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Adalimumab – Safe and Effective Therapy for an Adolescent Patient with Severe Psoriasis and Immune Thrombocytopenia

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ABSTRACT Psoriasis has been linked to several comorbidities, including metabolic syndrome, atopy, and celiac disease. However, the association between immune thrombocytopenia and psoriasis has rarely been described. We report the case of an adolescent with severe psoriasis and concomitant immune thrombocytopenia who obtained remission during treatment with adalimumab. Increased concentration of tumor necrosis factor-α seems to be a pathogenic linkage and therapeutic target for both diseases.

KEY WORDS: adalimumab, immune thrombocytopenia, psoriasis, tumor necrosis factor-alpha

INTRODUCTION

Psoriasis is a chronic inflammatory disease that affects about 2% of the population worldwide. The pediatric subset of the psoriasis population is an important subgroup since nearly one third of patients with psoriasis experience disease onset in childhood (1,2). The affected children and adolescents face a combination of physical and psychosocial challenges. Pediatric psoriasis is associated with pronounced effects on self-esteem, stigmatization, and social relationships compared with their disease-free peers (3). Recent research has linked psoriasis to several comorbidities, including metabolic syndrome, atopy, celiac disease, vitiligo, and alopecia areata (4).

Immune thrombocytopenia is one of the most common acquired bleeding disorders in children secondary to the production of autoantibodies against platelets (5). The association of immune thrombocytopenia and psoriasis has rarely been described (6,7).

CASE PRESENTATION

We present a case of 16-year-old girl with an 8-year history of plaque psoriasis. Over the course of disease, the patient was treated with topical agents, narrow band UVB phototherapy (3 sessions/week for 4 months), acitretin (0.5 mg/kg bw/day for 5 months), methotrexate (20 mg/week for 7 months), and cyclosporine (3.5 mg/kg bw/day for 6 months); however, no clinically meaningful response was observed. The patient was also diagnosed with immune thrombocytopenia at the age of 12.

On admission to our Department, physical examination revealed extensive erythematous scaly plaques involving 48% of the body surface area (BSA) (Figure 1). The psoriasis area severity index (PASI) score was assessed as 34.9. Psoriasis had a profound negative impact on the patient's quality of life (Children's Dermatology Life Quality Index – CDLQI – 27 points).

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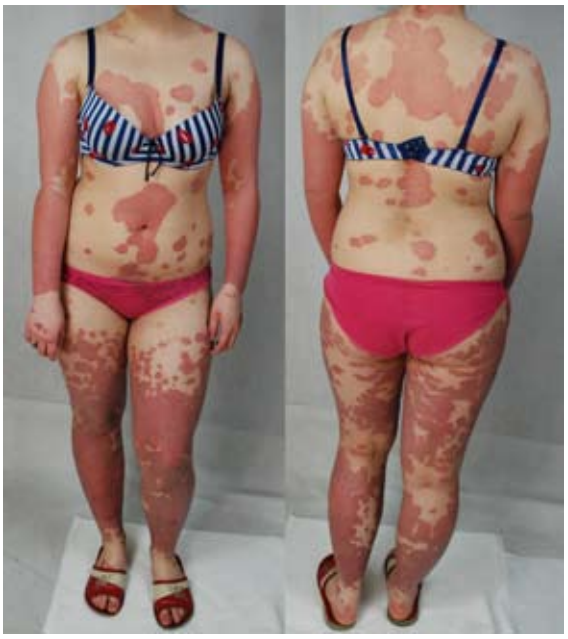

Figure 1. Diffuse erythematous scaly plaques before treatment with adalimumab.

Figure 2. Clinical improvement after 12 weeks of therapy with adalimumab.

Total blood count test revealed isolated thrombocytopenia (82×10^3/dL). Kidney and liver function tests, fasting blood glucose, and lipid profile showed no abnormalities. Serological markers for hepatitis B and C, human immunodeficiency virus, and interferon-γ release assay were negative.

Because of the severity of the disease and lack of response to standard systemic therapies, the patient received 40 mg adalimumab subcutaneously every 2 weeks. A rapid improvement was observed after the first two injections, with almost complete remission in the following weeks (outcomes at week 12: PASI – 2.4; BSA – 4%; CDLQI – 3; Figure 2). No adverse events were observed during biologic therapy. The platelet count increased moderately to 121×10^3/dL.

DISCUSSION

Although pediatric psoriasis generally has a mild clinical course, a certain group of patients is refractory to conventional systemic agents. Biological treatment targeting specific immune components in the pathophysiological cascade of psoriasis is becoming a promising therapeutic alternative (2,8). We described the case of a 16-year-old girl with severe psoriasis poorly controlled by conventional treatments and concomitant immune thrombocytopenia.

Immune thrombocytopenia is a benign condition and one of the common causes of thrombocytopenia in adults and children that resolves spontaneously. However, 20-30% of patients develop the chronic form that requires more intensive treatment including corticosteroids, intravenous immunoglobulin, rituximab, or splenectomy (9). Due to potential platelet-lowering effect of immunosuppressive drugs, systemic treatment of pediatric psoriasis concomitant with immune thrombocytopenia poses a substantial clinical challenge.

Our patient demonstrated a good clinical response to adalimumab, which has been approved in 2015 by the European Medicines Agency for the treatment of severe plaque psoriasis in children aged 4 years or older. Adalimumab is a fully human monoclonal antibody against tumor necrosis factor α (TNFα), a key cytokine in a number of autoimmune diseases (10).

Increased blood concentration of TNFα has been reported in patients with immune thrombocytopenia (11). Additionally, single-nucleotide polymorphism in the TNFα gene (308G/A) was reported to affect gene transcription by increasing TNFα production and was speculated to increase the risk and exacerbate the outcome of ITP (12).

We decided to use adalimumab in our patient due to inadequate response to conventional treatment, relatively short half-life of the drug (in case of adverse events), and the possibility of continuing the therapy with health care reimbursement after reaching adulthood. Monocytes and macrophages are considered to be the main producers of soluble TNFα, although activated CD4 T-cells highly express transmembrane TNFα which provides a co-stimulatory signal for human B-cell activation, a remarkable feature of ITP (13). The possibility of neutralizing the soluble and membrane-bound TNFα was an additional argument for starting therapy with adalimumab for both diseases.

On the other hand, the literature provides very few reports of thrombocytopenia in patients with psoriasis who were treated with biologics such as etanercept, adalimumab, infliximab, ustekinumab, or secukinumab (14-16). The exact mechanism by which biological drugs may induce thrombocytopenia in psoriasis remains unclear. This reaction may be due to the relative excess of Th2 lymphocytes, which may in turn stimulate antiplatelet antibody production, leading to platelet destruction and thrombocytopenia. Another explanation is that biologics are associated with formation of immune complexes, which in turn bind to the surface of platelets and activate the complement cascade. Some authors suggest that thrombocytopenia is an idiosyncratic reaction in genetically predisposed patients (17).

It is important for clinicians to be aware of this side effect of biological drugs. However, the potential risk of drug-induced thrombocytopenia does not represent a contraindication for the administration of biologics in psoriasis. Instead, as illustrated by this case, it may be applied as an attractive treatment for both psoriasis and immune thrombocytopenia. Since all agents pose a substantial risk, platelet counts should be regularly monitored in patients receiving anti-TNFα/IL-23/IL-17 biologics to facilitate early recognition of thrombocytopenia.

CONCLUSION

Psoriasis and immune thrombocytopenia are quite common in the pediatric population, but their coexistence is rare. We would like to emphasize that altered TNFα expression may be a pathogenic linkage and therapeutic target for both diseases.

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