

1. Templeton AJ, McNamara MG, Šeruga B, *et al.* Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *J Natl Cancer Inst* 2014; 106: dju124.
2. Templeton AJ, Ace O, McNamara MG, *et al.* Prognostic role of platelet to lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev* 2014; 23: 1204-12.
3. Fujisawa Y, Yoshino K, Otsuka A, *et al.* Baseline neutrophil to lymphocyte ratio combined with serum LDH level associated with outcome of nivolumab immunotherapy in a Japanese advanced melanoma population. *Br J Dermatol* 2018; 179: 213-5.
4. Nakamura Y, Kitano S, Takahashi A, *et al.* Nivolumab for advanced melanoma: pretreatment prognostic factors and early outcome markers during therapy. *Oncotarget* 2016; 7: 77404-15.
5. Chasseuil E, Saint-Jean M, Chasseuil H, *et al.* Blood predictive biomarkers for nivolumab in advanced melanoma. *Acta Derm Venereol* 2018; 98: 406-10.
6. Garnier M, Zaragoza J, Bénétou N, *et al.* High neutrophil-to-lymphocyte ratio before starting anti-PD1 immunotherapy predicts poor outcome in patients with metastatic melanoma. *J Am Acad Dermatol* 2018; 79: 165-7.
7. Minowa T, Kato J, Hida T, *et al.* Prognostic role of neutrophil to lymphocyte ratio in advanced melanoma treated with anti-programmed death-1 therapy. *J Dermatol* 2018; 45: e250-1.
8. Khoja L, Atenafu EG, Templeton A, *et al.* The full blood count as a biomarker of outcome and toxicity in ipilimumab-treated cutaneous metastatic melanoma. *Cancer Med* 2016; 5: 2792-9.
9. Failing JJ, Yan Y, Porrata LF, Markovic SN. Lymphocyte-to-monocyte ratio is associated with survival in pembrolizumab-treated metastatic melanoma patients. *Melanoma Res* 2017; 27: 596-600.
10. Zaragoza J, Caille A, Beneton N, *et al.* High neutrophil to lymphocyte ratio measured before starting ipilimumab treatment is associated with reduced overall survival in patients with melanoma. *Br J Dermatol* 2016; 174: 146-51.

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Successful treatment of psoriatic arthritis associated with adrenal hypoplasia congenita using infliximab

Psoriatic arthritis (PsA) is inflammatory arthritis associated with psoriasis, which often leads to impaired function and reduced quality of life [1]. Adrenal hypoplasia congenita (AHC) is a rare congenital disorder typically presenting with primary adrenal insufficiency (PAI) during infancy [2]. PsA associated with AHC is extremely rare, and limited information is available in the English literature. Moreover, efficient and safe therapeutic strategies for this combination have not been established. Here, we report a case of PsA associated with AHC, successfully treated with infliximab. A 21-year-old Japanese woman with a five-year history of psoriasis was referred to our hospital. She showed typical clinical and pathological features of psoriasis (*figure 1A-D*). She also had swollen toes (*figure 1E*) and arthralgia

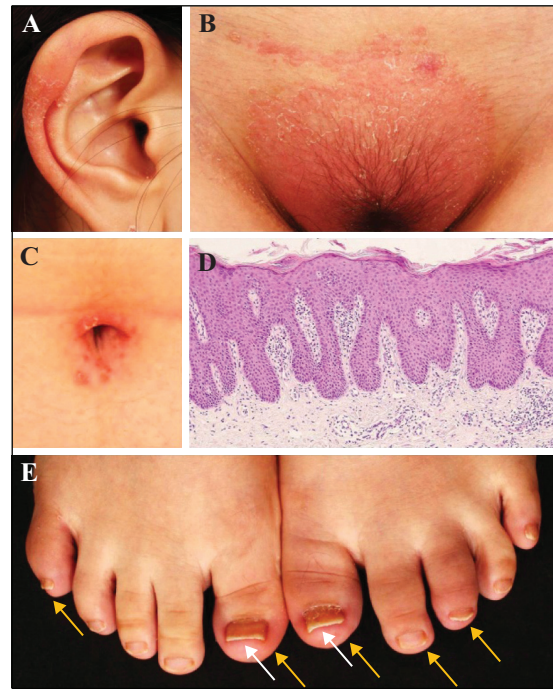


Figure 1. Clinical cutaneous manifestations and histological findings of the case. Well-demarcated, erythematous, scaly plaques are present on the auricle of the ear (A), pubic region (B), and umbilicus (C). D) A skin biopsy specimen obtained from the scaly erythema in the umbilical area shows parakeratosis and acanthosis with downward elongation of rete ridges. E) Discolouration of the big toenails (white arrows) and sausage toes (dactylitis) (yellow arrows) are seen.

of the knees for one year. The laboratory results were as follows: rheumatoid factor and anti-cyclic citrullinated peptide antibodies were negative, erythrocyte sedimentation rate (ESR) of 54 mm/h (reference: <15 mm/h), C-reactive protein at 32.5 mg/L (reference: <3.0 mg/L), and matrix metalloproteinase-3 at 179.2 ng/mL (reference: 1.25-20.0 ng/mL). The patient did not carry HLA-B27 alleles. Based on these findings, she was diagnosed with PsA. The psoriasis area and severity index (PASI) score was 5.4, while the 28-joint disease activity score based on ESR was 5.5, which was considered to represent a high level of disease activity.

It should be noted that the patient had been diagnosed with AHC in early infancy, followed by a diagnosis of hypergonadotropic hypogonadism in adolescence. She had no family history of AHC. She had been treated with oral hydrocortisone (20 mg/day), fludrocortisone (0.075 mg/day), and oestrogen-progestogen replacement therapy, and there were no symptoms of adrenal failure. Infliximab was initiated at 5 mg/kg along with methotrexate (4 mg/week). Rapid and significant improvements were noted two weeks after the initial infliximab injection, and her American College of Rheumatology (ACR) Criteria score indicated an ACR50 response. After the second injection (Week 6), the number of tender and swollen joints decreased from 2 to 0 and 7 to 0, respectively. Subsequently, she achieved an ACR70 response and PASI-100 response at 14 weeks. Although she received infliximab for more than

two years, no adverse events were observed throughout the treatment course.

Here, we present a case of PsA associated with AHC, which was successfully treated with infliximab. This case offers two important clinical suggestions.

First, PsA can occur with AHC. Because of the rarity of AHC, the precise rates of AHC with rheumatic diseases, such as PsA, have not been well established. However, it was recently reported that PAI was significantly associated with PsA. A population-based case-control study was conducted to investigate a potential association between PAI and PsA. It revealed that the adjusted odds ratio was 3.48 (95% CI: 1.54-7.81; $p = 0.003$) for PsA in individuals with PAI [3]. This rare combination of PsA and PAI may be biologically plausible. In patients with PAI, the blood cortisol level under conditions of stress is low [4]. Previous studies have shown that cortisol suppresses tumour necrosis factor (TNF)- α expression by affecting gene transcription and post-translational events [5]. In addition, synovial samples from patients with PsA showed marked expression levels of proinflammatory cytokines including TNF- α [6]. Thus, we hypothesized that adrenal insufficiency in PsA patients might fail to suppress TNF- α levels in the synovium and synovial fluid, and may consequently result in severe joint damage.

Second, infliximab can be a treatment option for PsA patients with AHC. According to evidence-based treatment recommendations for PsA, anti-TNF- α agents should be prescribed as initial treatment for those with active articular disease [7, 8]. However, there are limited data to guide treatment for PsA patients with PAI. In our case, AHC was stable with hormone replacement therapy, therefore we selected infliximab with consideration of the severity of the articular disease. Consequently, the patient achieved marked clinical improvement without a harmful influence on AHC. To the best of our knowledge, this is the first report to show the efficacy and safety of infliximab for PsA associated with PAI and AHC.

In conclusion, PsA can occur with AHC, and infliximab may be used as treatment for PsA patients with AHC. Although a long-term follow-up and further studies are required to clarify the safety of infliximab, our experience, in this case, provides evidence of successful treatment for PsA patients with PAI. ■

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1. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med* 2017; 376: 957-70.

2. Suntharalingham JP, Buonocore F, Achermann AJ, Achermann JC. DAX-1 (NROB1) and steroidogenic factor-1 (SF-1, NR5A1) in human disease. *Best Pract Res Clin Endocrinol Metab* 2015; 29: 607-19.

3. Jensen P, Egeberg A, Thyssen JP, Gislason G, Skov L. Psoriatic arthritis, but not psoriasis, is associated with primary adrenal insufficiency. *Acta Derm Venereol* 2017; 97: 519-21.

4. Minari R, Vottero A, Tassi F, et al. A novel mutation in the NROB1 gene in a family with monozygotic twin sisters and congenital adrenal hypoplasia affected children. *Hormones (Athens)* 2015; 14: 160-6.

5. Steer JH, Kroeger KM, Abraham LJ, Joyce DA. Glucocorticoids suppress tumor necrosis factor-alpha expression by human monocytic THP-1 cells by suppressing transactivation through adjacent NF-kappa B and c-Jun-activating transcription factor-2 binding sites in the promoter. *J Biol Chem* 2000; 275: 18432-40.

6. Ritchlin C, Haas-Smith SA, Hicks D, Cappuccio J, Osterland CK, Looney RJ. Patterns of cytokine production in psoriatic synovium. *J Rheumatol* 1998; 25: 1544-52.

7. Coates LC, Kavanaugh A, Mease PJ, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis. *Arthritis Rheumatol* 2016; 68: 1060-71.

8. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis* 2016; 75: 499-510.

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Infantile bullous pemphigoid following vaccination

Bullous pemphigoid (BP) is a rare autoimmune blistering disease associated with circulating autoantibodies against the hemidesmosomal proteins, BP180 (BPAG2) and BP230 (BPAG1) [1]. In particular, BP180 autoantibodies are critical for disease induction [1]. BP mostly affects the elderly and manifests with generalized tense blisters and eczematous- or urticarial-like lesions [1], while infantile BP is considered rare and characterized by major acral involvement [2]. BP diagnosis is based on clinical features and laboratory findings. Histological examination reveals subepidermal blisters and inflammatory infiltrates consisting mainly of eosinophils and neutrophils [1]. Direct immunofluorescence (DIF) represents the gold standard for diagnosis and shows linear deposition of IgG and C3 along the basement membrane zone (BMZ) [1]. Indirect immunofluorescence (IIF) on normal human salt-split skin (IIF-SSS) shows linear IgG deposits at the epidermal side in 96% of patients [3]. Enzyme-linked immunosorbent assays (ELISAs) are an additional highly sensitive test for BP diagnosis.

A five-month-old female was referred to our hospital due to a two-week history of asymptomatic urticarial plaques with vesicles on the extremities (*figure 1A-D*). Mucous membranes were not involved. She had received a first dose of hexavalent (diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and Haemophilus influenzae B) and pneumococcus vaccination four weeks before the onset of skin lesions. Laboratory investigations revealed leukocytosis with eosinophilia. Histopathological examination of an urticarial lesion of the leg showed vacuolization along the dermoepidermal junction and a perivascular infiltrate of lymphocytes and eosinophils in the papillary dermis (*figure 1E*). DIF microscopy of perilesional skin revealed continuous linear deposits of IgG and C3 along the BMZ