

Case Report

A Case of Psoriasis Complicated by Breast Cancer after Systemic Treatments Including Biologics

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Psoriasis is a common chronic inflammatory skin disorder that is characterized by scaly, erythematous, sharply demarcated plaques. The treatment for psoriasis has dramatically changed over the last 10 years with the introduction of biologics. However, the risk of cancer induced by biologics for psoriasis has not been fully analyzed, since these agents have such a short history of use. Here we report the case of a 74-year-old woman with psoriasis vulgaris and psoriatic arthritis complicated by breast cancer after systemic treatments including etretinate, cyclosporine, methotrexate, adalimumab, and ustekinumab.

Key words: psoriasis, systemic therapy, biologics, malignancy

Psoriasis is a common chronic inflammatory skin disorder that is characterized by scaly, erythematous, sharply demarcated plaques in different sizes and shapes [1]. Abnormal epidermal proliferation and cellular infiltration including T-cells and neutrophils are histologically observed in the skin lesions [1]. The numbers of Th1 and Th17 cells are particularly elevated in psoriatic patients, and these cells are thought to play critical roles in the pathogenesis [1, 2]. Some patients with psoriasis will develop psoriatic arthritis, which is characterized by diverse clinical features including dactylitis, enthesitis, nail pitting, onycholysis, and axial involvement [3].

The treatment for psoriasis has dramatically changed over the last 10 years with the introduction of biologics. While biologics including anti-TNF- α , anti-IL12/IL-23, anti-IL-17A, and anti-IL-17RA antibodies are all quite effective, they are known to exert immunosuppressive

effects that might increase the risk of infectious diseases or malignancies. Few reports have examined the risk of cancer induced by biologics for psoriasis, since these agents have such a short history of use.

Case Report

A 74-year-old woman was treated at our hospital for psoriasis vulgaris and psoriatic arthritis complicated by breast cancer. She had first developed eruptions and received a diagnosis of psoriasis when she was 17 years old. Decades later, at the age of 55 years, she developed joint pain and was diagnosed with psoriatic arthritis. She underwent several systemic treatments: etretinate (details unknown), adalimumab at 40-80 mg every 2 weeks for 1 year, ustekinumab at 45 mg every 3 months for 7 months, cyclosporine at 150-200 mg/day for 9 months, and methotrexate at 6-12 mg/week for 5 months. Breast tumor was identified at 72 years of age,

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when she was receiving methotrexate at 8 mg/week. Contrast-enhanced T1-weighted fat-saturated magnetic resonance imaging showed regions of clumped, non-mass-like enhancements in all four quadrants of the right breast (Fig. 1A). Cytology of a specimen from fine needle aspiration biopsy showed class V results, and breast cancer was diagnosed. Methotrexate was discontinued and the patient underwent dissection and sentinel lymph node biopsy, which yielded negative results (T3N0M0, stage IIb). The histological type was mucinous carcinoma (Fig. 1B). The patient has since been receiving hormone therapy of anastrozole at 90 mg/day, and no recurrence has been seen. However, her psoriatic skin lesions gradually worsened with an elevated Psoriasis Area and Severity Index (PASI) of 14.0 (Fig. 2A,B). We therefore decided to re-introduce methotrexate at day 90 after its discontinuation, and her PASI promptly decreased to 2.0. No joint symptoms were observed. No recurrence of breast cancer has been seen as of the time of writing, 2 years after re-introducing methotrexate.

Discussion

Psoriasis patients are thought to have an increased risk of some cancers, especially lymphoma, and long-term psoriasis and more severe disease might increase the risk [4]. There are very few case reports of patients with psoriasis and breast cancer [5-7], and the association of psoriasis with the incidence of breast cancer had been controversial [4, 8-11]. However, Chiesa Fuxench *et al.* performed a large-scale cohort study (198,366 psoriasis and 937,716 control group patients) and showed that there was no association of psoriasis with cancer of the breast, colon, prostate, or leukemia, although sig-

nificant associations between psoriasis and each of non-melanoma skin cancer, lymphoma, and lung cancer were identified [12]. In our patient, the breast cancer was diagnosed after systemic treatments for psoriasis including etretinate, cyclosporine, methotrexate, adalimumab, and ustekinumab. Therefore, we considered the possibility that these systemic treatments could have triggered breast cancer in our patient.

Etretinate is a synthetic retinoid in common use in Japan. In general, retinoid is thought to have anticancer activity and fewer immunosuppressive effects. Retinoid therapy alone has not been reported to be associated with a risk of malignancy [13]. Cyclosporine is a calcineurin inhibitor originally used as an immunosuppressive agent for organ transplantation and is well-known to increase the risk of malignancy [14]. In particular, psoriatic patients treated with cyclosporine have been reported to show an increased risk of non-melanoma skin cancers [15]. Methotrexate is a classical antifolate and was originally developed as an anti-cancer agent. In addition, low-dose methotrexate has been widely used as an immunosuppressive agent for inflammatory diseases such as rheumatoid arthritis. The association between methotrexate and risk of malignancy has not been considered significant [16]. Adalimumab is a humanized anti-TNF- α monoclonal antibody that has been in clinical use for around a decade. Very recently, an increased incidence of cutaneous squamous cell carcinomas among patients with psoriasis treated using TNF- α inhibitors has been reported [17]. Ustekinumab is a humanized anti-IL-12/23p40 monoclonal antibody that has been in clinical use since 2010, and has not been reported as associated with any increased risk of malignancy [18]. Although neither of these biologics has been associated with an increased

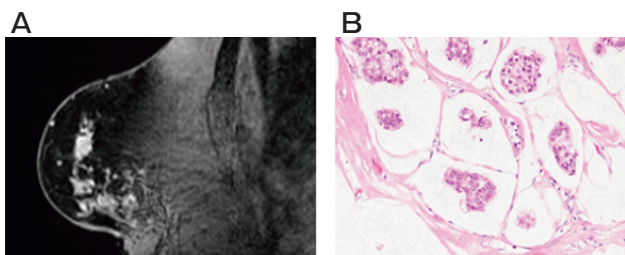


Fig. 1 Findings of breast cancer.

A, Contrast-enhanced T1-weighted fat-saturated image of the right breast; B, Pathological finding of breast cancer (200 \times , hematoxylin and eosin stain).

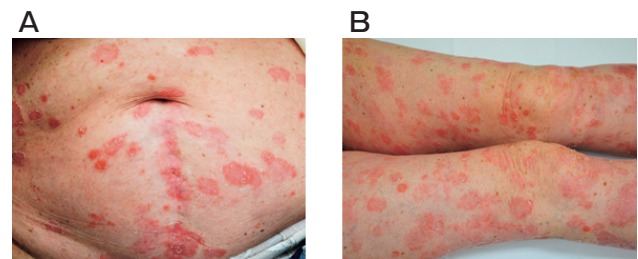


Fig. 2 Findings of psoriatic plaques at recurrence.

A, Psoriatic plaques on the abdomen; B, Psoriatic plaques on the lower extremities.

risk of breast cancer so far, our patient did receive both of them, which might have affected her anti-cancer immunity. Alternatively, the combined use of immune-suppressive agents and biologics might have affected the anti-cancer immunity, although the duration of each treatment was short. Further accumulation of cases followed over the long term will be needed to estimate the effects of the various biologics for psoriasis on the risk of malignancy.

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