

Does So Frequent Use Of It Make Innocent? Another Brick In The Wall: Serum Sickness Induced By Horse-Antithymocyte Globulin In A Patient With Bone Marrow Failure

Gokhan Ozgur¹, Adem Aydin², Musa Baris Aykan³, Murat Yildirim⁴, Selim Sayin⁵, Cengiz Beyan⁶

¹Gülhane Training and Research Hospital, Clinical of Hematology, Etlik, Ankara, Turkey

²Health Sciences University, Gulhane School of Medicine, Department of Internal Medicine, Etlik, Ankara, Turkey

³TOBB University of Economics and Technology Faculty of Medicine, Department of Internal Medicine, Çankaya, Ankara, Turkey

*Corresponding author

Adem Aydin

Article History

Received: 22.09.2017

Accepted: 09.10.2017

Published: 30.10.2017

DOI:

10.36347/sjmcrr.2017.v05i10.005



Abstract: Aplastic anemia is a condition characterized by the absence or decrease of hematopoietic progenitor cells in the bone marrow. The disease is considered to occur as a result of immune response triggered by the environmental factors, infective agents or endogenous antigens. Cyclosporine and antithymocyte globulin is recommended as first line therapy in patients have no unidentified suitable donor or hematopoietic stem cell transplantation cannot be done. However, despite skin testing for hypersensitivity and concomitant steroids, adverse effects are sometimes unavoidable. 30-year-old female patient, followed with aplastic anemia since 2012, was admitted to hospital with painful swelling in the neck, rash and joint pain began after ATG. Laboratory examination revealed pancytopenia, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). C4 and C3 were lower in tests carried to show complement consumption. Skin biopsy was reported consistent with leucocytoclastic vasculitis. The diagnosis based on clinical and laboratory investigations: serum sickness triggered by h-ATG. Firstly, ATG and tacrolimus therapy was discontinued. Methylprednisolone was started. But plasmapheresis was performed due to failure to provide relief on clinical symptoms and implementation of the h-ATG will be continued until a suitable donor identified. Recovery was experienced after three sessions of plasmapheresis and the patient is discharged. We thought that; to contribute to the literature should always not be perceived as presenting a very rare case so we find worth sharing it with the hope of shedding light on the pathophysiology, managements and current treatment methods of serum sickness.

Keywords: Antithymocyte globulin, Aplastic anemia, Plasmapheresis, Serum sickness

INTRODUCTION

Aplastic anemia is a condition characterized by the absence or decrease of hematopoietic progenitor cells in the bone marrow. The disease is considered to occur as a result of immune response triggered by the environmental factors, infective agents or endogenous antigen [1]. Blood-forming cells are destroyed by lymphocytes. Therefore, immunosuppressive agents are widely used in therapy. Cyclosporine and antithymocyte globulin is recommended as first line therapy in patients have no unidentified suitable donor or hematopoietic stem cell transplantation cannot be done [2]. However, despite skin testing for hypersensitivity and concomitant steroids, adverse effects sometimes unavoidable.

CASE REPORT

30-year-old female patient following with diagnoses of aplastic anemia was admitted to hospital

with painful swelling in the neck, rash and joint pain began ten days ago. The patient was diagnosed with aplastic anemia in 2012. Tacrolimus was began due to transaminase elevation induced by cyclosporine and bilateral aseptic necrosis of the humeral developed after steroids. During this time no longer needs blood products and two months ago immunosuppressive therapy has been started combined with horse ATG (h-ATG) in consequence of relapse. The last therapy was administered ten days ago. Physical examination revealed painful, mobile bilateral cervical and suboccipital lymphadenopathy. There was generalized erythematous and macular lesions on anterior lower trunk, groin. Knee, shoulder, hip and wrist movements were painful and range of motions was limited. But there was no red or swollen joints. Laboratory examination revealed pancytopenia, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The urine analysis to demonstrate the

renal involvement was normal. Urea, creatinine and liver function tests indicated no pathology. C4 and C3 was lower in tests carried to show complement consumption. Hepatitis B, one of the possible infectious agents, serology was negative. Cervical ultrasound laid out a large number of lymphadenopathy without blood flow signal. Skin biopsy was reported consistent with leucocytoclastic vasculitis. The diagnosis on the basis of clinical and laboratory investigations: serum sickness triggered by h-ATG. Firstly; ATG and tacrolimus therapy was discontinued. Methylprednisolone was started. After the patients were followed for a week, plasmapheresis was performed due to failure to provide relief on clinical symptoms and implementation of the h-ATG will be continued until a suitable donor identified. Recovery was experienced after three sessions of plasmapheresis and the patient is discharged.

DISCUSSION

Heterologous immunoglobulins had been used in children with diphtheria disease for the first time by Von Behring and in the following process toxic reactions has been identified with the widespread use [3]. The classic presentation characterized by fever, skin rash, lymphadenopathy and polyarthralgia has been observed in patients treated with horse serum in 1905 [4]. In that period, it has been shown that the risk of disease is directly proportional to the amounts and the number of previously applied dosage; but with the current technological capabilities it has not been able to explain the underlying pathological mechanism. In the next process, with the wide use of the heterologous immunoglobulins in areas such as infectious diseases, bone marrow failure and organ transplantation; a large number of cases had been defined including adverse effects, as well as it have been demonstrated the disease develops through the of immunocomplexes formed by the immunoglobulin generated against the protein in the serum [5]. Under normal circumstances the immune complexes are removed by mononuclear cells from the circulation. However, in case of excessive immune complex production or exceeds the capacity of the mononuclear system deposition in tissues is inevitable. These complexes can trigger the complement system and with the resultant inflammatory response, mononuclear phagocyte system is facilitated to eliminate immunocomplexes. The opinion that disease development is dominated by of IgG-mediated response has lost its significance, by demonstration that IgM, IgA and IgE is more dominant in the skin biopsies [6]. Serum sickness, classically, occurs with the administration anti-thymocyte globulins (ATG) derived from the rabbit and equine [7]. In a prospective study including 35 patients with bone marrow failure, ATG was given and SS has been observed in 86% of the patient's [3]. Serum sickness; is a clinical condition presenting with fever, rash, polyarthralgia, polyarthritis occurs after exposure to the agents within one to two weeks. After removal of the culprit antigen, symptoms

regresses within weeks. The macular itchy erythematous lesions, begin at the lower anterior of the body and groin, subsequently spread to the upper regions is characteristic and often the first signs of the disease. The absence of mucosal involvement is important in the differential diagnosis of disease. Fever is often the remittent and malaise becomes apparent in febrile period. Arthralgia observed in two thirds of patients and can be felt in almost all joints. More rarely, in severe cases, joint swelling and restricted range of motion can be defined. Headache, blurred vision, neuropathy, and lymphadenopathy are other rare clinical presentations. In the treatments of SS; there is no evidence-based guidelines and controlled clinical trials. Glucocorticoids can be preferred in cases with higher fever, significant arthralgia or arthritis. The plasmapheresis can be performed in patients with recurrent and refractory to treatment diseases or the causative agent could not be interrupted [8].

CONCLUSION

To contribute to the literature should always not be perceived as presenting a very rare case, to discover a new molecule or design studies with broad participation. Did we describe a novel clinical entity? Maybe not. Did we propose a new diagnosis and treatment methods? Maybe not. Our case is just another brick in a big wall. However; we find worth sharing it with the hope of shedding light on the pathophysiology, managements and current treatment methods of serum sickness as a brief review.

REFERENCES

1. Young NS. Acquired aplastic anemia. *Annals of Internal Medicine*. 2002 Apr 2;136(7):534-46.
2. Frickhofen N, Kaltwasser JP, Schrezenmeier H, Raghavachar A, Vogt HG, Herrmann F, Freund M, Meusers P, Salama A, Heimpel H, German Aplastic Anemia Study Group*. Treatment of aplastic anemia with antilymphocyte globulin and methylprednisolone with or without cyclosporine. *New England Journal of Medicine*. 1991 May 9;324(19):1297-304.
3. Bielory L, Gascon P, Lawley TJ, Young NS, Frank MM. Human serum sickness: a prospective analysis of 35 patients treated with equine anti-thymocyte globulin for bone marrow failure. *Medicine*. 1988 Jan 1;67(1):40-57.
4. von Pirquet CF, Schick B. Die Serumkrankheit von---und B (ela) Schick. Deuticke; 1905.
5. Lawley TJ, Bielory L, Gascon P, Yancey KB, Young NS, Frank MM. A prospective clinical and immunologic analysis of patients with serum sickness. *New England Journal of Medicine*. 1984 Nov 29;311(22):1407-13.
6. Bielory L, Yancey KB, Young NS, Frank MM, Lawley TJ. Cutaneous manifestations of serum

- sickness in patients receiving antithymocyte globulin. *Journal of the American Academy of Dermatology*. 1985 Sep 1;13(3):411-7.
7. Rizkallah J, Cordova F, Malik A, Zieroth S. Serum sickness after antithymocyte globulin administration in a cardiac transplant patient. *Transplantation*. 2012 Dec 15;94(11):e68-9.
 8. Bayraktar F, Akinci B, Demirkan F, Yener S, Yesil S, Kirmaz C, Comlekci A. Serum sickness-like reactions associated with type III insulin allergy responding to plasmapheresis. *Diabetic Medicine*. 2009 Jun 1;26(6):659-60.