Case Report

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EVAN'S SYNDROME – A RARE ENTITY

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ABSTRACT

The Evans syndrome was first identified by Robert Evans in 1951. Primary thrombocytopenic purpura and acquired hemolytic anemia are related by a rare autoimmune disease. Immunological thrombocytopenia (ITP) and autoimmune hemolytic anemia (AIHA) may develop in this illness simultaneously or consecutively, and immunological neutropenia may also follow ITP. About 2–5% of ITP patients and 5–10% of warm autoimmune hemolytic anemia cases have Evans syndrome, which is often identified by exclusion. Our case report focuses on a female patient, age 15, who complained of anemia, jaundice, and petechiae. Her lab tests revealed higher amounts of reticulocytes, lactic dehydrogenase, positive Coomb's test, and indirect bilirubin. Due to the presence of thrombocytopenia and hemolytic anemia that tested positive for Coomb's, she was diagnosed with Evan's syndrome. There was no main autoimmune illness indicated by the negative ANA profile for SS-A. Evans syndrome can be hard to diagnose and treat. Corticosteroids and other immunosuppressive drugs are commonly used in treatment.

KEYWORDS: Evans syndrome, Autoimmune hemolytic anemia, Idiopathic thrombocytopenia.

INTRODUCTION

The Evans syndrome was first identified by Robert Evans in 1951. An autoimmune disease called primary thrombocytopenic purpura is linked to acquired hemolytic anemia. This uncommon illness is characterized by the simultaneous or subsequent development of immune thrombocytopenia (ITP), which is occasionally followed by immune neutropenia, and autoimmune hemolytic anemia (AIHA). Two to five percent of cases of ITP and five to ten percent of cases of warm autoimmune hemolytic anemia are caused by Evans syndrome.

Less than 5% of individuals with AIHA or ITP at first get identified with the illness, which is characterized by B cells attacking the body's own cells with auto-antibodies. The typical diagnosis age, with a 3:2 F:M ratio, is 52 years old; nevertheless, the diagnostic rate is greater in females.

Although often seen in children, Evans syndrome also affects adults and is typically sporadic with no specific genetic links, though rare familial cases do exist. The disease's progression can vary, ranging from self-limited to relapsing-remitting. Treatments often provide temporary relief, but relapses are frequent.Symptoms of Evans syndrome depend on which blood cell lines are affected. The symptoms of AIHA include pallor, exhaustion, lightheadedness, dyspnea, and decreased physical activity. Pallor and jaundice may be found on physical examination. Diagnosing Evans syndrome involves excluding other conditions and confirming with tests such as a complete blood count showing low hemoglobin, reduced platelets, peripheral blood smear indicating reticulocytosis, and a positive direct coombs test hemolytic anemia.Treatment for Evans syndrome varies based on the condition's severity, the symptoms present, and the individual's response to the therapy (2-4).

CASE REPORT

A 15-year-old girl was admitted to Era's Lucknow Medical College and Hospital's pediatric unit. she came with a 15-days history of nose and lip bleeding, petechiae across her body, generalized weakness, and shortness of breath. Additionally, she reported vaginal bleeding, yellowing of the eyes for three weeks, and dark-colored urine. She was born from parents who are not related by blood. No previous history of similar symptoms. Physical examination revealed that the patient had petechiae, jaundice, anemia, and was afebrile. Her organomegaly was not found during the systemic examination, and her vitals remained steady. Mean corpuscular volume (MCV) was 90.2 fL, mean corpuscular hemoglobin (MCH) was 24.9 pg, and mean corpuscular hemoglobin concentration (MCHC)

was 27.6 g/dl, according to laboratory results. 4.0 g/dl was the hemoglobin level. Her WBC and platelet counts were 7,400 and 10,000 cells/cumm, respectively, at admission.

The peripheral blood smear indicated reduced red cell density with anisopoikilocytosis, predominantly microcytic hypochromic cells mixed with normocytes, some elliptocytes, a few macrocytes, macroovalocytes, and occasional spherocytes. The reticulocyte count was 4%, and lactate dehydrogenase (LDH) levels were significantly elevated. The erythrocyte sedimentation rate was raised i.e 68 mm in the first hour. Positive results were obtained from both the direct and indirect Coombs tests. She had normal renal and liver function tests, non-reactive serology, and total and direct bilirubin levels of 1.0 mg/dl and 2.7 mg/dl, respectively, according to her liver function tests. Although the international normalized ratio and activated partial thromboplastin time are both normal, the prothrombin time was somewhat longer. Furthermore, a chest X-ray, 2D echocardiography, and abdomen USG all showed no signs of splenomegaly. The patient was diagnosed with Evan's syndrome based on low platelet count, or thrombocytopenia, and Coombs positive hemolytic anemia.

An underlying autoimmune condition was ruled out by the negative results of the ANA immunofluorescence and ANA profile testing. Ten units of platelets and three units of packed red blood cells were first administered to the patient. After receiving 60 mg of methylprednisolone twice a day and 5g/100 ml of intravenous immunoglobulin (i.v. Ig), she was given a progressively lowered dosage of oral prednisolone, beginning at 30 mg twice a day. Hemoglobin was at 7.1 mg/dl, platelets were at 40,000/cumm, and total bilirubin was at 1.3 mg/dl after nine days, according to laboratory data (Table 1). Her response to therapy was good, and her symptoms much improved.

DISCUSSION

Robert Evans originally described the Evans syndrome in 1951(1).The diagnosis is uncommon and necessitates a high degree of doubt in order to rule out other conditions that exhibit AIHA and thrombocytopenia. The cause of this condition is not known, but immune dysregulation may play important role in pathogenesis (2). Defects in the immune response, common to many autoimmune diseases, may lead to the constitutive production of IL-10 and INF, which can stimulate autoreactive, antibody-producing B cells. Recent research highlights that immunization might trigger the onset of disease in genetically predisposed individuals. Evans syndrome can manifest with symptoms related to thrombocytopenia, such as purpura, petechiae, ecchymoses, mucosal bleeding (including menorrhagia, hematuria, and gastric hemorrhage), or symptoms which are associated with anemia, such as pallor, fatigue, and dizziness (5). Diagnosis of hemolytic anemia is confirmed by positive direct agglutination test (DAT), (11) and peripheral smears showing spherocytes can provide additional diagnostic clues, along with lab findings of elevated lactate dehydrogenase, reticulocytosis, and increased indirect bilirubin levels (12). In 2009 study we found that Evans syndrome was primary in 50% of cases, with the other 50% were associated with conditions such as systemic lupus, lymphoproliferative diseases (10).

Evans syndrome, which alternates between periods of remission and aggravation, can be difficult to manage(8). Relapses are common, however the majority of patients respond to corticosteroids and/or intravenous immunoglobulin as first-line treatments(8). Corticosteroids are usually given daily to isolated ITP patients at a dose of 1-2 mg/kg, with a progressive tapering off of the medication over a few weeks (3,8). Immunosuppressive medications such as vincristine, mycophenolate mofetil, ciclosporin, and danazol are used in second line treatment. Rituximab/splenectomy (requiring at least 15 mg of prednisone daily to prevent relapses) may be recommended for those who are dependent on steroids and do not respond to standard therapy (7) .

First-line therapy (1) - for this condition typically involves corticosteroids and or administration of a mixture of antibodies (immunoglobulins) through an intravenous route. Prednisolone can be administered at daily doses ranging from 1 to 4 mg per kilogram of body weight, according to certain research. Intravenous methylprednisolone has had good clinical and analytical responses. The dose is 30 mg/kg per day for the first three days of therapy and 20 mg/kg per day for the next four days.After this first stage, the dose is gradually reduced in compliance with a tapering schedule: After the first doses, the regimen proceeds as follows: Take 10 mg/kg/day for one week, 5 mg/kg/day for the next, 2 mg/kg/day for the week after that, and 1 mg/kg/day for the week after that.

Norton et al suggests using i.v immunoglobulin (2 g/kg in divided dose) for those who do not respond to steroids or who need excessively higher doses to stay in the remission. In severe cases, blood transfusion and platelet transfusions may be necessary to ease the symptoms, but routine use is not recommended. If first-line therapy failsimmunosuppressive drugs such

as ciclosporin (5 mg/kilogram twice day on alternate days), mycophenolate mofetil, vincristine (1.5 mg/m³/week intravenously for three weeks), and danazol (200 mg/day) may be taken into account. Rituximab is a monoclonal anti-CD20 antibody that, when combined with steroids at a dose of 375 mg/m² per week for four weeks, has demonstrated promise in treating Evans syndrome, a condition resistant to first-line therapy. Rituximab may be a better alternative than splenectomy, which often results in transient increases in blood cell counts and recurring flare-ups quickly after the treatment, despite the lack of experience with the drug in pediatric patients.

CBC TEST	29/04/24	30/04/24	02/05/24	03/05/24	04/05/24	05/05/24	07/05/24
Hemoglobin	4.0	4.8	6.3	5.5	4.8	6.7	7.1
Neutrophils	73	80	80	83	85	90	68
Lymphocyte	22	16	18	14	12	07	26
Eosinophils	01	01	01	01	01	01	01
Monocytes	04	03	01	02	02	02	05
Hematocrit	14.1	16.1	22.5	18.1	17.8	21.7	25.0
Total Leukocyte Count	7400	8200	8200	7200	7000	11800	10000
M.C.V	90.2	89.9	96.1	98.5	98.2	87.5	93.4
M.C.H.C	27.6	29.6	28.0	26.9	27.0	31.1	28.2
Platelet Count	10000	5000	10000	12000	8000	25000	40000
RBC	1.56	1.79	2.34	1.83	1.81	2.47	2.68
M.C.H	24.9	26.6	26.9	26.6	26.5	27.3	26.3
Serum bilirubin (Total)	2.7						1.3
Direct bilirubin	1.0						0.3

Table 1: Laboratory finding during Treatment of the Patient in Pediatric Ward

Third line of therapy - Treatment possibilities include oral cyclophosphamide administered at a rate of 1-2 miligram per kilogram per day for two to three months, or intravenous monoclonal anti-CD52 antibodies (10 mg/day for 10 days). The only individuals who can benefit from allogeneic and autologous stem cell transplantation are those who did not respond to medication-based therapy. Finally, we recommend the following: Evan's syndrome initially manifested clinically as autoimmune thrombocytopenia. Six months after the diagnosis of ITP, concurrent involvement of both the erythroid and myeloid lines can occur. The diagnosis of this syndrome is confirmed by autoimmune hemolytic anemia, reduced platelet counts, and a positive direct Coombs test.

Prior to starting steroid therapy, a bone marrow examination can rule out cancer and validate the initial diagnosis. The first line of therapy is immunoglobulin infusion and high dosage methylprednisolone, with steroid maintenance therapy coming next, according to international literature.

Laboratory reports after 9 days showed haemoglobin of 7.1 mg/dl, platelet count was 40,000/cumm and total bilirubin was 1.3 mg/dl. Her symptoms were improved and she responded dramatically.

CONCLUSION

The study's findings allow us to conclude that: 1) autoimmune thrombocytopenia was the initial clinical manifestation of Evan's syndrome; 2) concurrent involvement of the erythroid and myeloid lines can happen six months after the illness is diagnosed with ITP; and 3) declining platelet counts, autoimmune hemolytic anemia, and a positive direct Coombs test are markers for the diagnosis of the illness. According to international literature, the mainstays of treatment are immunoglobulin infusion and high-dosage methylprednisolone, with steroid maintenance therapy following. We saw a positive clinical outcome in our case report.

ABBREVIATIONS

ITP idiopathic thrombocytopenic purpura AIHA autoimmune haemolytic anaemia SLE systemic lupus erythematosus TTP thrombotic thrombocytopenic purpura.

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