negative for known KIT, BRAF, MEK, or NRAS gene mutations in melanomas. In recent study on multiple primary superficial spreading melanomas, CDKN2A gene mutation was statistically significant in these cases other than non-multiple melanoma cases[5]. Therefore, we suggest comparing genetic mutations in acral MPMs with solitary cases for the further studies.

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Infliximab for Treatment of Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis Syndrome: A Case Report

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Dear Editor:

A 26-year-old Japanese man presented with high fever (>38.0°C). He had a history of intractable acne of the face, chest, and back beginning from his early teens. The facial acne had worsened during the previous 2 weeks, and was accompanied by diffuse arthralgia followed by high fever. On admission, the patient had multiple erythematous follicular papules and pustules on his forehead, lower jaw, and posterior neck (Fig. 1A). The white blood cell count was $11.8\times10^3/\mu l$ (normal 4.0 to $8.5\times10^3/\mu l$) with 66% neutrophils (normal 38% to 58%), 25% lymphocytes (normal 27% to 46%), and 9% monocytes (normal 3% to 7%). The C-reactive protein level was 4.86 mg/dL (normal <0.3 mg/dl), the tartrate-resistant acid phosphatase-5b level was 638 mU/dl (normal 170 to 590 mU/dl), and the serum type I collagen cross-linked N-telopeptides (s-CTx) level was 66.9 nmol bone collagen equivalent (BCE)/mmol・Cr (normal <35.3 nmol BCE/mmol・Cr). All other laboratory values were normal. Culture of a facial pustule was negative; histological examination of the pustule folliculitis. Bone scintigraphy and enhanced magnetic resonance imaging showed sacroiliac arthritis (Fig. 2). We diagnosed synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome, because he ex-

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hibited severe acne and sacroiliac arthritis. We initiated treatment with a single dose of intravenous ibandronic acid (1 mg) and 60 mg oral loxoprofen 2 to 3 times daily, but the symptoms persisted and worsened. Therefore, we changed the treatment to intravenous infliximab (5 mg/kg ×1 dose at week 0, 2, 4, 6, and 8, and every 8 weeks thereafter). The acne and arthritis exhibited rapid and dramatic improvement after a single infusion of infliximab and he has been relapse-free during 10 months of treatment (Fig. 1B).

SAPHO syndrome was first described in 1987 and it has been predominately asspociated with hyperostosis of the anterior chest and with various skin abnormalities, including palmoplantar pustulosis, hidradenitis suppurativa, acne conglobata, and acne fulminans[1]. *Propionibacterium acnes* has been suggested as a possible etiologic agent, and tumor necrosis factor (TNF)-α may have a role in the pathogenesis. *P. acnes* infection stimulates keratinocyte production of interleukin (IL)-1α and TNF-α in cases of acne conglobata[2], and Wagner et al have found TNF-α -producing cells in bone biopsy specimens from patients with SAPHO syndrome[3].

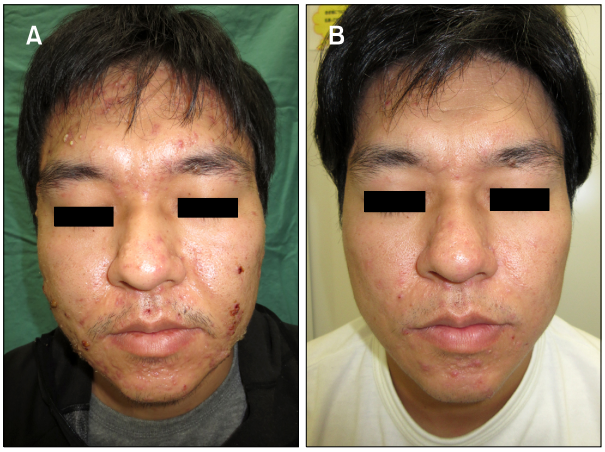

Fig. 1. Physical findings. (A) On admission, the patient had multiple erythematous follicular papules and pustules, approximately 5 mm in diameter, on the forehead, lower jaw, and posterior neck. Multiple scars from healed acne lesions on the back and bilateral forearms were also noted. (B) Physical findings after a single intravenous dose of ibandronic acid and fifth infusion of infliximab. The acne lesions almost disappeared from the face.

There is no standard treatment for SAPHO syndrome. First-line treatment options include non-steroidal anti-inflammatory drugs, colchicine, corticosteroids, bisphosphonates (i.e., ibandronic acid), and disease-modifying agents such as infliximab[4]. Bisphosphonates inhibit bone remodeling by osteoclasts and exhibit anti-inflammatory activity through suppression of IL-1, IL-6, and TNF-α. Response to bisphosphonates in cases of SAPHO syndrome is measured by monitoring bone resorption markers including s-CTx, but improvement may take several months[5]. Infliximab is a monoclonal anti-TNF-α antibody that neutralizes TNF-α, leading to a reduction in pro-inflammatory cytokines including IL-1 and IL-6. In our patient, infliximab, but not ibandronic acid, was associated with rapid and dramatic remission of severe acne and osteitis. Accumulation of additional cases of infliximab-responsive SAPHO syndrome is necessary to determine whether infliximab can be discontinued upon remission.

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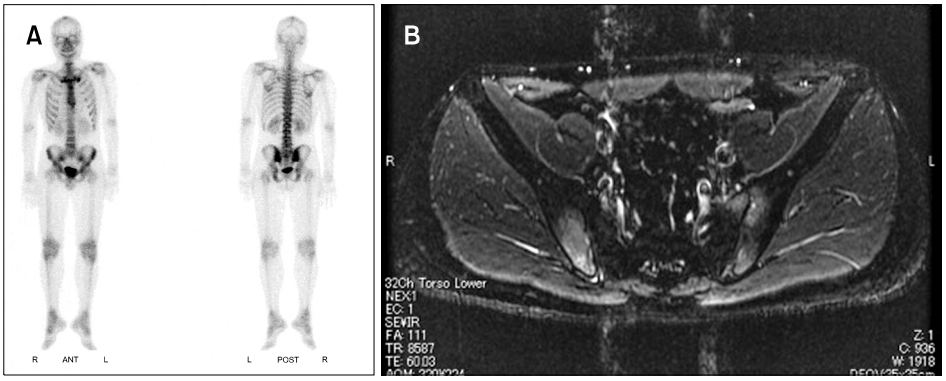

Fig. 2. Evaluation of bone and joint lesions before the infusion of infliximab. (A) Bone scintigraphy shows abnormal radioisotope accumulation at the sacroiliac joints. (B) Enhanced magnetic resonance imaging using short inversion time (TI) inversion recovery sequences shows increased signal intensity at the sacroiliac joints and the iliums.

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