Case Report
Volume 12:7, 2022

Journal of Clinical Case Reports

ISSN: 2165-7920 Open Access

Ascorbic Acid-A Useful Adjuvant in Refractory Immune Thrombocytopenic Purpura: A Case Report

Eindrini C Muhandiram*, Wasanthi Wickramasinghe, Inoshi Atukorala, Lallindra V Gooneratne

Department of Pathology, University of Colombo, Colombo, Sri Lanka

Abstract

Immune Thrombocytopenic Purpura (ITP) is a heterogeneous disease with unpredictable treatment responses. This unpredictability is attributed in part to different pathogenic mechanisms including oxidative stress. The anti-oxidant effect of ascorbic acid in treatment of ITP has been described but evidence on its efficacy is contentious.

We describe a patient with refractory ITP in whom ascorbic acid was used as a useful adjuvant treatment. A 60-year old man with diabetes and hypertension presented with myocardial infarction and underwent primary coronary intervention. He had steroid dependent ITP, with a poor response to azathioprine, rituximab and splenectomy. He had drug induced cholestasis with dapsone. Therefore high doses of steroids were required to maintain safe platelet counts for antiplatelet drugs, which lead to poor glycemic control. High dose ascorbic acid was started, following which his platelet count remained above 100 x 10^9/L, permitting tailing off of prednisolone while continuing dual antiplatelet therapy.

Keywords: Ascorbic acid • Idiopathic • Purpura • Thrombocytopenic

Introduction

Immune Thrombocytopenic Purpura (ITP) is a heterogeneous disease with multiple postulated pathogenic mechanisms and diverse response to treatment. Significant numbers of adults have relapsing and remitting disease. The majority responds to high dose steroids but steroid dependency is also common. There are many steroid sparing treatment options, including agents with proven benefit such as rituximab, thrombopoetin receptor agonists and splenectomy. There is weak evidence for antioxidants like ascorbic acid in refractory ITP. We describe a patient with refractory ITP whose platelet count showed dramatic response to high dose Ascorbic Acid (AA) [1].

Case Study

A 60-year old Sri Lankan was diagnosed with ITP in 2010. He had type-2 diabetes and hypertension for nearly 20 years. He was steroid dependant and was started on azathioprine. Azathioprine together with a low dose of prednisolone maintained the platelet count above 30 x 10^9/L. However, he had frequent relapses which necessitated recommencement of high dose of steroids. Rituximab was tried in 2015 with a poor response. The patient underwent a splenectomy in 2016 to which he had a response for about 18 months. He relapsed in November 2017 and was started on dapsone with which his platelet count increased. However, dapsone was discontinued due to drug-induced cholestatic hepatitis.

In May 2019 a person with myocardial infarction while patient platelet count was 74 x 10^9/L and underwent Primary Coronary Intervention (PCI). To maintain an adequate platelet count for dual antiplatelet therapy, he was given IVIG (total dose of 2 g/kg), followed by 1mg/Kg of oral prednisolone to which he responded with platelet counts rising to >100 x 10^9/L. However, platelets dropped to <20 x 10^9/L once the steroid was being tailed off. This made continuation of even a single antiplatelet agent a challenge. His glycemic control fluctuated due to prolonged use of high dose steroids. Eltrombopag, which is the only thrombopoietin receptor agonist available in Sri Lanka, was deferred due to its potential hepatotoxicity and risk of thrombosis.

Results

It was decided to give a trial of high dose ascorbic acid as per 2011 American Society of hematology guidelines on treating

***Address for Correspondence:** Eindrini C Muhandiram, Department of Pathology, University of Colombo, Colombo, Sri Lanka, Tel: +94 777 513 703; E-mail: eindrinimec@gmail.com*

Received: 08-Jul-2020, Manuscript No. JCCR-20-11124; **Editor assigned:** 09-Jul-2020, Pre QC No. P-11124; **Reviewed:** 14-Jul-2020, QC No. Q-11124; **Revised:** 20-Jul-2022, QI No. Q-11124; Manuscript No. R-11124; **Published:** 27-Jul-2022, DOI: 10.37421/2165-7920.2022.12.1519.

refractory ITP. He showed an impressive response to vitamin C 2 g daily with platelets reaching 348 x 10^9 /L within 2 weeks. It persisted above 100 x 10^9/L despite tailing off of prednisolone. The platelet count dropped to below 100 x 10^9 /L on 2 occasions when the vitamin C dose was reduced below 1.5 g. The patient did not have any class 3 or 4 side effects due to high dose AA. The platelet response in parallel with treatment he received is shown in Figure 1 [2].

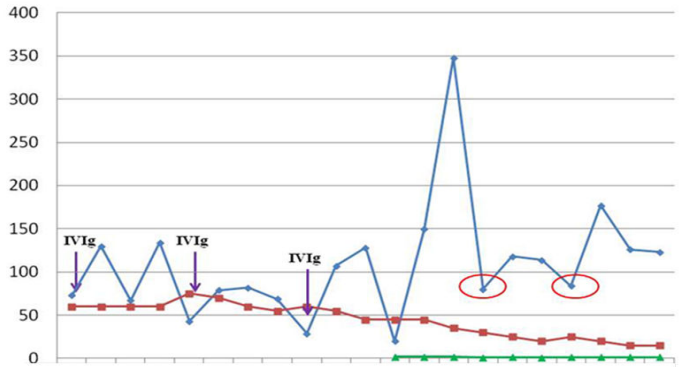

Figure 1. Platelet Response to AA with tailing off of prednisolone.

Note: plt x 10^9/lit, pred (mg), AA (g)

After the commencement of ascorbic acid, the platelet count was maintained above 100x 10^9/L even with the tailing off of prednisolone, except on 2 occasions (circled in red) where it dropped below 100 x 10^9/L when the dose was reduced below 1.5 g. [AA: Ascorbic Acid, IVIg: Intravenous immunoglobulin, Ptl; platelet count, pred; oral prednisolone].

The pathophysiology of ITP is complex. Heterogeneity of ITP and its treatment response may be consequent to different causative mechanisms of thrombocytopenia. Peripheral destruction of antibody-coated platelets remains the main pathogenic mechanism. However, it has been reported that auto-antibodies also inhibit megakaryocytes and that there is significant T cell involvement in its pathogenesis. More recently, oxidative stress was identified as an initiating factor of autoimmunity in patients with ITP [3-8].

Overproduction of reactive oxygen species in ITP has been described in few studies. In a study, the ratio of reduced to oxidized glutathione (GSH/GSSG) was found to be significantly lower in patients with ITP than in healthy controls. It is known that persistent oxidative stress causes lipid peroxidation and formation of reactive aldehydes. Two studies have demonstrated elevated levels of reactive aldehydes like malondialdehyde in the plasma of ITP patients. Significant evidence for high oxidative stress in ITP raises an important question: will targeting antioxidant pathways alter the course of the disease? [9-11].

Discussion

Several small-scale studies have been done to assess the usefulness of ascorbic acid in ITP. A study reported on the effectiveness of ascorbic acid in the treatment of ITP in 1988. In this study, there was a significant increase in platelet count in 9 out of 11 patients treated with a single daily 2 g dose of ascorbic acid. However, subsequent studies by other groups have reported less impressive results. A study have reported a good response in only one of 14 and 12 patients respectively. Another study reported good response in only two of 11 patients. There are few case reports in literature describing the effectiveness of ascorbic acid in ITP [12-17].

In addition, there is evidence for antithrombotic properties of ascorbic acid. A study demonstrated administration of vitamin C significantly reduces platelet.

Adhesion and aggregation in patients with coronary artery disease. Prothrombotic state is commoner in diabetic patients and is attributed to hyperglycemia induced oxidative stress leading to endothelial dysfunction. Studies have shown, supplementation of ascorbate could enhance the synthesis of nitric oxide by neutrophils and thereby decrease the thrombotic tendency in these patients [18,19].

In our patient with refractory ITP, a safe platelet count for antiplatelet therapy after PCI was achieved with a trial of ascorbic acid. This effect persisted and allowed gradual tailing off of prednisolone and continuation of antiplatelet drugs. In addition to increasing platelet counts in ITP, AA has antioxidant and antithrombotic properties that are beneficial in patients like ours with many vascular risk factors.

Conclusion

The role of ascorbic acid in the overall and long-term management of refractory ITP is yet to be determined. However, ascorbic acid is a relatively non-toxic, inexpensive, widely available agent that can be trialed in this cohort of refractory ITP patients. Further, it has additive anti-oxidant properties which may be otherwise beneficial. Therefore, use of ascorbic acid in refractory ITP, especially in resource limited settings warrants further investigation.

Conflict of Interests

The authors declare that they have no conflict of interest.

Acknowledgements

We thank the staff of the University Medical Unit of the National Hospital of Sri Lanka and the Department of Pathology, Faculty of Medicine, Colombo, for their continuous support in patient care. We also thank the patient for providing consent to publish this case report.

References

1. Cuker, A, and Neunert. C E. "How I Treat Refractory Immune Thrombocytopenia." *Blood* 128 (2016): 1547-1554.
2. Neunert, C, Lim W, Crowther M, and Cohen A, et al. "The American Society of Hematology 2011 Evidence-Based Practice Guideline for Immune Thrombocytopenia." *Blood* 117 (2011): 4190-4207.
3. Zufferey, A, Kapur R, and Semple J W. "Pathogenesis and Therapeutic Mechanisms in Immune Thrombocytopenia (ITP)." *J Clin Med* 6 (2017): 16.
4. McMillan, Robert, Wang L, Tomer A, and Nichol J, et al. "Suppression of *In Vitro Megakaryocyte Production by Antiplatelet Autoantibodies from Adult Patients with Chronic ITP*." *Blood* 103 (2004): 1364-1369.
5. Rocha, A M C, Souza C, Rocha G A, and De Melo F F, et al. "The Levels of Il-17a and of the Cytokines Involved in Th17 Cell Commitment

are Increased in Patients with Chronic Immune Thrombocytopenia." *Haematologica* 96 (2011): 1560-1564.

6. Bao, W, Bussel J B, Heck S, and He W, et al. "Improved Regulatory Cell Activity in Patients with Chronic Immune Thrombocytopenia Treated with Thrombopoietic Agents." *Blood* 116 (2010): 4639-4645.
7. Zhang, F, Chu X, Wang L, and Zhu Y, et al. "Cell-Mediated Lysis of Autologous Platelets in Chronic Idiopathic Thrombocytopenic Purpura." *Eur J Haematol* 76 (2006): 427-431.
8. Zhang, B, and Zehnder J L. "Oxidative Stress and Immune Thrombocytopenia." *Semin Hematol* 50 (2013): e1-e4.
9. Akbayram, S, Dogan M, Akgün C, and Mukul Y, et al. "The Association of Oxidant Status and Antioxidant Capacity in Children with Acute and Chronic ITP." *J Pediatr Hematol Oncol* 32 (2010):281.
10. Polat, G, Tamer L, Taniriverdi K, and Gorkan E, et al. "Levels of Malondialdehyde, Glutathione and Ascorbic Acid in Idiopathic Thrombocytopaenic Purpura." *East Afr Med J* 79 (2002): 446-449.
11. Brox, Alan G., Jan H K, and Fauser A A. "Treatment of Idiopathic Thrombocytopenic Purpura with Ascorbate." *Br J Haematol* 70 (1988): 341-344.
12. Verhoef, GE G., Boonen S, Boogaerts M A, and Brox A. "Ascorbate for the Treatment of Refractory Idiopathic Thrombocytopenic Purpura." *Br J Haematol* 74 (1990): 234-325.
13. Jubelirer, S J. "Pilot Study of Ascorbic Acid for the Treatment of Refractory Immune Thrombocytopenic Purpura." *Am J Hematol* 43 (1993): 44-46.
14. Godeau, B, and Bierling P. "Treatment of Chronic Autoimmune Thrombocytopenic Purpura with Ascorbate." *Br J Haematol* 75 (1990): 289-290.
15. Zhang, B, Lo C, Shen L, and Sood R, et al. "The Role of Vanin-1 and Oxidative Stress–Related Pathways in Distinguishing Acute and Chronic Pediatric ITP." *Blood* 117 (2011): 4569-4579.
16. Masugi, J, Iwai M, Kimura S, and Ochi F, et al. "Combination of Ascorbic Acid and Methylprednisolone Pulse Therapy in the Treatment of Idiopathic Thrombocytopenic Purpura." *Intern Med* 33 (1994):166.
17. Bordia, A., and Verma S. K. "Effect of Vitamin C on Platelet Adhesiveness and Platelet Aggregation in Coronary Artery Disease Patients." *Clin Cardiol* 8 (1985): 552-554.
18. Ting, Henry H., Timimi F K, Boles K S, and Creager S J, et al. "Vitamin C Improves Endothelium-Dependent Vasodilation in Patients with Non-Insulin-Dependent Diabetes Mellitus." *J Clin Investig* 97 (1996): 22-28.
19. Huang, A, Vita J A, Venema R C, and Keaney J F. "Ascorbic Acid Enhances Endothelial Nitric-Oxide Synthase Activity by Increasing Intracellular Tetrahydrobiopterin." *J Biol Chem* 275 (2000): 17399-17406.

How to cite this article: Muhandiram, Eindrini C. "Ascorbic Acid: A Useful Adjuvant in Refractory Immune Thrombocytopenic Purpura- A Case Report. *Clin Case Rep* 12 (2022) : 1519.