Partial Remission of Psoriasis Following Rituximab Therapy for Non-Hodgkin Lymphoma

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Rituximab, a human-mouse, chimeric, monoclonal antibody that targets the B-cell CD20 antigen and causes rapid and specific B-cell depletion, is indicated for the treatment of low-grade or follicular, relapsed or refractory, CD20+ B-cell, non-Hodgkin lymphoma (NHL). We report the case of a middle-aged woman with psoriasis who experienced a partial sustained remission of her psoriasis after treatment with rituximab for NHL and discuss potential pathophysiologic mechanisms for this unexpected effect in a condition known to be mediated by T cells.

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Psoriasis is a chronic inflammatory disease involving the skin and joints. It is widely accepted that the development of the disease is due to a combination of genetic and environmental factors. Research has demonstrated the prominent role of T cells in the pathogenesis of psoriasis.[1-3] These cells comprise the lymphocytic infiltrate seen in biopsy specimens of psoriatic skin and are responsible for both the induction of changes in psoriasis and the maintenance of plaques.[2,3] The mechanism by which T cells induce the phenotypic changes in psoriasis consist of the activation of T cells; the migration of T cells into the skin; and the secretion of cytokines by T cells into the skin, resulting in the magnification of the inflammatory cascade.[3]

Rituximab is a human-mouse, chimeric, monoclonal antibody that targets the B-cell CD20 antigen and causes rapid and specific B-cell depletion. The drug was approved in the United States in 1997 to treat low-grade or follicular, relapsed or refractory, CD20+ B-cell, non-Hodgkin lymphoma (NHL). Rituximab, alone and with other therapies, has been evaluated in indolent and aggressive NHL, as well as other B-cell lymphoproliferative disorders.[4] The use of rituximab for autoimmune disorders, such as rheumatoid arthritis (RA), autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, systemic lupus erythematosus, and multiple sclerosis, is also under investigation.[4]

We report the case of a middle-aged woman with psoriasis who experienced a partial sustained remission of her psoriasis after treatment with rituximab for NHL. Given the T-cell nature of psoriasis and the B-cell depletion induced by rituximab, this remission would be an unexpected effect of the medication. However, we will discuss potential pathophysiologic mechanisms that may explain the effect of rituximab on psoriasis.

Case Report

A 60-year-old white woman presented in June 2001 with a diffuse eruption on her arms, legs, and scalp. She noted that the eruption had developed over the previous several months. The patient had NHL that had been diagnosed in May 1996. Since that time, she had received 2 courses of oral chemotherapy with chlorambucil, as well as radiation therapy.

Findings of the physical examination included psoriatic plaques covering the patient's arms, legs, and scalp. The plaques covered about 50% of the surface of her extremities. She was diagnosed with psoriasis and instructed to apply fluocinonide 0.05% ointment and calcipotriene 0.005% ointment twice daily to her arms and legs. In addition, she was prescribed fluocinonide 0.05% solution to

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apply twice daily to her scalp. Four months later, treatment with halobetasol propionate 0.05% ointment twice daily and clobetasol propionate 0.05% solution twice daily was initiated, and the fluocinonide ointment and solution were discontinued. The topical medications were continued but resulted in minimal improvement; in February 2002, UVB phototherapy was added 3 times per week. After 5 treatments, the patient discontinued therapy; however, she received 12 additional treatments in July and August 2002. She noted minimal improvement with the phototherapy and was subsequently lost to follow-up.

In January 2004, the patient returned for an examination. She reported that she had received 2 courses of rituximab in September and October 2002 and September and October 2003. She reported that, during her first course of rituximab, the psoriatic plaques on her arms and legs "melted away." The patient's arms and legs had cleared completely, and she exhibited minimal scalp involvement. Since that time, she has had no recurrence in the extremities, with no increase in scalp lesions. As of October 2004, she had noted no increase in her disease.

Comment

Rituximab functions by complement-dependent and antibody-dependent, cell-mediated cytotoxicity, inducing CD20+ B-cell lysis and promoting apoptosis of CD20+ B cells.[5] Although the role of B cells in psoriasis is not clear at present, mounting evidence from studies of RA suggests that B cells may be important in the pathogenesis of both RA and psoriatic arthritis, and possibly cutaneous psoriasis, as well.[5-8]

It has been suggested that B cells contribute to the evolution of RA by functioning as antigen-presenting cells that provide costimulatory signals required for CD4+ T-cell clonal expansion and effector functions and for the secretion of proinflammatory cytokines such as tumor necrosis factor α and chemokines.[5] Previously published case reports and preliminary study results suggest that the use of rituximab with methotrexate or cyclophosphamide to treat RA has shown promising results.[5,8] It has been postulated that the efficacy of rituximab might arise from its favorable effects on immune complexes that control the production of tumor necrosis factor α, an agent whose role in both RA and psoriasis has been clearly elucidated.[9,10]

CD20+ B cells have been noted in the skin of patients with psoriatic arthritis.[6] Results of immunohistologic analysis by Veale et al[6] showed a statistically significant CD20+ immunoreactive population of B cells in the skin lesions of patients with psoriatic arthritis compared with normal skin and skin from patients with skin findings of psoriasis alone ($P<.02$).[6] In contrast, Mahmoud et al[7] identified a subset of patients with cutaneous psoriasis (and no psoriatic arthritis) who had a preponderance of B cells in the skin.[7] In this study, the lymphocyte subpopulations in peripheral blood from 21 Kuwaiti patients exhibited elevated levels of the T-cell activation marker CD25, as well as increased expression of HLA-DR antigen, compared with a group of age- and sex-matched control subjects. In addition, there was a tendency toward an increase in the CD4+/CD45RO+ (memory cell) population, which was also consistent with peripheral T-cell activation. Immunohistologic results showed a heavy infiltrate of all cell types into the lesional tissue including, as expected, activated T cells.

An unexpected finding was higher levels of B cells infiltrating the psoriatic lesions, numerically exceeding the T cells.[7] The authors noted that this phenomenon had previously been reported only in cases of psoriasis with concurrent arthritis. None of the subjects in the study had arthritis. The authors concluded that their findings were suggestive of an immunopathologic variant of psoriasis specific to their study population.[7] It is therefore possible that patients with psoriasis who have a majority of B cells in the skin might be more likely to respond to an antibody to CD20 antigen.

Although CD20 antigen is considered a representative marker for B cells, the antigen is weakly expressed on a small subset of normal T cells.[11] Takami et al[11] reported the case of a 60-year-old man who developed pancytopenia and hepatosplenomegaly because of clonal proliferation of atypical lymphocytes that were weakly positive for CD20 antigen. This was the first report of a case of clonal expansion of CD20+ T cells. The presence of CD20+ T cells in a given psoriasis patient would also provide another potential mechanism of action for rituximab.

In light of these and other studies, anti-CD20 antibody therapy may ameliorate psoriasis via several potential mechanisms. Although a B-cell therapy would not be a first-line choice for most patients with psoriasis, it is useful to keep rituximab in mind for cases refractory to other therapies. Further reports of cases of successful treatment also will help clarify the potential role of B cells or CD20 antigen in the pathogenesis and treatment of psoriasis.

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