

Coexistence of immune thrombocytopenic purpura and alopecia areata: Possible relationship

İDogan Kose¹, İAbdullah Solmaz², İAhmet Guzelcicek², İHalil Aslan²

¹Division of Pediatric Hematology Oncology, Department of Pediatrics, Harran University Faculty of Medicine, Sanliurfa, Turkey

²Department of Pediatrics, Harran University Faculty of Medicine, Sanliurfa, Turkey

Copyright@Author(s) - Available online at www.annalsmedres.org

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



Abstract

ITP and AA are common immune-mediated disorders in childhood. Both AA and ITP have been described with different autoimmune disorders. However, their coexistence has been reported in only a few cases in the literature. In our patient, both ITP and AA spontaneously improved within 5 months and suggesting a pathophysiological relationship. In this article, we present a case of a six-month-old boy diagnosed as ITP associated with AA.

Keywords: Alopecia areata; immune thrombocytopenia; purpura; childhood

INTRODUCTION

Immune thrombocytopenic purpura (ITP) and alopecia areata (AA) are common immune-mediated disorders in childhood.

ITP is an autoimmune disease characterized by autoantibody formation against platelet membrane glycoproteins (1). ITP alone has an incidence of 10 per 100,000 children per year (2).

AA is often manifested by patchy hair loss on the scalp and beard area. The disease has a rapid onset and can progress to severe forms (3). Approximately 20% of all cases of AA are children (4). Disease, in 80% of cases in the form of a single plaque and frequency; scalp, beard, eyebrows and extremities begin. 15-25% of cases progress to total forms. The risk of progression to alopecia totalis (AT) is 50% in patients before the puberty (5). AT is defined as the loss of all hair, eyebrows, beard, mustache and eyelashes (6). Alopecia universalis (AU) is 100% loss of hair on the scalp and body (3).

Although both AA and ITP have been described with different autoimmune disorders, their coexistence has been reported in only a few cases in the literature (7-10). In another case of AA, an autoimmune thrombocytopenic disease has been reported, but the temporal relationship between the two conditions is not indicated (11).

The aim of our study was to discuss the youngest case in the literature diagnosed with AA and ITP.

CASE REPORT

A six month old boy presented with diffuse hair loss over the scalp of one month duration. Her mother noticed a significant increase in shedding of hair one month back which had gradually progressed to diffuse baldness over scalp. He was born 37 weeks and 2900 g from the first pregnancy of the 27-year-old mother. There was no parental consanguinity. In the antenatal period, the ultrasonographic follow-up examinations were found to be normal. The patient had no family history of chronic disease, and his vaccinations were made according to his age.

The baby had a body weight of 6500 g (3-10%), a height of 67 cm (25-50%) and a head circumference of 43 cm (10-25%). The patient was fed only with breastfeeding, and the neurological development was appropriate for his age. Dermatological examination revealed total eyebrows and eyelashes; almost complete hair loss was detected in the scalp (Figure 1). General physical examination was normal with no evidence of lymphadenopathy or hepatosplenomegaly. There was no lesion in the skin and mucosa due to thrombocytopenia. Other system examinations were normal.

Received: 11.11.2019 **Accepted:** 13.05.2020 **Available online:** 27.01.2021

Corresponding Author: Dogan Kose, Division of Pediatric Hematology Oncology, Department of Pediatrics, Harran University Faculty of Medicine, Sanliurfa, Turkey, **Email:** drdogankose@gmail.com



Figure 1. Alopecia areata on admission

Initial laboratory findings revealed thrombocytopenia, and mild absolute neutropenia. His laboratory data showed Leukocytes 8900 (reference; 6,000–17,500) / μ l, Absolute neutrophil counts 970 (reference; 1,000–8,500) / μ l, platelet count 30,000 (reference; 150,000–400,000) / μ l, hemoglobin (Hb) 10,9 (reference; 9,5–16) g/dl. On peripheral blood smear, erythrocyte, leukocyte and platelet morphologies were found to be normal and 1-2 clusters was observed in the platelets. Bleeding time; 20 (1-13 minutes), pre-prandial blood glucose level; 85 (70-100 mg/dL), Vitamin B12 level; 210 pg / mL, folic acid level; 10.3 ng/mL, Vitamin D level; 39.9 ng/mL, C reactive protein level; <2 mg/L. Liver function tests and renal function tests were evaluated as normal.

The immunoglobulin profile was performed for the patient in our laboratory. The levels of IgG were 460 (normal range for age: 304-1230) mg/dL, IgM were 54 (normal range for age: 32-203) mg/dL and IgA were 25 (normal range for age: 7-123) mg/dL. The serum complement levels, of C3 were 88 (normal range for age: 60-125) mg/dL and of C4 were 20 (normal range for age: 8-42) mg/dL.

Thyroid function tests were as follows: free thyroxin (fT4): 1.22 ng/dL (N: 0.7-2 ng/dL), TSH: 1,84 uIU/L (N: 0.5-4.5 uIU/L), anti-tyroglobulin: 1,18 IU/ml (N: 0-50 IU/ml), anti-thyroidperoxidase: 0,07 IU/ml (N:0-50 IU/ml).

Anti-double stranded DNA, antinuclear antibody, anticardiolipin antibody, rheumatoid factor and lupus anticoagulant were found to be negative. Screening for celiac disease was done using tissue transglutaminase IgA and IgG, were found to be negative. Antibody (IgM) tests were performed for HIV, EBV, TORCH, hepatitis B and hepatitis C infections. The results were negative.

Patient with normal abdominal ultrasound was consulted dermatology and etiology was not found.

Anti-platelet antibody and anti-neutrophil antibody tests could not be performed.

Biopsy was not performed on the scalp of the patient.

There were no etiologic factors to explain thrombocytopenia and AA. The patient was followed up without any treatment. The patient was followed for approximately 3 months with an interval of 15 days and the platelet count gradually increased to the normal range after 3 months of follow-up. Alopecia began to improve approximately 2 months after thrombocytopenia improved and resolved completely over time. (Figure 2).



Figure 2. Alopecia began to improve approximately 2 months after thrombocytopenia improved

DISCUSSION

AA has been associated with many pathological conditions. These are endocrinological (autoimmune polyglandular syndrome-1, Addison disease, diabetes mellitus, Hashimoto thyroiditis), dermatological (vitiligo, psoriasis, pemphigus vulgaris), hematological (pernicious anemia) and neurological diseases (multiple sclerosis). Autoimmunity plays an underlying role in most of these diseases (12-14). Other connections include drugs, infections and vaccinations (15). In our case, tests related to these diseases were performed and resulted in negative.

ITP is a fairly rare, generally benign autoimmune bleeding disorder characterized by isolated thrombocytopenia, defined as a platelet count <100,000/ μ l in the absence of other conditions that may cause thrombocytopenia. ITP can occur with immunodeficiency, systemic infections, some tumors, rheumatological diseases, lymphoproliferative disorders, and various drugs. Also, diseases such as ulcerative colitis, celiac disease, systemic lupus erythematosus, and rheumatoid arthritis have been individually associated with ITP and AA. (16). In

our case, there were no signs and symptoms of bleeding secondary to thrombocytopenia. In addition, Intravenous immunoglobulin (IVIg) or steroid treatment was not given, since the platelet count was over 20,000 / μ l. No specific cause was found in the studies for the reasons mentioned above.

Simultaneous onset and remission of both diseases in this patient, similar pathophysiology including autoimmune, genetic and environmental factors suggest that coexistence of ITP and AA is not coincidental.

It has been suggested that the coexistence of ITP and AA may be due to a single factor that activates an autoimmune response to hair follicles and platelets. It is also claimed to be due to cross-reaction with different antigens in hair follicles and platelets (9,10).

Although different target tissue such as dermal papilla cells, keratinocytes of the matrix and the bulb of melanocytes have been proposed in the pathological process of AA, there is no consensus on this issue (17).

Hair follicles (HFs) have a different immunological mechanism, in particular, including downregulation of MHC class I expression. This interesting situation makes HFs immune privileged (IP). Normally, CD56 + (natural killer) cells attack cells that do not have MHC class I expression or are low. However, NK cells do not attack hair follicles through this IP. The disappearance of this IP is thought to initiate hair loss in patients with AA. Studies have shown that Natural killers (NK cells), cytotoxic T (CD8 +) cells, and T helper (CD4 +) cells were rarely seen around the HFs in the scalp of normal people. It was observed that these cells were found in high density in the HFs of patients diagnosed with AA. The increase in the number of CD56 +, CD8 +, or CD4 + cells explains the immune mechanism in AA (18).

In genetic studies, cytokine gene polymorphism and human leukocyte antigens (HLA) DQ3 were significantly associated with AA. HLA DQ3 association was found in 80% of cases. In addition, HLA DQ7 and DR4 were particularly associated with AT and AU (3). While 34-50% of mild cases with AA recover spontaneously within a year, this rate is below 10% for AT and AU (5).

HLA Typing could not be performed in this patient. Vitamin A and E levels have also not been studied. This situation limited our work.

CONCLUSION

In this article, we present a rare association of ITP and AA in a six-month-old boy who presented with thrombocytopenia and hair loss. Considering the few published cases to date, we think that patients diagnosed with AA should be carefully examined for bleeding symptoms and it is appropriate to evaluate suspicious cases for ITP. We believe that the common pathogenesis between these two diseases will be demonstrated by future studies.

Competing interests: The authors declare that they have no competing

interest.

Financial Disclosure: There are no financial supports.

Patient informed consent: Written informed consent was given by the patient's parents.

REFERENCES

1. Cines DB, Cuker A, Semple JW. Pathogenesis of immune thrombocytopenia. *Presse Med* 2014;43:49–59.
2. Lilleyman JS. Management of childhood idiopathic thrombocytopenic purpura. *Br J Haematol* 1983;54:11–4.
3. Gilhar A, Etzioni A, Paus R. Alopecia areata. *N Eng J Med* 2012;366:1515–25.
4. Xiao FL, Yang S, Liu JB, et al. The epidemiology of childhood alopecia areata in China: a study of 226 patients. *Pediatr Dermatol* 2006;23:13–8.
5. Rakowska A, Slowinska M, Kowalska-Oledzka E, et al. Alopecia areata incognita: true or false? *J Am Acad Dermatol* 2009;60:162–3.
6. Madani S, Shapiro J. Alopecia areata update. *J Am Acad Dermatol* 2000; 42: 549– 66.
7. Salman A, Eser A. Concurrence of Immune Thrombocytopenic Purpura and Alopecia Areata: A Rare Association. *Int J Trichology* 2016;8:52–3.
8. Ahmed AM, Barahmani N, Duvic M; National Alopecia Areata Registry. Familial alopecia areata and chronic thrombocytopenia. *J Am Acad Dermatol* 2008; 58:75–7.
9. Cohn SM, Buchanan GR. Immune thrombocytopenia and alopecia areata: spontaneous occurrence and resolution in the same patient. *Pediatr Blood Cancer* 2014;61:2110–1.
10. Levin RM, Travis SF, Heymann WR. Simultaneous onset of alopecia areata and idiopathic thrombocytopenic purpura: A potential association? *Pediatr Dermatol* 1999; 16:31–4.
11. Tosti A, Bellavista S, Iorizzo M. Alopecia areata: A long term follow-up study of 191 patients. *J Am Acad Dermatol* 2006; 55:438–41.
12. Tan E, Tay YK, Goh CL, et al. The pattern and profile of alopecia areata in Singapore -- A study of 219 Asians. *Int J Dermatol* 2002;41:748–53.
13. Goh C, Finkel M, Christos PJ, et al. Profile of 513 patients with alopecia areata: Associations of disease subtype with atopy, autoimmune disease and positive family history. *J Eur Acad Dermatol Venereol* 2006; 20:1055–60.
14. Buzi F, Badolato R, Mazza C, et al. Autoimmune polyendocrinopathy – candidiasis – ectodermal dystrophy syndrome: time to review diagnostic criteria? *J Clin Endocrinol Metab* 2003; 88:3146–8.
15. Willemsen R, Vanderlinden J, Roseeuw D, et al. Increased history of childhood and lifetime traumatic events among adults with alopecia areata. *J Am Acad Dermatol* 2009;60:388–93.
16. Teachey DT, Lambert MP. Diagnosis and management of autoimmune cytopenias in childhood. *Pediatr Clin*

North Am 2013;60:1489–511.

17. McDonagh AJ, Messenger AG. The etiology and pathogenesis of alopecia areata. *J Dermatol Sci* 1994;7(suppl): 125–35.
18. Ito T, Ito N, Saatoff M, et al. Maintenance of hair follicle

immune privilege is linked to prevention of NK cell attack. *J Invest Dermatol* 2008;128:1196-206.