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A-50-Year-Old Woman with Autoimmune Hemolytic Anemia (AIHA): A Case Report

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Abstract: ***Autoimmune Hemolytic Anemia (AIHA) is a disorder of red blood cells characterized by the destruction of erythrocytes by autoantibodies in the patient's body. A 50-year-old woman came to Emergency Room Pertamina Balikpapan Hospital with complaints of weakness throughout the body; three (3) days before admission to the hospital; accompanied by joint pain, back pain, and headaches. The patient had similar complaints a year ago, Hemoglobin (Hb) measurement at that time was 6.5gr/dL, and we have performed two (2) colf blood transfusion. No family member experienced this kind of complaint. On the physical examination, the patient was compos mentis, medium pain when joints were moved, conjunctiva anemic, pain in the epigastric region, palpation of tactile fremitus, and vesicular auscultation. On the laboratory examination, the patient's Hemoglobin (Hb) around 7.7gr/dL, erythrocytes 2.74 million/mm3 with morphology's finding mild normochromic anisocytosis, positive agglutination, positive young erythrocytes, and has indicated anemia normochrome anisopoikilocytosis with erythrocytes activation. Low hematocrit (24.3%), high neutrophils (50), high reticulocytes (2.9), a positive result of Coombs test, abnormal iron and bilirubin content, and high ferritin found in the blood tests result. From all those parameters, the diagnosis (Dd) has led to Autoimmune Hemolytic Anemia. We have advised a patient to perform an Antinuclear Antibody (ANA) profile; also haptoglobin (Hp) and the results were positive. We have treated a patient with IVFD RL 15 TPM, methylprednisolone 2x62.5mg/12h injections, Bionemi 1x1, Ranitidine 2x1, folic acid 1x1, monitor the transfusion, and periodic vital measurements. We have discharged a patient from the hospital with the improvement of her condition and Hemoglobin (Hb) level has reached to 12,5g/dL.***

Keywords: autoimmune, ANA, coombs test, DAT, hemolytic anemia

1. Introduction

Autoimmune Hemolytic Anemia (AIHA) is a disorder of red blood cells characterized by destruction of erythrocytes by autoantibodies in the body of the patient.[1] Though uncommon, but the disease is not rare. The overall incidence is one (1) in 80.000 to 100.000 of a given population/year in the Caucasians.[2] More than 70% of new cases are seen annually in patients above 40 years of age. The peak incidence is between 60 and 70 years of age, and the frequency of the disorder is usually more in women than in men. The men to women ratio is 40:60 with mortality rate is approximately 11%.[3] Based on temperatures at which autoantibodies react with red blood cells, AIHA is classified into warm and cold antibody types. Warm antibody AIHA occurs predominantly in children aged 2–12 years. They belong to the IgG class, react at temperatures ≥37°C, do not require complement for activity, and do not produce agglutination in vitro.

On the other hand, cold antibody AIHA occurs less commonly in children. Antibodies are of IgM class which react at temperatures <37°C, require complement for activity, and produce spontaneous agglutination of red blood cells in vitro.[4] Mixed warm and cold antibody AIHA is the presence of both warm and cold autoantibodies.[5] About 50 percent of all AIHA cases are idiopathic splenomegaly. AIHA can occur at any point in life and can develop suddenly or gradually. If AIHA is not idiopathic, it is caused by an underlying disease or medication, such as lymphoproliferative syndrome (20%), autoimmune disease as systemic lupus erythematosus (SLE) or splenomegaly (20%) to infections and tumors.[6-8] Clinical manifestations of AIHA will generally appear slowly over a few months to years depending on the severity of anemia, from compensated asymptomatic reticulocytosis with mild hyperbilirubinemia to fulminant hemolysis with jaundice, hepatosplenomegaly, tachycardia, and angina.

The clinical manifestations are also distinguished based on the presence of primary disease and hemolysis degree depending on the type of autoantibodies. Patients with warm reactions to IgM were reported likely to have severity hemolysis and its mortality rate higher than AIHA type cold. The degree of anemia generally depends on the body's compensation ability with increased reticulocytes. The patients with reticulocytopenia generally have worse clinical circumstances and require appropriate red blood cell transfusion.[9] Diagnostic approach of AIHA requires proof of anemia caused by the hemolysis process and the results of serological examinations that prove the presence of anti-erythrocyte antibodies detected with Direct Antiglobulin Test (DAT).[10]

2. Case Report

A 50-year-old woman came to Pertamina Balikpapan Hospital's emergency room with the main complaint of weakness three (3) days before being admitted to the hospital. A whole day, complaints were felt throughout the body, become heavy during activities, and not disappeared after resting. The patient did not take any vitamins or drugs to resolve this problem. The patient also complains of frequent joint pain (4-5 scale) in the same spots between the right and left limbs. She also felt headaches, lost appetite, and abdominal pain. The patient had some similar complaints a year ago, at that time Hemoglobin (Hb) was 6.5gr/dL, and

had a blood transfusion of 2 colf. No family member has experienced this kind of symptoms.

On the physical examination **(Table 1)**, the patient's condition was in moderate pain, compos mentis, pressure blood 100/70 mmHg, pulse rate 72 times per minute, regular rhythmic, respiration rate 20 times per minute, body temperature 36.6 degrees of Celsius, two (2) kgs of weight loss, conjunctiva anemic from both eyes, auricular and ear canal normal, neck normal; no indication of thyroid enlargement or lymphadenopathy, and neurological status within normal limits. On the chest examination **(Table 2)**, lung inspection in a normal shape, no retraction, symmetrical vocal fremitus in the left and right lungs, sonor percussion in all lung fields, vesicular auscultation, no rhonchi, no wheezing, and heart sound was normal I and II without murmurs.

The abdominal examination **(Table 2)** was in a normal condition, flat shape, no scar or trauma, normal bowel sounds, tenderness on the palpation of epigastric region, palpation of the spleen undetected, tympanic percussion without any signs of abnormality. On the examination of the extremities **(Table 2)**, the pain was found when the patient did a range of motion active, akral palpable warm, capillary refill <2 seconds, positive pulse was sufficient and regular, cyanosis (-), and edema (-). On the laboratory examination **(Table 3)**, the patient had hemoglobin (Hb) 7.7 gr/dL, leukocytes 5750/µL, hematocrit (Ht) 24,3%, platelets 170.000/µL. We have performed a morphological examination of the peripheral blood smear (ADT) and observed a picture **(Figure 1)** in the form of mild normochromic anisocytosis, agglutination (+), young erythrocytes (+), reactive lymphocytes, and indicated anemia normochrome anisopoikilocytosis with erythrocytes activation. Other parameters such as low hematocrit (24.3%), high neutrophils (50), high reticulocytes (2.9), Coombs test (+), iron contents (150ug/dL), high bilirubin (1.95mg/dL), and high ferritin (1084 ng/dL). All of those parameters has led to Autoimmune Hemolytic Anemia diagnosis.

We have advised a patient to check the ANA, LDH profile, and haptoglobin levels. While the patient was waiting for the ANA profile results, we have treated a patient for one week to manage the symptoms. In non-pharmacotherapy treatment, we encouraged the patient to rest for a while, and we informed a patient and family member regarding this disease. We have given pharmacotherapy treatment such as ringer lactate 2000cc per 24 hours, methylprednisolone 2x62.5mg intravenous, bionemi 1x1 tab, ranitidine 2x1 tab, and folic acid 1x1 tab. We also have performed transfusion monitoring and periodic vital measurements to monitor and observe the patient. LDH profile was standard, but the ANA profile test was positive. After seven (7) days of being hospitalized, we have discharged a patient from the hospital because of getting better, and the level of hemoglobin (Hb) has reached 12,5g/dL

Table 1: Physical Examination Results

General Status	
Condition	Moderate Pain
Conciousness	Compos Mentis
Vital Signs	
Pulse (mins)	72x/mins
Breath Frequency (mins)	20x/mins
Blood Pressure (mmHg)	100/70
Temperature (deg C)	36.6
Weight (kgs)	48
Height (cms)	150

Table 2: Physiology and Chest Examination Results

External Examination	
Skin	Normal skin and no rash
Head	Normocephaly
Eyes	Icteric sclera -/-, conjunctiva anemic +/+, strabismus -/-.
Ear, Nose, Throat	Ear: auricular and canal normal, secretions -/-, nose: septal deviation (-), normal infundibulum, secretions -/-, throat: T1/T1 tonsils, pharyngeal arch is not hyperemic, uvula deviation (-)
Neck	Normal, no indication of thyroid enlargement or lymphadenopathy
Chest Examination	
Lung	Inspection: normal in shape, symmetrical lung movements Palpation: tactile fremitus +/+ Percussion: sonor percussion and resonant Auscultation: Inspiration>Expiration, Vesicular +/+, Rhonchi -/-, Wheezing -/-
Heart	S1S2 Regular. S3 (-), S4 (-), Murmur (-), Gallop (-)
Abdomen	Inspection: flat shape, scar or trauma (-), bowel contour (-) Auscultation: normal (+) bowel sounds Percussion: tympanic Palpation: tenderness (+) in the epigastric region Special Palpation Palpation of the liver: 2 fingers palpable under the arch of the ribs, soft edges Palpation spleen: not palpable
Extremities	Akral warm Capillary refill <2 seconds The pulse (+) is sufficient, regular Cyanosis (-) Edem (-)

Table 3: Laboratory Test Results

Complete Blood Tests	
Hemoglobin	**: 7,7 gr/dL (12,8-16,8)**
Leukocytes	: 5750 / (mm^3)
Erythrocytes	**: 2.74 million/mm^3 (4,20-5,40)**
Platelets	: 170000/mm3 (150-400)
Hematocrit	**: 24,3 % (38,4-50,4)**
MCV	: 89 fL (81-99)
MCHC	: 32 g/dL (33-37)
MCH	: 28 pg (27-31)
Diff Count	
Basophils	: 0 (0-1)
Eosinophils	: 1 (0-7)
Neutrophils	**: 50 (40-47)**
Lymphocytes	: 42 (19-48)
Monocytes	: 7 (3-9)
Blood Type	: A
Rhesus	: +
Coomb's test	**: +**
Reticulocytes	**: 2,9 (0.5-1,5)**
Blood Chemical Results	
Iron Content	: 150ug/dL (37-145)

TIBC	: 218ug/dL (228-428)
Ferritin	**: 1084 ng/dL (13-150)**
SGPT	: 26 (0-33)
SGOT	: 22 (0-40)
Creatinine	: 0,8mg/dL (0,5-0,9)
Ureum	: 27,8 mg/dL (10-50)
LDH	: 303 U/L (240-480)
Bilirubin Total	**: 1,95 mg/dL (<10)**
Bilirubin Direct	: 0.08 mg/dL (<0.25)
Bilirubin Indirect	**: 1,87 mg/dL (<0.85)**
ANA Test	**: (+) 2.0 (neg <20 Unit)**

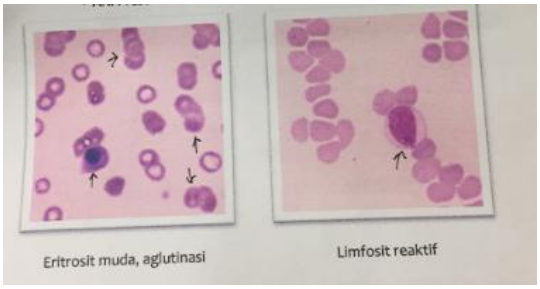

Figure 1: Morphology of Peripheral Blood

3. Discussion

Autoimmune Hemolytic Anemia (AIHA) is usually caused by intrinsic defects in red blood cells as seen typically in membrane defects, red cell enzyme deficiencies, or hemoglobin abnormalities, and most of them are inherited in nature. AIHA is one group of acquired hemolytic anemias that results from the development of autoantibodies directed against antigens on the surface of patient's red blood cells. Warm reactive autoantibodies mediate most of the cases while AIHA due to cold reactive antibodies are less common.[12] Mixed type of AIHA is rare in the pediatric age group. Review of literature revealed very few cases of mixed type of AIHA.[13, 14–17]

AIHA diagnosis is based on evidence of hemolytic anemia, jaundice, splenomegaly, reticulocytosis, raised serum bilirubin, and a positive Direct Antiglobulin Test (DAT).[11] Once AIHA has been identified, differentiation between warm and cold antibodies can be observed by monospecific DAT, which identifies responsible mechanisms. If the reaction is positive with anti-IgG and negative with anti C3d, it is usually due to warm antibodies common in idiopathic or drug-associated AIHA. If the response is positive with both anti-IgG and anti C3d, it also indicates warm autoantibodies and is more common in patients with Systemic Lupus Erythematosis (SLE) and idiopathic AIHA. In cold agglutinin disease (CAD), the reaction is positive with anti C3d but negative with anti IgG.[22] There is an agglutination of red blood cells at temperatures <37°C in a cold type of AIHA.[12]

In this case, we have diagnosed the AIHA based on anamnesis, physical and other supporting examinations (chest, lung, heart, abdomen, laboratory test, etc.). The clinical manifestations of AIHA are not much different from other manifestations of hemolytic anemia. Patients will give clinical signs of anemia, pale skin, conjunctiva anemic, and in hemolytic anemia to get jaundice and enlargement of organs reticuloendothelial.[11] Autoimmune hemolytic anemia is also associated with infection, malignancy, or other autoimmune diseases, but in most cases, it is idiopathic.[11-12] Cause of AIHA remains obscure in the majority of cases labelling them as idiopathic or primary.[18-19] Associated medical conditions linked to AIHA such as viral infections, Systemic Lupus Erythematosus (SLE), Mycoplasma Pneumonia, immunization, tuberculosis, diabetes mellitus, Hodgkin's lymphoma, autoimmune hepatitis, sepsis with bacterial endocarditis due to Staphylococcus aureus, Guillain-Barré syndrome, and Langerhan cell histiocytosis have been reported.[13,14-17,19-20]

Treatment options for AIHA depend on several factors. If the anemia is mild, it often passes without treatment. Between 70 and 80 percent of people need no treatment or minimal intervention. However, some people will need medication, surgery, or blood transfusion. If there is an underlying cause—such as cancer, an infection, or the use of some medicines—treating the condition or changing the medication may reduce AIHA symptoms. In this case, we have treated a patient with IVFD RL 15 TPM, methylprednisolone 2x62.5mg/12h injections, Bionemi 1x1, Ranitine 2x1, folic acid 1x1, transfusion monitoring, and periodic vital measurements.

4. Conclusion

In summary, this is a case of a 50-year-old woman with Autoimmune Hemolytic Anemia (AIHA). The patient was diagnosed based on the anamnesis, chest examination, and also laboratory test results. Coombs and ANA tests' positive result was strengthening the clinical manifestations of AIHA in this patient. We have treated a patient with IVFD RL 15 TPM, methylprednisolone 2x62.5mg/12h injections, Bionemi 1x1, Ranitine 2x1, folic acid 1x1, transfusion monitoring, and periodic vital measurements. We have discharged a patient from the hospital because of getting better, and the hemoglobin levels reached 12,5g/dL. Although AIHA is not an uncommon clinical disorder and requires advanced, efficient immunohematological, and transfusion support, we can handle and manage this disease very well with adequate knowledge, skills, and appropriate management and treatment.

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Author Profile

Fransisca Kristina Elisabet received MD degree in Faculty of Medicine, Maranatha Christian University (2017). Worked as a General Practitioner (GP) for various hospitals in Indonesia (2017-2019), such as Pertamina Hospital Balikpapan, Siloam Hospital Balikpapan, Medika Utama Permata (RSPKT Group) Hospital, and as a medical check-up doctor in Indomec Clinic Balikpapan. Currently, she is working as a Research Assistant at Infectious Disease Management and Control Research Center, Padjadjaran University, Bandung, and being involved in Indonesia Brain Infection Study.