SUMEJ
Sumatera Medical Journal
Journal homepage: https://talenta.usu.ac.id/smj

Case Report

Warm Autoimmune Hemolytic Anemia with Chronic Hepatitis B

Adefri Wahyudi[1] , Fadrian[*2] , Rudy Afriant[3]
[1]*Department of Internal Medicine, Faculty of Medicine, Universitas Andalas, Padang, 25163, Indonesia*
[2]*Division of Tropical and Infectious Diseases, Department of Internal Medicine, Faculty of Medicine, Universitas Andalas, Padang, 25163, Indonesia*
[3]*Division of Medical Hematooncology, Department of Internal Medicine, Faculty of Medicine, Universitas Andalas, Padang, 25163, Indonesia*
*Corresponding author: fadrian@med.unand.ac.id

ARTICLE INFO

Article history:
Received 14 April 2023
Revised 20 December 2023
Accepted 04 December 2023
Available online 01 January 2024

E-ISSN: 2622-1357
P-ISSN: 2622-9234

How to cite:
Adefri Wahyudi, Fadrian, Rudy Afriant, "Warm Autoimmune Hemolytic Anemia in a Patient with Chronic Hepatitis B Infection", SUMEJ, Vol. 07, No. 01, January 2024.

https://doi.org/10.32734/sumej.v7i1.11836.

ABSTRACT

Background: Warm autoimmune hemolytic anemia (wAIHA) is caused by erithrocytes destruction by IgG or IgG plus C3d-mediated autoantibody. **Objective:** To present a case of warm autoimmune hemolytic anemia (wAIHA) in a patient with chronic hepatitis B infection. **Methods:** This is a case report that showed a special case. **Results:** Man, 64 y.o, hospitalized with diagnosis wAIHA and chronic hepatitis B. Diagnosis of wAIHA is built by: severe normocytic normochromic anemia, reticulocytosis 42.29%, increasing *lactate dehydrogenase* 397 U/L, direct Coombs test (+4), antibody screening IgG (+4). Anothers laboratorium findings: HbsAg (+), albumin 3.5 g/dL, ALT U/L, rapid HIV (-), anti HCV (-). There is no blast found in peripheral blood and bone marrow smear. Patient also diagnosed chronic hepatitis B inactive phase with negative HbeAg, HBV DNA 547 IU/L, normal liver finding in abdominal USG and moderate fibrosis from fibroscan. Washed red cell transfussion was administered, 2 x 125 mg methilprednisolone iv (3 days) tapering off until to 40 mg/day doses. He did not get antiviral prophylaxis and be planned to reevaluate in next 6 months. **Conclusion**: Steroid is first line therapy in wAIHA. When wAIHA is diagnosed, determination of chronic hepatitis B status should confirmed. There is a risk of reactivation of chronic hepatitis B infection so monitoring is needed.

Keywords: chronic hepatitis b, steroid, warm, AIHA

1. Introduction

Autoimmune hemolytic anemia (AIHA) is a hemoglobin level that is less than normal due to damage to erythrocytes caused by autoantibodies against erythrocytes [1]. Based on the optimal temperature at which hemolysis occurs, AIHA can be divided into: warm type, cold type, mixed type, and paroxysmal cold hemoglobinuria. Warm-type AIHA is characterized by optimal hemolysis occurring at 37°C with involvement of IgG immunoglobulin [2]. Based on the etiology, AIHA can be classified into primary and secondary AIHA. About 50% of cases of warm-type AIHA are secondary type. Some conditions that can predispose to AIHA are chronic infection, malignancy, lymphoproliferative disorders, systemic lupus erythematosus, kidney disease, and the use of immunoglobulin drugs. One infection that can predispose to AIHA is chronic hepatitis B [3].

2. Case Presentation

A 64-year-old male was admitted with chief complaints of fatigue and weakness accompanied by looked pale since 2 weeks ago. There is no history of bleeding. He also complained of yellowish sclera and subfebrile fever since 1 week ago. There was no history of previous transfusion, drug abused, and hepatitis.

From physical examination was found conjunctiva anemic, sclerae icteric, with splenomegaly *Schuffner* 2. There are no enlarged of lymph nodes. Laboratory tests results haemoglobin 3.6 g/dl, leukocytes 14,430/mm^3, and platelets 263,000/mm^3. From peripheral blood examination, reticulocytes were 42.29 % and no blasts were found. There was mild hyperbilirubinemia with indirect bilirubin of 2.8 mg/dL, increased lactate dehydrogenase 397 U/L, with positive direct Coombs test results (+4). Antibody screening examination obtained IgG results (+4).

Other laboratory findings are HbsAg (+), AntiHCV (-), rapid HIV (-), HbeAg (-), HBV DNA 547 IU/ml, albumin 3.5 g/dl, globulin 4.4 g/dl, and ALT 9 U/L. Abdominal ultrasound examination result in normal liver and splenomegaly. Fibroscan examination showed moderate fibrosis. The patient was then treated with washed red cell transfusion, 2 x 125 mg methylprednisolone injection tapering off and continued with 40 mg/day methylprednisolone. In addition, the patient was given lansoprazole 30 mg/day and calcium tablets 1000 mg/day. The patient was not given antiretroviral prophylaxis and is planned for re-evaluation in 6 months.

3. Discussion

A 64-year-old male patient was treated with a final diagnosis of severe anemia ec AIHA warm type and chronic hepatitis B. The above diagnosis is based on anamnesis, physical examination and support. The flow of diagnosis of AIHA is if normochromic normocytic anemia with reticulocytosis is found, signs of hemolysis and a positive Coombs test [4]. Clinical signs of hemolysis are anemic conjunctiva, yellowish sclera, splenomegaly. Laboratory signs found were normocytic anemia, reticulocytosis, increased LDH, and increased serum haptoglobulin. The next step is to determine whether the anemia is immune or non-immune by using the direct antiglobulin test (DAT) or the direct Coombs test [1].

The next step is to determine the type of AIHA with a serological test to determine the type of AIHA. As much as 65% of AIHA is a warm type with the presence of IgG or IgG and anti-C3d. If IgM is found then it is cold type AIHA which causes agglutination at cold temperatures. About 50% of cases of warm-type AIHA are secondary. Some conditions that can predispose to AIHA are chronic infection, malignancy, lymphoproliferative disorders, systemic lupus erythematosus, kidney disease and use of immunoglobulin drugs [1]. Primary screening tests that can be performed are HIV, HBV, HCV, dsDNA, ANA profile, and a CT scan of the chest and abdomen if needed. In patients who are more than 60 years old and have lymphoproliferative abnormalities from peripheral blood preparations, bone marrow investigation can be performed.

In addition, if reticulocytopenia is found, parvovirus examination is necessary. If no cause is found above, then primary warm type AIHA can be enforced. Positive HbsAg is an indication of hepatitis B infection in the patient. If the infection has lasted more than 6 months it is known as chronic hepatitis B [5]. Before giving therapy for chronic hepatitis B, it is necessary to evaluate: hepatitis B and HBeAg infection status, assess the degree of liver damage through liver enzyme examination and ultrasound, other causes of liver disease such as HIV, HCV, and steatosis. Indications for antiretroviral therapy were determined based on a combination of criteria: HBV DNA value, HBeAg status, ALT value, and liver histology [6].

In patients, the results showed a minimal increase in indirect bilirubin 2.8 mg/dL, direct bilirubin 1.2 mg/dL, normal albumin levels 3.5 g/dL, globulin 4.4 g/dL, ALT 9 U/L, HBV DNA 547 IU/mL, with HBeAg negative. Ultrasound examination of the abdomen revealed a normal liver and splenomegaly. Examination of the fibroscan results showed moderate fibrosis. Based on the examination, the patient was concluded to be in the inactive phase of chronic hepatitis B with hepatic abnormalities in the compensated phase.

Patients were treated with 2 units/day of WRC transfusion, given 2 × 125 mg of methylprednisolone IV tapering off and continued with 16-16-8 mg of methylprednisolone p.o (equivalent to prednisone 1 mg/kg/day) for 2 weeks and tapering off. Apart from that, they were also given lansoprazole 30 mg p.o/day, and calcium tablets 1000 mg/day. Corticosteroids are the first-line treatment for warm-type AIHA patients. Steroid administration with an initial dose of prednisone 1.0–1.5 mg/kg/day or equivalent for 1–3 weeks until an Hb level of more than 10 g/dL is achieved. Administration of methylprednisolone at a dose of 250–1000 mg/d within 1–3 days intravenously can be done if signs of severe hemolysis are found [3].

Barcellini et al. (2020) explained that the response to steroid therapy in warm-type AIHA cases reached 75–80%. Side effects that can occur with long-term use of steroids (>1 month) include infection, osteoporosis, and Cushing's syndrome. To prevent these effects, it is necessary to give calcium supplementation and mucoprotector drugs [3]. Blood transfusions in cases of AIHA need to be done if life-threatening conditions

are found in the form of severe anemia <6 g/dL and increased oxygen demand. If possible, crossmatching to antigen erythrocytes can be done [3].

There is no prophylactic use of antivirals for steroid use in Indonesia. Hatano et al. (2018) conducted a study of the reactivation rate of hepatitis B in patients receiving steroid therapy for 8–10 years with a population of adrenal insufficiency and rheumatoid arthritis as samples. The average prednisone dose for adrenal insufficiency is 5 mg and for rheumatoid arthritis is 50 mg. Of the 80 samples, reactivation of hepatitis B occurred in 2 people (2.5%). The mechanism for the reactivation of the hepatitis B virus is thought to be through two mechanisms, namely: direct initiation of steroids against the receptor glycoproteins of the hepatitis B virus which induce replication and conditions of immunotolerance that occur due to the use of steroids [7].

Zhong et al. (2021) in their study concluded that patients using steroids equivalent to prednisone >20 mg/day for more than 1 month are included in the high-risk group for flares and reactivation, so they need to be given antiviral prophylactic therapy [8]. On the other hand, Jeong et al. (2021) explained that the use of low-dose steroids (prednisone equivalent <10 mg/day) did not result in hepatitis B reactivation, so antivirals did not need to be given [9-12]. Based on the above, the patient was not given antiviral prophylaxis according to the algorithm in chronic hepatitis B cases with negative HBeAg and will be reevaluated by assessing HBV DNA, alpha-fetoprotein (AFP), and ALT after 6 months of steroid administration.

4. Conclusion

Warm autoimmune hemolytic anemia (wAIHA) is a condition requiring prompt diagnosis and initiation of steroid therapy as the first-line treatment. In patients with concurrent chronic hepatitis B infection, it is important to assess the risk of viral reactivation when initiating steroids. Although prophylactic antivirals are generally recommended for high-dose, long-term steroid use, in cases with low viral load, negative HBeAg, and moderate fibrosis without active hepatitis, careful monitoring without antiviral prophylaxis can be considered. Regular follow-up to reassess HBV DNA levels, liver function, and hepatitis activity is essential to prevent complications.

5. Data Availability Statement

The datasets generated and analyzed during the current study are not publicly available due to privacy and ethical considerations but are available from the corresponding author upon reasonable request.

6. Ethical Statement

Sumatera Medical Journal (SUMEJ) is a peer-reviewed electronic internationaljournal. This statement clarifies ethical behavior of all parties involved in the act of publishing an article in Sumatera Medical Journal (SUMEJ), including the authors, the chief editor, the Editorial Board, the peer-reviewer and the publisher (TALENTA Publisher UniversitasSumatera Utara). This statement is based on COPE's Best Practice Guidelines for Journal Editors.

7. Author Contributions

All authors contributed to the design and implementation of this research, data analysis, and finalizing the manuscript.

8. Funding

No funding.

9. Acknowledgement

The authors thank to the staff and member for their valuable assistance during data collection and analysis.

10. Conflict of Interest

Authors declares no conflict of interest.

References

[1] Parjono E. et al (eds). Buku Ajar Ilmu Penyakit Dalam Volume VII. Jakarta: Interna Publishing. 2018;663–8.
[2] Barcellini W, Zaninoni A, Giannotta A, et al. Review: New insights in autoimmune hemolytic anemia: from pathogenesis to therapy. Journal of Clinical Medicine. 2022;3859(9):1–19
[3] Hill A, and Hill QA. Autoimmune hemoliytic anemia. Hemolytic Anemia: Cornucopia of causes. American Society of Hematology. 2018:382–9

[4] Parjono E, et al (eds). Buku Ajar Ilmu Penyakit Dalam Volume VII. Jakarta: Interna Publishing. 2018;632–5
[5] Zanella A, and Barcellini W. Review: Treatment of autoimmune hemolytic anemias. Haematologica. 2014;99(10):1547–54
[6] Perhimpunan Peneliti Hati Indonesia. Konsensus Nasional Penatalaksanaan Hepatitis B. Jakarta: Perhati. 2018.
[7] Hatano M, Mimura T, Shimada A, et al. Original article: Hepatitis B virus reactivation with corticosteroid therapy in patiens with adrenal insuficiency. Endocrinology, Diabetes & Metabolism. 2019;2:1–7.
[8] Zhong Z, Liao W, Dai L, et al. Average corticosteroid dose and risk for HBV reactivation and hepatitis flare in patients with resolved hepatitis B infection. Annals of the Rheumatic Diseases. 2022;81:584–91.
[9] Jeong W, Choe JY, Song BC, et al. Effect of low dose corticosteroid use on HBV reactivation in HbsAg positive rheumatoid arthritis patient. 2021.
[10] Barros, M. M. L., Blajchman, M. A., & Bordin, J. O. (2021). Warm autoimmune hemolytic anemia: recent progress in understanding the immunobiology and the treatment. *Transfusion Medicine Reviews*, 35(2), 129–138.
[11] Loomba, R., & Liang, T. J. (2017). Hepatitis B reactivation associated with immune suppressive and biological modifier therapies: current concepts, management strategies, and future directions. *Gastroenterology*, 152(6), 1297–1309.
[12] Terrault, N. A., Lok, A. S. F., McMahon, B. J., Chang, K. M., Hwang, J. P., Jonas, M. M., & Brown, R. S. (2018). Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*, 67(4), 1560–1599.