

A case of psoriasis accompanied by arthritis after delivery

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Summary

Psoriasis and psoriatic arthritis are chronic inflammatory diseases of the skin and joints, but the relationship between them has not been fully understood. Since the delay of treatment for psoriatic arthritis can result in the severe deformities, it is important to identify the pathological triggers of the arthritis. On the other hand, many reports suggest that the changes of immune balance during pre/postpartum period are associated with the state of autoimmune diseases. Here, we report a female case with psoriasis whose arthritis may be triggered by the delivery. Our report suggests that immune tolerance may diminish in the postpartum period, which may alter the susceptibility to arthritis. Female patients should be followed-up carefully during postpartum period against the development of arthritis.

Keywords: Autoimmune diseases, immune tolerance, psoriatic arthritis

1. Introduction

Psoriasis is a chronic inflammatory dermatosis of the skin affecting as many as 1-2% of Caucasian and 0.02-0.1% of Japanese people (1). Among them, some cases are thought to be accompanied with arthritis. Psoriatic arthritis is different from rheumatoid arthritis (RA) in terms of its predilection for the distal interphalangeal joints and negative rheumatoid factors (RF), and therefore is included in seronegative spondyloarthritis. The arthritis is associated with cutaneous psoriasis in more than 90% of cases, and is preceded by the cutaneous lesion in 75% cases (2). Though treatment with monoclonal antibodies against tumor necrosis factor (TNF) (*e.g.* infliximab and adalimumab) or soluble TNF receptor (etanercept) have been in clinical use recently, the delay of treatment may result in the reduced quality of life and the severe deformities resembling the joint changes seen in RA. Therefore, the early detection and treatment of arthritis is necessary in psoriasis patients, and it is important to identify the pathological triggers of the arthritis. Until today, genetic factors, mechanical stimulations,

infections, drugs, and immunologic factors are reported as triggers of psoriatic arthritis (2). Here, we report a female case with psoriasis whose arthritis may be triggered by the delivery.

2. Case reports

A 37-year-old Japanese female visited our hospital, for the treatment of the eruption and arthritis. There was no record of similar conditions in her family history. She had been diagnosed as having psoriasis vulgaris more than 20 years ago, and treated with corticosteroid ointments. She had never had arthralgia. She got her first child 3 months before the first visit, without any problems related to the delivery. However, she started to complain of arthralgia after the delivery, and the arthritis as well as the eruption worsened gradually. On physical examination, the patients had the skin lesions in the trunk and extremities. The each lesion was well-demarcated, erythematous plaque covered by silver-white scales (Figure 1). Neither pustules nor nail changes were observed. She could not stand up by herself because of her joint swelling and pain, which was present in finger, wrist, elbow, knee, and ankle joints.

As laboratory findings, the white blood cell (WBC) count and C-reactive protein (CRP) levels was slightly increased at 9,000/uL and 2.07 mg/dL, respectively. Antinuclear antibody or anti-cyclic citrullinated

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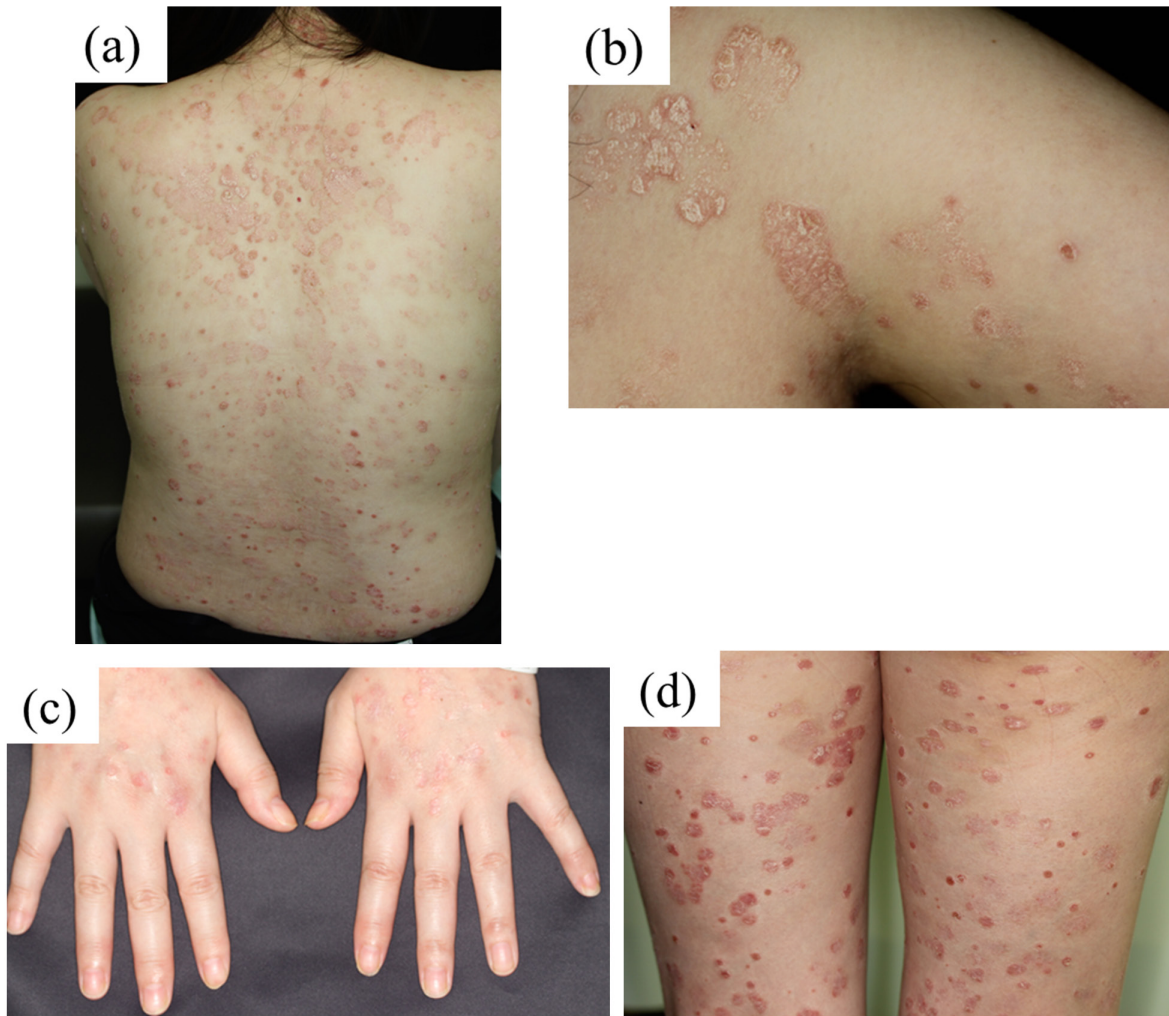


Figure 1. Well-demarcated, erythematous plaques covered by silver-white scales in the back (a), upper arm (b), hands (c), and thighs (d).



Figure 2. ^{99m}Tc -MDP bone scintigraphy showing the increased uptake in finger, wrist, elbow, knee, and ankle joints.

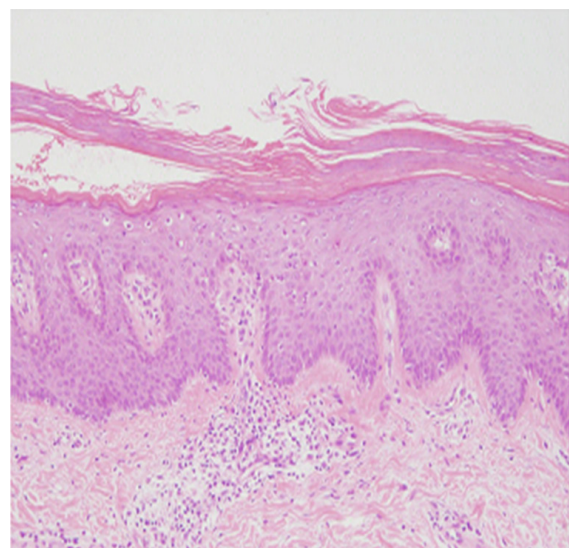


Figure 3. Haematoxylin and eosin (H&E) staining of biopsy specimen from cutaneous lesion.

peptide (CCP) antibody was not detected. RF was also negative (7 IU/mL, normally < 20 IU/mL), and the serum level of matrix metalloproteinase (MMP)-3 was not increased (32.1 ng/mL, normally < 59.7 ng/mL). Laboratory results of other blood cell counts, blood chemistry analysis (including serum albumin, p-glucose or HbA1c), urinalysis, and chest radiography were within normal limits. Bone scintigraphy showed increased uptake in multiple joints (Figure 2), which were identical to the swollen and painful joints.

A skin biopsy from the affected area revealed acanthosis, hypogranulosis and extensive overlying parakeratotic scale in the epidermis. Perivascular infiltration of neutrophils and lymphocytes in the dermis was also seen (Figure 3).

Based on the findings of blood examination, bone scintigram and skin biopsy, she was diagnosed as having psoriasis and postpartum development of

arthritis. Her Psoriasis Area and Severity Index (PASI) of the cutaneous lesion, DAS28-CRP and visual analogue scale (VAS) of the arthritis was 22.6, 3.9, and 60, respectively.

The patient was treated with infliximab immediately. After three times of administration, her eruption and arthritis have disappeared completely (Figure 4). The PASI and VAS was also improved dramatically as shown in Figure 5.

3. Discussion

Though the aetiology of psoriasis and psoriatic arthritis is multifactorial, one of the most likely pathogenic agents may be T cell (2). This suggestion is supported by many clinical studies for the treatment of psoriasis and psoriatic arthritis: e.g. the clinical efficacy of cyclosporin, a highly selective antagonist of T-cell proliferation and activation (2). Psoriasis has been regarded as the Th1-mediated disease like RA and Crohn disease (2-5). However, in the last few years, Th17, a new subset of CD4 T cells, has been identified, based on their production of IL-17 (6). There are many reports that indicate IL-17 is associated with the pathogenesis of psoriasis (7). In addition, it was reported that regulatory T cells (Treg), which suppress CD4 helper T cells, are impaired in many autoimmune diseases (8). Psoriatic Treg have also been found to defect the activity, which may result in the auto-reactive T cell activation and contribute to the pathogenesis for psoriasis (9). Taken together, in psoriasis and psoriatic arthritis, Th1 and Th17 should be predominant rather than Th2 and Treg, like RA.

On the other hand, although the change of immune system during pregnancy has not been fully clarified,

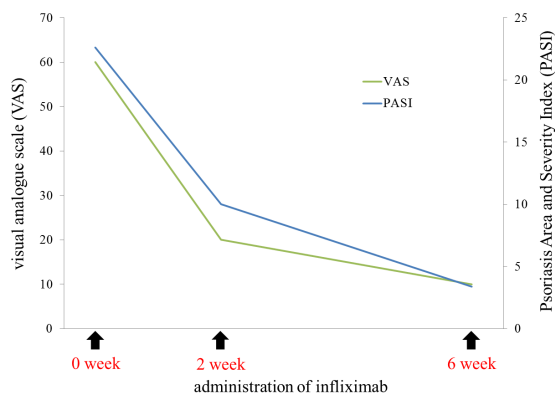


Figure 5. The time course of the changes of PASI of the cutaneous lesions and VAS of the arthritis during the treatment with infliximab, which was administered three times (0, second and, sixth week).

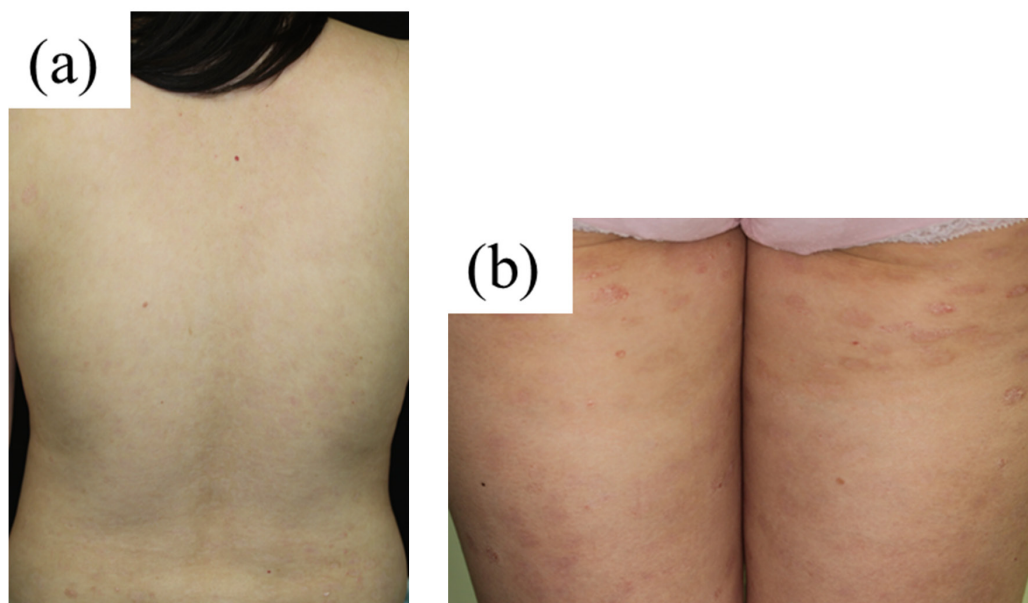


Figure 4. Macroscopic appearance of the back (a) and thighs (b) of the patient after three times of infliximab administration.

many studies have reported a predominant Th2/Treg-type immunity and a suppressed Th1/17-type immunity during normal pregnancy (10). These immunological changes seem to be necessary for successful pregnancy, because the predominance of Th1/17-type immunity over Th2/Treg-type immunity is observed in abortion patients (10). Estrogens and progesterone are known to inhibit Th1 immune responses including TNF- α and IL-12 production, while induce Th2 immune responses like IL-10 and IL-4 production (11). These hormones are significantly increased during pregnancy in comparison with the postpartum period. In addition, during pregnancy, Th1-type immunity is well controlled to avoid its overstimulation, probably due to the suppression by Treg, which are observed to increase in decidua (11). Furthermore, the level of IL-17 in normal pregnancy is lower than that in non-pregnancy, and Th17 is thought to be inhibited in the former condition (12). Taken together, in pregnancy, Th2/Treg-type immunity should be predominant over Th1/Th17-type immunity by the above changes in the hormones and cytokines, and the subsequent rebound of Th1/Th17 may occur after delivery.

The above notions suggest that immune tolerance may diminish in the postpartum period, which may alter the susceptibility to autoimmune diseases including RA. Actually, postpartum onset of RA by the Th1/Th17 activation has been well described (13). On the other hand, psoriasis is known to be one of the diseases which are improved during pregnancy (14). Furthermore, there is a very old report that states 6 of 20 psoriasis patients developed arthritis during postpartum period (15). Since then, however, there have been no reports describing similar cases. Our case is the second to suggest that the changes in immune balance after delivery may be the newly described trigger of arthritis in female patients with psoriasis. From this point of view, female patients should be followed-up carefully during postpartum period against the occurrence of arthritis.

Recent papers have shown that serum IL-17 level is reduced and Treg level is increased after infliximab treatment in psoriasis (16,17). As the limitation of the paper, because blood samples of the patient were not collected, we could not perform time course measurement of IL-17 levels and the number or activity of Treg before and during the treatment with infliximab, which may support our hypothesis. To confirm the immunologic mechanism in female patients with psoriatic arthritis during pre/postpartum period, further studies are needed in a large number of patients in the future.

References

1. Takahashi H, Nakamura K, Kaneko F, Nakagawa H, Iizuka H, Japanese Society for Psoriasis Research.

- Analysis of psoriasis patients registered with the Japanese Society for Psoriasis Research from 2002-2008. *J Dermatol.* 2011; 38:1125-1129.
2. Ciocon DH, Kimball AB. Psoriasis and psoriatic arthritis: separate or one and the same? *Br J Dermatol.* 2007; 157:850-860.
3. Jacob SE, Nassiri M, Kerdel FA, Vincek V. Simultaneous measurement of multiple Th1 and Th2 serum cytokines in psoriasis and correlation with disease severity. *Mediators Inflamm.* 2003; 12:309-313.
4. Berner B, Akça D, Jung T, Muller GA, Reuss-Borst MA. Analysis of Th1 and Th2 cytokines expressing CD4+ and CD8+ T cells in rheumatoid arthritis by flow cytometry. *J Rheumatol.* 2000; 27:1128-1135.
5. Parronchi P, Romagnani P, Annunziato F, Sampognaro S, Becchio A, Giannarini L, Maggi E, Pupilli C, Tonelli F, Romagnani S. Type 1 T-helper cell predominance and interleukin-12 expression in the gut of patients with Crohn's disease. *Am J Pathol.* 1997; 150:823-832.
6. Weaver CT, Harrington LE, Mangan PR, Gavrieli M, Murphy KM. Th17: An effector CD4 T cell lineage with regulatory T cell ties. *Immunity.* 2006; 24:677-688.
7. Li J, Li D, Tan Z. The expression of interleukin-17, interferon- γ , and macrophage inflammatory protein-3 α mRNA in patients with psoriasis vulgaris. *J Huazhong Univ Sci Technolog Med Sci.* 2004; 24:294-296.
8. Buckner JH. Mechanisms of impaired regulation by CD4(+)CD25(+)FOXP3(+) regulatory T cells in human autoimmune diseases. *Nat Rev Immunol.* 2010; 10:849-859.
9. Goodman WA, Cooper KD, McCormick TS. Regulation generation: The suppressive functions of human regulatory T cells. *Crit Rev Immunol.* 2012; 32:65-79.
10. Saito S, Nakashima A, Shima T, Ito M. Th1/Th2/Th17 and regulatory T-cell paradigm in pregnancy. *Am J Reprod Immunol.* 2010; 63:601-610.
11. Robinson DP, Klein SL. Pregnancy and pregnancy-associated hormones alter immune responses and disease pathogenesis. *Horm Behav.* 2012; 62:263-271.
12. Santner-Nanan B, Peek MJ, Khanam R, Richarts L, Zhu E, Fazekas de St Groth B, Nanan R. Systemic increase in the ratio between Foxp3+ and IL-17-producing CD4+ T cells in healthy pregnancy but not in preeclampsia. *J Immunol.* 2009; 183:7023-7030.
13. Ostensen M, Villiger PM. The remission of rheumatoid arthritis during pregnancy. *Semin Immunopathol.* 2007; 29:185-191.
14. Murase JE, Chan KK, Garite TJ, Cooper DM, Weinstein GD. Hormonal effect on psoriasis in pregnancy and post partum. *Arch Dermatol.* 2005; 141:601-606.
15. McHugh NJ, Laurent MR. The effect of pregnancy on the onset of psoriatic arthritis. *Br J Rheumatol.* 1989; 28:50-52.
16. Kagami S, Rizzo HL, Lee JJ, Koguchi Y, Blauvelt A. Circulating Th17, Th22, and Th1 cells are increased in psoriasis. *J Invest Dermatol.* 2010 ; 130:1373-1383.
17. Diluvio L, Romiti ML, Angelini F, Campione E, Rossi P, Prinz JC, Chimenti S, Lamioni A. Infliximab therapy induces increased polyclonality of CD4+CD25+ regulatory T cells in psoriasis. *Br J Dermatol.* 2010; 162:895-897.

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