Management of Autoimmune Hemolytic Anemia in the Midst of Coronavirus Disease 2019 Pandemic: A Case Report

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Abstract

Introduction : The novel coronavirus disease 2019 (COVID-19) has become a pandemic COVID-19 has involved all people, it can be severe and life-threatening in a certain population such as those with comorbidity. Autoimmune hemolytic anemia (AIHA) is an autoimmune hematologic disease characterized with antibodies production that binds to red cell surface antigens. In this pandemic, several concerns have been raised by autoimmune disease clinicians and patients regarding the use of immunosuppressive drugs. In this case report, we illustrate the problems of autoimmune hemolytic anemia patient when she got active case.

Case Illustration : A 28 years old lady was admitted to the hospital owing to fatigue and tired during exercise for two weeks. She had been diagnosed with autoimmune hemolytic anemia before and was not comply with the treatment. This patient has been reevaluated of having AIHA from the symptoms of fatigue, enlarged spleen, low hemoglobin, increased reticulocytes, signs of hemolytic in blood smear examination, increased indirect bilirubin, LDH and the Combs' test result was given positive. She received methylprednisolone 2 mg/kg of body weight intravenously, washed packed red cells (PRC), calcium and proton pump inhibitor. She was discharged at the seventh day since admission and she was prescribed oral methylprednisolone equal to 1 mg/kg body weight.

Conclusion :
This is an educated case of non-compliance of AIHA that should be given high dose steroid and blood transfusion during hospitalization amid the COVID-19 pandemic. The recommendation of treatment for AIHA was still the same as before the pandemic occur.

Introduction

The novel coronavirus disease 2019 (COVID-19) has become a pandemic since it was announced by World Health Organization (WHO) at the end of January 2020. The COVID-19 pandemic is worsening globally. Nowadays, the virus has rapidly spread around the world. Until this article was written, the positive cases have increased to 4,524,679 and 303,345 deaths worldwide. In Indonesia there were 16,006 positive cases and 1,043 death cases.[1] According to the current literature, COVID-19 has involved individuals aged 30-80 years and has low mortality in healthy individuals but it can be severe and life-threatening in certain population such as those with comorbidity.[2]

Autoimmune hemolytic anemia (AIHA) is the clinical condition in which antibodies of immunoglobulin G (IgG) and/or immunoglobulin M (IgM) bind to red cell surface antigens and initiate red cell destruction via the complement system and the reticuloendothelial system. AIHA is characterized by the production of autoantibodies directed against red blood cells (RBC). The treatment of AIHA depends on the type of antibodies and the course of the disease. Steroid and immunosuppressant agent were the mainstay of treatment beside splenectomy. In certain cases, the autoimmune hemolytic anemia needs blood transfusion for patient with extremely severe anemia.[3]

During the pandemic, several concerns have been raised by hematologist, autoimmune disease clinicians, and as well as autoimmune patients who took Immunosuppressive drugs. There is a concern whether immunosuppressant treatment might increase the risk of severe COVID-19.[4] The other concern was on the blood availability in the community. The blood supply from the donor was decreased during the pandemic.[5] In this case report, we illustrated the problems of autoimmune hemolytic anemia patients when they got active case. As the COVID-19 cases had unfolded worldwide, the information would be so crucial for patients and clinicians to make evidence-based decision in how we should manage AIHA during the pandemic.

Case illustration

A 28 years old lady admitted to the hospital owing to fatigue and tired during exercise for two weeks. She was diagnosed autoimmune hemolytic anemia one year ago. She was hospitalized three times with the similar complaints, fatigue and tiredness. She took prednisone 50 mg daily with other vitamins. However, she frequently stopped to consume it when there were no symptoms felt. Her condition had ever been complicated with tuberculosis peritoneal and she took the tuberculosis drugs for 9 months. There is no history of blood transfusion in one month before.

When she arrived in the emergency ward, firstly, she was screened for COVID-19 and the result was negative. The vital signs were stable. The eye looked pale and slightly icteric. The spleen was enlarged with the size of *schuffner* 4. The others physical examination was unremarkable. The initial hemoglobin was 3.2 g/dl, normal leucocyte and low platelet 99,000/mcL. The mean corpuscular volume was 120 fl and the reticulocyte was increased to 3.5%. The blood smear showed normocytic anemia, spherocyte, and helmet cells. Both indirect bilirubin and lactate dehydrogenase (LDH) was increased to 3mg/dL and 1027 U/liter, respectively. The combs test showed autoantibodies to red blood cells with positive IgG and complement 3 (C3).

She was diagnosed warm type autoimmune hemolytic anemia with severe anemia. She was given methyl prednisolone 2 mg/kg body weight intravenously, calcium tablet 500 mg three times daily, and proton pump inhibitor omeprazole 20 mg daily. She was planned to receive washed packed red cells (PRC), but there was a delay and given on the second day after admission. A total of 5 unit washed PRC with furosemide prophylaxis were given, the hemoglobin was increased to 6.8 g/dl in the day four. She was discharged at the seven day of admission with hemoglobin 13 g/dl, and she was prescribed daily with methyl prednisolone equal to 1 mg/kg body weight, calcium, omeprazole and folic acid orally. The detail of hemoglobin results can be seen in figure 1.

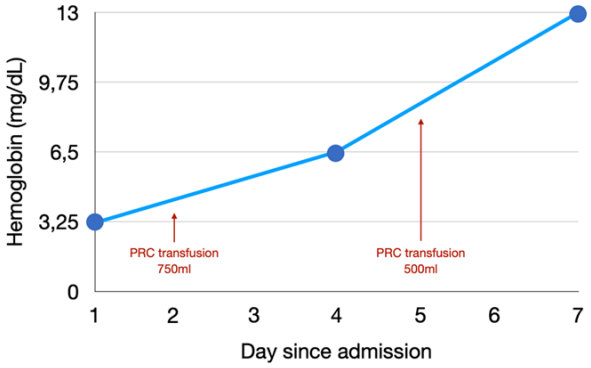

Figure 1. The hemoglobin results

Discussion

The diagnosis and management of AIHA continued to be challenging in current practice. It was related to an incomplete understanding of the pathophysiology of disease process, complexity of initiating factors and lack of evidence in the standardized therapy. However, it became more complicated throughout the pandemic era. This patient had been reevaluated of having hemolytic anemia from her complaints of fatigue, enlarged spleen, low hemoglobin, increased reticulocytes, signs of hemolytic in blood smear examination, increased indirect bilirubin and LDH. The Coombs test result confirmed her of having AIHA warm type. The algorithm of AIHA diagnosis can be seen in figure 2. The low platelet should be thought several differential diagnoses such as thrombotic microangiopathy or Evan syndrome.[6]

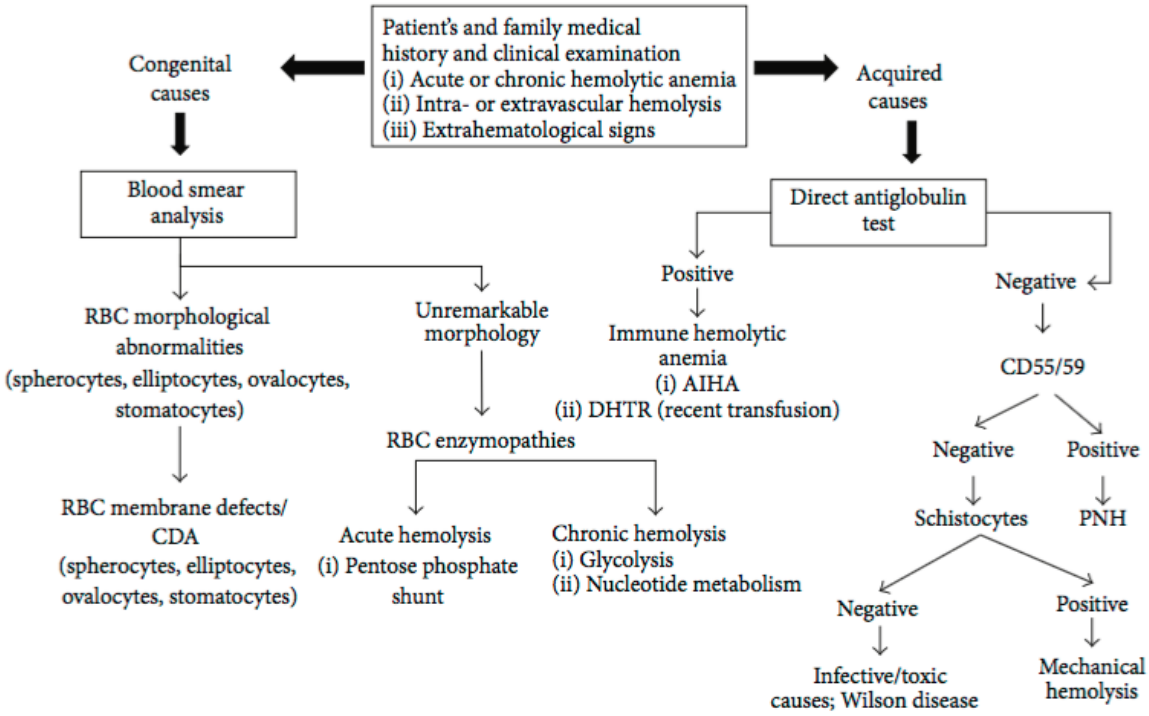

Figure 2. Diagnostic algorithm of hemolytic anemia.[6] RBC: red blood cells; AIHA: autoimmune hemolytic anemia; DHTR: delayed hemolytic transfusion reactions; CDA: congenital *dyserythropoetic* anemia; PNH: paroxysmal nocturnal hemoglobinuria

She was planned on the first day of hospital stay to received blood transfusion of washed PRC due to her condition, severe anemia. Unfortunately, there was limited supply of blood in the red cross society. Thus, she was transfused in the second day. The challenges faced by the blood banks were to secure and protect the blood supply while the demand for blood and blood product my decrease during a pandemic due to postponement of elective surgeries, measures such as physical distancing and a large scale social restricted policy in the city may result in a larger decline in blood supply and an overall shortage of blood products.[5]

The patient was given high dose of steroid due to severe acute of AIHA. The first line treatment of warmed type AIHA was steroid with immunosuppressant dose. The patient had previous three episodes of severe anemia in the past year. Evaluation of refractory of AIHA should be in a consideration. Barcelini et al proposed the definition of refractory AIHA in the following scenarios: (1) Requirement of >20 mg of prednisone daily (or equivalent corticosteroid) to maintain hemolysis control; (2) Clinically significant relapse (hemoglobin <11 g/dl or symptomatic anemia with ongoing evidence of hemolysis); or (3) Intolerance to a currently effective treatment. If the hemolysis continued when the prednisone was being tapered, the second-line treatment with immunosuppressant can be considered.[7]

The dose of steroid was tapered after the hemoglobin value increased in day 5 of hospitalization. The increasing of hemoglobin might be due to the blood transfusion. The steroid would work after 5-7 days of administration. After the fifth day of given high dose steroid, the steroid was tapered to 1 mg/kg body weight dose. On the seventh day, the patient's hemoglobin became normal 13 g/dl. She was discharged on day seven of hospitalization with orally steroid equal to 1 mg/kg body weight dose. Although steroid had led good response in warmed type AIHA, the complication of the treatment especially, the risk of infections remained as major area of concern. When it was used as pulse or high dose therapy, steroid might cause side effects on cardiac. This concern became even more pronounced during the COVID-19 pandemic. Existing clinical data have not confirmed the use of corticosteroid towards the risk of COVID-19 infection and manifest as more severe case.[8] The universal precaution related to the prevention of contracting the disease should be done, such as using face mask, physical distancing and hand washing with soap and water regularly.[9]

The patient was educated to discuss any further complaints by teleconference with the physician. The dose of steroid was planned to be tapered at home after three weeks of treatment with a stable hemoglobin value. In many locations, going to a health care facility might increase the risk of being contracted by COVID-19. Most autoimmune disease patients should therefore be managed by phone, text, or email to follow-up their symptoms and should have less frequent blood counts. Nonetheless, certain condition who was unstable may need monitoring by regular check of blood counts. The patients should be educated to decrease the steroid dose weekly and called the healthcare if they develop symptoms of fatigue.[8]

AIHA patients, like other hematologic autoimmune disease who were stable on low dose of immunosuppressive drugs, should be maintained without treatment adjustment during COVID-19 pandemic. Changing the treatment were requiring increased in monitoring and could potentially result in relapse, thus it might be riskier than making no changes. For patients on higher doses of corticosteroid or immunosuppressive drugs, there were still no data to decrease or change to alternative

treatment because of limited options of treatment.[8]

Conclusion

This is an educational case of non-compliance patient in AIHA treatment that should be given high dose steroid and in need of blood transfusion during hospitalization during the COVID-19 pandemic. There was still a scarce evidence to associate between high dose steroid consumption and the risk of severe COVID-19 infection. The recommendation of treatment of AIHA was still the same as before the pandemic occurred. Further study is needed to be done for evaluating the risk of using high dose steroid regarding the risk of COVID-19 infection.

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