



CASE REPORT

Treatment of Hidradenitis Suppurativa Patient with Klinefelter Syndrome by Adalimumab

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Hidradenitis suppurativa (HS) is a chronic, inflammatory and painful skin disease with recurrent nodules and tracts involving the intertriginous regions. It is known that the patient with HS shows an increased risk of metabolic disorders such as diabetes, metabolic syndrome and autoimmune diseases. Klinefelter syndrome (KS) is a sex chromosomal disorder occurring in males due to an abnormality of sexual differentiation, characterized by 47, XXY karyotype. Also, KS is related with somatic comorbidities such as metabolic syndrome, autoimmune and rheumatologic disorders as HS is. We report a HS patient with KS who shows a big improvement while on tumor necrosis factor-alpha inhibitor treatment. (*Ann Dermatol* 31(4) 446~449, 2019)

-Keywords-

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INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic recurrent suppurative skin disorders, mostly involving axillae, inguinal

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area, buttock and perineum. It occurs more frequently in females than in males. Although the etiology of HS remains poorly understood, an inappropriate immunologic reaction to unknown antigen is suggested to play a role¹. HS patients are at high risk for various metabolic diseases such as diabetes mellitus, dyslipidemia, and obesity². Obesity is associated with the increased levels of cytokines such as tumor necrosis factor-alpha (TNF- α), derived from adipocyte. And overexpressed TNF- α is shown to be related to the development and the severity of HS³. Klinefelter syndrome (KS) is chromosomal abnormality in males, characterized by 47, XXY. Symptoms include gynecomastia, small testes and low testosterone levels. A number of cases have suggested that the coexistence of KS and autoimmune diseases may result from hypogonadism⁴ and decreased testosterone level⁵. Furthermore, patients with KS tend to have more metabolic diseases such as diabetes and obesity compared to normal male⁶. We report a rare case of HS who was already suffering KS, diabetes and metabolic syndrome. We thought these comorbidities played an important role in HS development and exacerbation in our case, although an exact mechanism is unknown.

CASE REPORT

A 30-year-old male patient was referred to the dermatologic clinic with purulent nodules and fistulas around the anus and perineal area. The patient was diagnosed with perianal abscesses. Then he received drainage and surgical resection several times for recurrent purulent nodules and took third generation cephalosporine antibiotics intermittently. But the symptoms got worse, so he was referred to Department of Dermatology, Soon Chun Hyang University College of Medicine, Cheonan. Multiple puru-

lent nodules with tenderness and odor were present around the anus and perineum, accompanied by scar and sinus on the periphery (Fig. 1A). Hemorrhoid and anal fistula were ruled out by the clinical features and relapsing course of disease despite several times of surgical resection. Endoscopic examination revealed no significant findings for inflammatory bowel disease. Similar purulent nodules had previously existed on his both axilla which had disappeared after surgical resection. Only post-operative scar remained on axilla (Fig. 1B).

He has been diagnosed with KS (genetic testing, 47XXY) (Fig. 2), diabetes and cataracts in the past. Besides, he was obese (body mass index, 31.6 kg/m²) and mentally retarded. His luteinizing hormone (LH) (30.56 mIU/ml) and follicle-stimulating hormone (FSH) (52.40 mIU/ml) levels were high and his testosterone level was low (2.16 ng/ml). We diagnosed him as HS (Hurley stage III) based on clinical findings, and then, we prescribed minocycline 400 mg daily for 15 months with intralesional triamcinolone injection twice a month. However, the patient experienced a recurrence of his symptoms repeatedly, so we did punch biopsy and tissue cultures from the perineal lesion to differentiate other infectious diseases. Histological examination revealed extensive fibrosis and inflammatory cell infiltration in the dermis to subcutis (Fig. 3). Tissue cultures were negative for bacteria, mycobacteria, and fungi. Finally, we started adalimumab (HUMIRA[®]; AbbVie, Maidenhead, UK). He reported that symptoms including pain, pus, odor, and erythema improved immediately after the first treatment with adalimumab 160 mg. Currently, he is maintaining treatment with adalimumab 40 mg weekly, and is

showing continuous improvement (Fig. 4). We received the patient's consent form about publishing all photographic materials.

DISCUSSION

HS is a chronic inflammatory skin disease affecting apocrine gland-rich areas and presenting with painful nodules, abscesses, sinus tracts and scarring. The etiology of HS is still not clearly understood. But, its multi-factorial causes include folliculosebaceous anatomical abnormalities, genetic mutations, immunologic dysregulation and adnexal microbiota⁷.

Numerous studies have reported an increased level of TNF- α in the lesional and non-lesional skin of patients



Fig. 2. Chromosome analysis of the patient demonstrating the karyotype of KS, 47XXY.



Fig. 1. (A) Deep-seated, inflamed and painful nodules with odorous discharge from perianal lesions and scar. (B) Postoperative scar on the axilla after surgical resection.

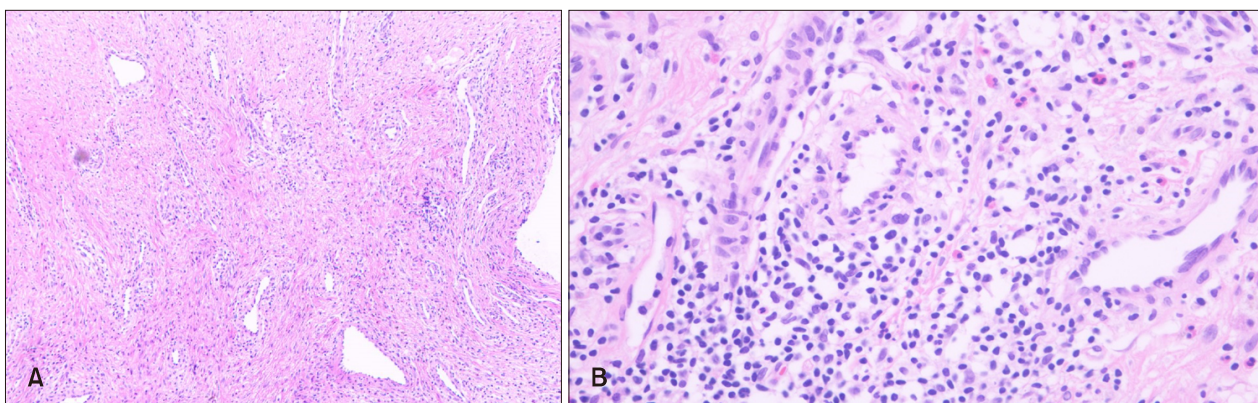


Fig. 3. (A, B) Histological examination revealed extensive fibrosis and inflammatory cell infiltration in the dermis to subcutis (H&E: A, $\times 100$; B, $\times 400$).



Fig. 4. Improved and decreased the painful and purulent nodules around the perianal lesions after 2nd adalimumab injection.

with HS, becoming for the basis of targeted treatment using TNF- α -biologics⁷. Previous studies have shown that when the patient is obese, macrophages in visceral fat secrete TNF- α , which exacerbates HS⁸. Adalimumab (HUMIRA[®]) is the only approved TNF- α monoclonal antibody for the treatment of moderate to severe HS⁸. And its clinical effect was confirmed again in this case.

Although a consensus about the relationship between HS and KS is not established yet, low testosterone level in KS may have contributed to exacerbate our patient's condition by increasing TNF- α . It may also be associated with the female predominance in HS⁸. And metabolic diseases such as diabetes and obesity may also synergistically affected the HS development in our case.

KS, known as 47, XXY or XXXY, is the set of symptoms that result from two or more X chromosomes in males due

to nondisjunction of the sex chromosomes. Various studies have determined KS incidence to be 1:1,000 in live male birth and only 25% are diagnosed through life⁹. The prototype of KS is a tall stature, gynecomastia, small testes with azoospermia and hypergonadotrophic hypogonadism. Hormone levels of gonadotropins such as FSH and LH in KS patients are increased¹⁰ and testosterone levels are decreased to about half of the normal.

It has been reported that various KS comorbidities such as osteoporosis, metabolic disease and diabetes are related with hypogonadism^{9,11}. Also, The coexistence of rheumatologic and autoimmune diseases associated with gonadal dysgenesis and/or KS is reported in many cases¹⁰. Seminog et al.¹² reported that the risk of female-predominant autoimmune disease, such as multiple sclerosis, acquired hypothyroidism, rheumatoid arthritis, Sjogren's syndrome and systemic lupus erythematosus, had increased in males with KS. Considering that KS is a disease related with an extra X chromosome (i.e., XXY), it is suggested that the abnormality of X chromosome contributed to the pathogenesis of the female-predominant autoimmunity in KS¹². It is known that males with deficient sex hormones have more prevalence of autoimmune diseases, which means that testosterone may cause immunosuppression. Testosterone is suggested to have anti-inflammatory functions via both cellular and humoral immune suppression. Testosterone deficiency is linked with an increase of various inflammatory markers, such as TNF- α ⁴. Furthermore, Bobjer et al.¹³ found males with lower testosterone, but without manifestations of systemic disease, had higher levels of pro-inflammatory markers including TNF- α in young age. Many cases of coexistence of KS and autoimmune diseases with female predominance have been reported, but no case has been reported with HS¹². As far as we know, this is the first case of a patient coexisting KS with HS. And

adalimumab showed marked improvement in our case. Thus, we supposed this may be associated with an increased TNF- α in our patient. Herein, we report a rare case of HS in which KS was concurrently present and great response occurred to adalimumab therapy.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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