

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

Mariusz Sikora, Patrycja Gajda, Magdalena Chrabąszcz, Albert Stec, Małgorzata Olszewska, Lidia Rudnicka

Department of Dermatology, Medical University of Warsaw, Warsaw, Poland

Corresponding author:

Mariusz Sikora, MD, PhD
Department of Dermatology
Medical University of Warsaw
Koszykowa 82A
02-008 Warsaw
Poland
msikora@wum.edu.pl

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- α

Received: January 16, 2019

Accepted: May 15, 2019

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).





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

Total blood count test revealed isolated thrombocytopenia ($82 \times 10^3/\text{dL}$). 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 $121 \times 10^3/\text{dL}$.

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



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

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 (TNF α), a key cytokine in a number of autoimmune diseases (10).

Increased blood concentration of TNF α has been reported in patients with immune thrombocytopenia (11). Additionally, single-nucleotide polymorphism in the TNF α gene (308G/A) was reported to affect gene transcription by increasing TNF α 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 TNF α , although activated CD4 T-cells highly express transmembrane TNF α 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 TNF α 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-TNF α /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 TNF α expression may be a pathogenic linkage and therapeutic target for both diseases.

References

1. Eichenfield LF, Paller AS, Tom WL, Sugarman J, Hebert AA, Friedlander SF, *et al.* Pediatric psoriasis: Evolving perspectives. *Pediatr Dermatol.* 2018;35:170-81.
2. Piekarska-Myślińska D, Pietrzak A, Myśliński W, Pietrzak D, Borysowicz M, Socha M, *et al.* Pediatric psoriasis. *Dermatology Review.* 2017;104:363-76.
3. Gonzalez J, Cunningham K, Perlmutter J, Gottlieb A. Systematic review of health-related quality of life in adolescents with psoriasis. *Dermatology.* 2016;232:541-9.
4. Kelati A, Baybay H, Najdi A, Zinoune S, Mernissi FZ. Pediatric psoriasis: Should we be concerned with comorbidity? Cross-sectional study. *Pediatr Int.* 2017;59:923-8.
5. Labarque V, Van Geet C. Clinical practice: immune thrombocytopenia in paediatrics. *Eur J Pediatr.* 2014;173:163-72.
6. Aboud N, Depre F, Salama A. Is autoimmune thrombocytopenia itself the primary disease in the presence of second diseases data from a long-term observation. *Transfus Med Hemother.* 2017;44:23-8.
7. Feudjo-Tepie MA, Le Roux G, Beach KJ, Bennett D, Robinson NJ. Comorbidities of idiopathic thrombocytopenic purpura: a population-based study. *Adv Hematol.* 2009;2009:963506.
8. Madiraca D, Šitum M, Prkačin I, Ožanić Bulić S. Treatment options for pediatric psoriasis. *Acta Dermatovenerol Croat.* 2016;24:175-80.
9. Osman ME. Chronic immune thrombocytopenia in a child responding only to thrombopoietin receptor agonist. *Sudan J Paediatr.* 2012;12:60-4.
10. Wu JJ, Valdecantos WC. Adalimumab in chronic plaque psoriasis: A clinical guide. *J Drugs Dermatol.* 2017;16:779-90.
11. Del Vecchio GC, Giordano P, Tesse R, Piacente L, Altomare M, De Mattia D. Clinical significance of serum cytokine levels and thrombopoietic markers in childhood idiopathic thrombocytopenic purpura. *Blood Transfus.* 2012;10:194-9.
12. Zhang J, Min QH, Xu YM, Deng LB, Yang WM, Wang Y, *et al.* Association between TNF-alpha -308G/A polymorphism and risk of immune thrombocytopenia: a meta-analysis. *Genet Test Mol Biomarkers.* 2017;21:80-5.
13. Talaat RM, Elmaghraby AM, Barakat SS, El-Shahat M. Alterations in immune cell subsets and their cytokine secretion profile in childhood idiopathic thrombocytopenic purpura (ITP). *Clin Exp Immunol.* 2014;176:291-300.
14. Nakahara T, Konishi S, Yasukochi Y, Esaki H, Tsuji G, Kido-Nakahara M, *et al.* Thrombocytopenia in a psoriatic patient sequentially treated with adalimumab, secukinumab and ustekinumab. *J Dermatol.* 2019;46:e157-e158.
15. Philippe L, Badie J, Faller JP, Krattinger É, Deconinck E, Aubin F. Fatal thrombotic thrombocytopenic purpura in a psoriasis patient treated with ustekinumab and methotrexate. *Acta Derm Venereol.* 2015;95:495-6.
16. Chen M, Holland MJ, Mir MR, Wong MG, Kelley BP, Grim KD, *et al.* Frequency of thrombocytopenia in psoriasis patients treated with tumor necrosis factor-a inhibitors. *J Drugs Dermatol.* 2011;10:280-4.
17. Casanova MJ, Chaparro M, Martínez S, Vicuña I, Gisbert JP. Severe adalimumab-induced thrombocytopenia in a patient with Crohn's disease. *J Crohns Colitis.* 2012;6:1034-7.