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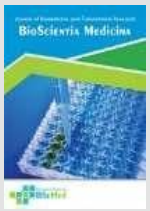

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Evans Syndrome in a Forty-Four Years Old Male Patient: A Case Report

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A B S T R A C T

Background: Evans syndrome (ES) is an autoimmune disease characterized by the presence of autoimmune hemolytic anemia (AIHA) and idiopathic thrombocytopenic purpura (ITP), together with unknown causes. ES disease is the least common, diagnosed in only 0.8% - 3.7% of all patients with AIHA or ITP. This study aimed to describe Evans syndrome in a 44-year-old male patient. **Case presentation:** A 44-year-old male patient was reported with complaints of weakness and fatigue, red spots, a history of bleeding gums, a history of bleeding from the nose, and a history of red urination. A routine blood examination revealed mild anemia, reticulocytosis, and thrombocytopenia, and the peripheral blood showed polychromatic erythrocytes. Other laboratory examinations revealed an increase in LDH. The results of a positive Comb's test and antibody screening examination showed the impression of warm-type AIHA. The diagnosis of Evans syndrome in this patient was confirmed by the presence of AIHA and ITP, which co-occur and are primarily due to unknown causes. **Conclusion:** ES is a rare disorder and a diagnosis of exclusion. The diagnosis of ES was established by the presence of signs and symptoms of AIHA and ITP accompanied by a positive direct antiglobulin test with no other etiology found.

1. Introduction

Evans syndrome (ES) is an autoimmune disease characterized by the presence of autoimmune hemolytic anemia (AIHA) and idiopathic thrombocytopenic purpura (ITP), together with unknown causes.[1] ES is classified into primary (idiopathic) and secondary (related to primary disease).[2] The etiology of ES is still unknown. ES is rarely diagnosed and found in only 0.8-3.7% of all patients with AIHA or ITP.[3] Incidence of ES is significantly increased from 1.8 to 21.3 in 1 million population per year. The mean survival rate in individuals with ES is 7.2 years.[4]

Evans syndrome is a diagnosis of exclusion. By definition, it cannot be accompanied by other disorders. Other disorders that must be excluded before diagnosing Evans Syndrome such as systemic lupus erythematosus (SLE), common variable immunodeficiency (CVID), IgA deficiency, acquired immunodeficiency syndrome (AIDS), and autoimmune lymphoproliferative syndrome (ALPS).[3] The first-line therapy for Evans Syndrome is steroids with or without intravenous immunoglobulin (IVIG).[3] Prednisone can be given with a daily dose of 1-2 mg/kgBW for 3-4 weeks.[5] Blood transfusions are only indicated in patients with severe symptoms and exacerbation risks.[3] This study aimed to describe

Evans syndrome in a 44-year-old male patient.

2. Case Presentation

A 44-year-old male patient presented with fatigue and malaise 1 month before admission. The patient also had red rashes on both arms 1 month before admission, with no history of trauma. The patient had hematuria 5 days before admission with normal frequency and volume, then stopped 2 days before admission. Pain or discomfort while urinating was denied. He also had a headache 2 days before admission, there was no referred pain, and the pain did not relieve with rest.

The patient had no history of nausea and vomitus, significant weight loss, cough, fever, shortness of breath, hair loss, and myalgia. Defecation is normal, and there is no history of black stool. The patient had received PRC and platelet transfusion recently. The patient had no history of hematology disorders, hypertension, diabetes, cardiovascular diseases, autoimmune diseases, and malignancy. There is no history of the family who has a similar condition as the patient.

The patient was cooperative and vital signs were normal. Physical examination showed the conjunctivas were anemic, and the patient had cardiomegaly. There were red rashes on both arms. Other physical examinations were in the normal range. Routine hematology test showed Hb 9.3 mg/dL, hematocrit 28%, leukocyte 10,970/mm^3, thrombocyte 2,000/mm^3, and reticulocyte 2.96%. Peripheral blood smears showed polychromatic erythrocytes. The patient was diagnosed with normochromic normocytic mild anemia due to acute bleeding, thrombocytopenia due to immune thrombocytopenic purpura, and heart failure stage B NYHA Fc I.

The patient was given therapies high carbohydrate high protein diet of 1700 kcal, IVFD NaCl 0.9% 500 cc every 8 hours, folic acid 1 mg per day, paracetamol 500 mg/8 hours, and was advised to check complete peripheral blood count, hemostasis, renal and liver function, lactate dehydrogenases, coombs test, anti-dengue, lipid profile, bone marrow puncture, and chest X-ray. Other laboratory parameters showed increased lactate dehydrogenase (LDH) (235 U/L), direct coombs test positive 3, and indirect coombs test positive 2. The patient was consulted by a hemato-oncology consultant and diagnosed with Evans syndrome. The patient was given additional therapies such as methylprednisolone 2x125 mg IV, lansoprazole 1x30 mg, calcium carbonate 1x1000 mg, 1 unit of WRC transfusion, and 10 units of platelet transfusion. Chest X-ray showed cardiomegaly, and the cardiovascular consultant diagnosed the patient with heart failure preserved ejection fraction. Bone marrow puncture is mixed with peripheral blood and cannot be identified. Antibody screening results showed the warm type of AIHA.

3. Discussion

This case report presented a 44-year-old man diagnosed with Evans syndrome. The diagnosis of Evans syndrome (ES) in this patient is based on a patient that had been complaining of fatigue and weakness, red rashes, gingival bleeding, epistaxis, and hematuria. The patient also had to receive PRC and platelet transfusion recently. A physical examination of the eye showed anemic conjunctivas. Other historical taking and physical examinations did not reveal any disorders that could be the cause of the anemia and thrombocytopenia of the patient.

The diagnosis of Evans syndrome in this patient was established from the presence of AIHA and ITP that occur coincidentally and is primarily due to an unknown cause.[1] Therefore, it is necessary to further observe the cause of ES, whether it is idiopathic, secondary to autoimmune, or lymphoproliferative disorders. Routine blood tests found mild anemia, reticulocytosis, and thrombocytopenia. In this case, the peripheral blood smear did not reveal any blast suggesting a hematological malignancy but showed polychromatic erythrocytes. Other laboratory parameters showed an increased LDH. The coomb test was positive. On the antibody screening examination, a warm type of AIHA was detected. In this case, the patient was not tested for antinuclear antibodies. The

diagnosis of SLE in this patient could not be acknowledged because only 1 of the 11 categories of the American Rheumatology Association (ARA) 1997 was found, which is positive hematological symptoms.

Anamnesis, physical examination, and laboratory tests did not support the presence of autoimmune and lymphoproliferative disorders as the cause of ES, so we suggest ES in this patient is caused by a primary disorder. Autoantibodies that target antigens on red blood cells and platelets are the basic pathogenesis for the manifestation of hemolytic anemia and thrombocytopenia in ES patients. A study by Michel et al. reported that 60% of the patients were women. The mean age at the onset of ITP and AIHA was 52 ± 33 years, and cytopenias occurred concomitantly in 37 cases (54.5%).[2]

AIHA was suspected in cases of anemia with reticulocytosis and positive signs of hemolysis, such as increased lactate dehydrogenase, low haptoglobin levels, and increased indirect bilirubin, with a positive direct antiglobulin test (DAT) for IgG with or without complement (C3d) due to cold agglutinins or cold type AIHA, not ES.[5] In 2019, the incidence of AIHA was estimated as 1.77/100000 cases per year, of which warm autoimmune hemolytic anemia (wAIHA) is the most common form and found in about 2/3 cases.[6]

ITP is a diagnosis of exclusion indicated in cases of early-onset thrombocytopenia that isn't associated with liver disease (cirrhosis and portal hypertension), splenomegaly (hematological malignancy, Gaucher's disease), drug-associated thrombocytopenia, bone marrow deficiency (dysmyelopoiesis syndrome, hematological malignancy, metastatic cancer), or congenital thrombocytopenia.[7-9] Due to the lack of specification or sensitivity of the various tests, the detection and recognition of antiplatelet antibodies are still not recommended in routine practice.

Thrombocytopenic patients have a risk of bleeding, although this risk isn't equal in all patients. Generally, thrombocytopenia is defined as mild if platelets are more than 70,000/mm^3, and patients with a platelet count of 50,000/mm^3 are generally asymptomatic. Thrombocytopenia is said to be severe if the platelets drop to 20,000-30,000/mm^3. Platelets count less than 30,000/mm^3 are at risk of bleeding triggered by trauma.[10-11] Meanwhile, platelets <10,000/mm^3 may increase the risk of spontaneous bleeding. Spontaneous bleeding is bleeding that occurs even in the absence of trauma. Manifestations of spontaneous bleeding can be mild in the form of petechiae, epistaxis, and bleeding gums but can also manifest as severe bleeding, such as gastrointestinal bleeding or urogenital bleeding, and can be life-threatening, such as intracranial bleeding.[12]

The primary goal of ES management is to achieve a complete long-term response. There is no established therapy regimen. Steroids with and without intravenous immunoglobulin (IVIG) are recommended as front-line therapy.[4,7] High-dose corticosteroids (daily dose of methylprednisolone with a maximum dose of 15 mg/kg per day for 3 days and not to exceed 1 g/day) are used with IVIG (1 g/kg/day for two consecutive days). To achieve rapid hemostasis, platelet transfusion is recommended in situations of high or severe bleeding that cannot be controlled and may be repeated every 8 hours until the bleeding resolves.[8,14]

The patient was given intravenous methylprednisolone with a dose of 2x125 mg for 3 days, followed by methylprednisolone oral with a maintenance dose of 3x8 mg. After administering intravenous methylprednisolone and a maintenance dose, the patient was found to be in remission. The response to steroid therapy in this patient was quite good, as indicated by the increased hemoglobin and platelet levels at the time of discharge.[12,13]

ES is generally characterized by recurrent episodes of relapse and remission of both ITP and AIHA. In some patients, long-term remission can only be achieved by shooting stem cells. On long-term follow-up, most researchers stated there were more frequent episodes of ITP compared to AIHA. The prognosis for the AIHA component is generally good, with zero mortality. The highest cause of mortality in ES is generally related to bleeding due to thrombocytopenia or sepsis.3,4,8 In this patient, the survival rate is high because primary

ES has a better survival rate compared to secondary ES (10.9 vs 1.7 years), with a 5-year survival rate of about 75% compared to 38% in the secondary ES.[4]

4. Conclusion

Evan syndrome is a rare disorder and a diagnosis of exclusion. The diagnosis of ES was established by the presence of signs and symptoms of AIHA and ITP accompanied by a positive direct antiglobulin test with no other etiology found. First-line therapy in ES is corticosteroids with or without IVIG, and most patients show a good response.

5. References

1. Jaime-Pérez JC, Elva P, Aguilar-Calderón, Salazar-Cavazos L, Gómez-Almaguer D. Evans syndrome: Clinical perspectives, biological insights, and treatment modalities. J Blood Med. 2018; 9: 171-84.
2. Michel M, Chanet V, Dechartres A, Morin A-S, Piette J-C, Cirasino L, et al. The spectrum of Evans syndrome in adults: new insight into the disease based on the analysis of 68 cases. Blood. 2009; 114(15): 3167-72.
3. Norton A, Roberts I. Management of Evans syndrome. Br J Haematol. 2006; 132(2): 125-37.
4. Hansen DL, Möller S, Andersen K, Gaist D, Frederiksen H. Evans syndrome in adults-incidence, prevalence, and survival in a nationwide cohort. Am J Hematol. 2019; 94(10): 1081-90.
5. Audia S, Grienay N, Mounier M, Michel M, Bonnotte B. Evans' syndrome: From diagnosis to treatment. J Clin Med. 2020; 9(12): 1-22.
6. Michalak S, Gawlik AO, Rupa-Matysek J. Autoimmune hemolytic anemia: current knowledge and perspectives. Immunity & Ageing. 2020; 17(38): 1-16.
7. Miano M. How I manage Evans syndrome and AIHA cases in children. Br J Haematol. 2016; 172(4): 524–34.
8. Provan D, Arnold DM, Bussel JB, Chong BH, Cooper N, Gernsheimer T, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. Blood Adv. 2019; 3(22): 3780-817.
9. Ariputra A. Evans syndrome in a 10 year old girl. Medicina. 2015; 46(1).
10. Angelopoulos A, Kirkilesis G, Kakavia K, Papanikolaou P. Diagnosis of Evans syndrome. Pan Afr Med J. 2021; 38: 314.
11. Porcaro F, Valenzise M, Candela G, Chiera F, Corica D, Pitrolo E, et al. Evans syndrome: a case report. Pediatr Med Chir. 2014; 36(4): 91.
12. Otaibi ZD, Rao R, Sadashiv SK. A case of Evans syndrome: a clinical condition with under-recognized thrombotic risk. J Hematol. 2015; 4(3): 205-9.
13. Mohammadien HA, Abudab LH, Ahmad AM. Evans syndrome as initial presentation of COVID-19 infection. Egypt J Bronchol. 2022; 16: 22.
14. Maqsood H, Shakeel HA, Gulraiz A, Khan MD. The spectrum of Evans syndrome: a literature review. Int J Res Med Sci. 2020; 8(5): 1961-7.