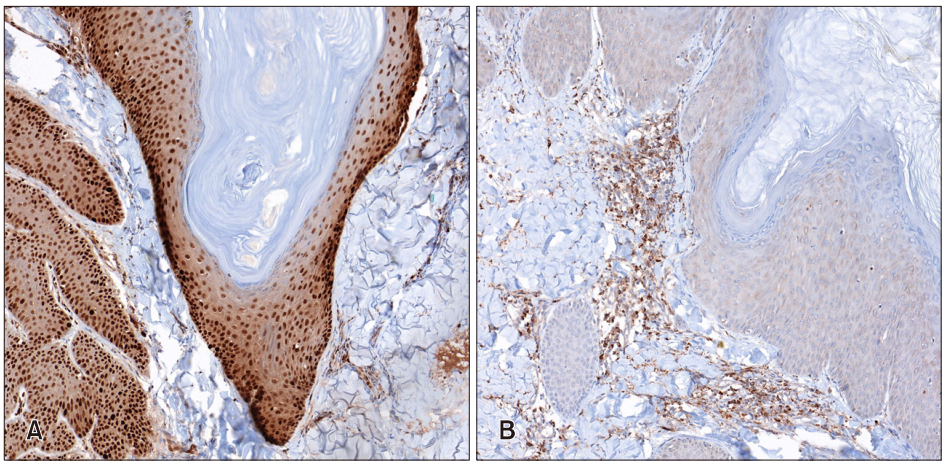

Fig. 3. Immunohistochemical staining (A: ×100, B: ×100) of extensive nevus comedonicus with proliferating cell nuclear antigen (PCNA) and CD68. Increased expression of (A) PCNA in the infundibular keratinocytes and (B) CD68 in the cells of the dermis near the proliferating infundibular keratinocytes is evident.

was first treated with systemic doxycycline (100 mg twice a day for 1 month), topical adapalene, incision & drainage, and triamcinolone intralesional injection (10 mg/ml), followed by systemic isotretinoin (10 mg twice a day for 3 months), incision & drainage, and triamcinolone intralesional injection (10 mg/ml). However, as we expected, they were not effective. Finally, he was treated with adalimumab (80 mg subcutaneously biweekly for 1 month, after then 40 mg subcutaneously weekly for 3 months). A flare-up of inflammatory nodules in nevus comedonicus was not seen during treatment with adalimumab. Comedones have also improved. Remarkable clinical improvement was obtained in physician global assessment and visual analogue scale (VAS) score. Physician global assessment was changed from "very severe" to "mild", and the pain that was difficult to fall asleep was relieved from 9 to 1 on the VAS score (Fig. 1D, E). Written informed consent form was obtained for publication of photographs.

DISCUSSION

Extensive nevus comedonicus is very rare, with only a few cases reported in Korea[4,5]. Nevus comedonicus is usually treated conservatively, with moisturizers, topical corticosteroids, and keratolytics[6]. Retinoids have also been used[7]. Topical tretinoin treatment has shown limited efficacy in nevus comedonicus[8]. Topical tazarotene as monotherapy or in combination with topical mometasone furoate or calcipotriene has yielded better results[9]. Oral isotretinoin may be an option in extensive nevus comedonicus with inflammatory nodules and cysts[10]. In addition, topical clindamycin 1% solution/gel, systemic tetracycline and systemic rifampicin, which are evidence-based medical therapeutic options for hidradenitis suppurativa, can be considered extensive nevus comedonicus with hidradenitis suppurativa-like lesions[11]. In patients refractory to medical treatment, adalimumab or second line therapy can be required[11]. Surgical excision can be used for the removal of sinus tract, scarring and localized nevus comedonicus[3]. Superficial shaving, comedo extraction and dermabrasion are also therapeutic options for nevus comedonicus[3]. Laser treatment with erbium YAG, CO_2 laser or diode laser has been successful in patients with nevus comedonicus[12-14]. Despite these various therapeutic options, complete resolution may not be achieved. There are no data available on the treatment of nevus comedonicus with topical adapalene and systemic or topical bexarotene. Other drugs of interest for treating nevus comedonicus are fibroblast growth factor receptor inhibitors, interleukin-1 α inhibitors, and γ-secretase-targeting agents[15-17]. Our patient's extensive nevus comedonicus with inflammatory nodules and cysts was successfully treated with subcutaneous injection of adalimumab, which is an inhibitor of tumor necrosis factor (TNF)-alpha[18]. TNF-alpha is one of the cytokines which are involved in hidradenitis suppurativa pathogenesis. Inflammatory nodules and cysts in this case can be hidradenitis suppurativa-like lesions complicating nevus comedonicus. Dermatologist taking care of patients with hidradenitis suppurativa-like lesions should be accustomed to disease severity scores, such as Hurley staging, modified Sartorius score, physician global assessment and hidradenitis suppurativa clinical response, and patient reported outcomes including visual analogue pain scale, dermatology life quality index, and work productivity and activity impairment questionnaire[19]. We assessed improvement of the patient with nevus comedonicus accompanying hidradenitis suppurativa-like lesions using physician global assessment and visual analogue pain scale. Mechanical stress and hormonal changes can be a triggering or worsening factor for hidradenitis suppurativa-like lesions in nevus comedonicus[20]. Only several reports have described hidradenitis suppurativa-like lesions in nevus comedonicus[20]. In addition, there was only one report on adalimumab used for treatment of hidradenitis suppurativa-like lesions complicating nevus comedonicus in a prepubertal child, and has not yet been reported in Korea[18]. Adalimumab may be a therapeutic option for patients with extensive nevus comedonicus and severe cutaneous inflammation. We herein report a case of extensive nevus comedonicus with inflammatory nodules and cysts controlled with adalimumab.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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