Evans Syndrome- An Unresolved Tale

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ABSTRACT

Evans syndrome is an uncommon hematologic autoimmune disease characterized by autoimmune hemolytic anemia and immune thrombocytopenic purpura with a positive antihuman globulin test. We report a rare case of Evans Syndrome of a 40 years old female who presented with bleeding per vaginal since 4 days with anemia and thrombocytopenia. The purpose of this case report is to increase the level of awareness among clinicians to instigate an appropriate diagnostic workup in patients presenting with anemia in the setting of ITP.

Evans syndrome (ES) is a hematologic disorder characterized by the sequential or simultaneous development of DAT positive autoimmune hemolytic anemia (AIHA), immune thrombocytopenia (ITP) and/or immune neutropenia in the absence of a known etiology. Evans’s syndrome is a rare disorder because it is diagnosed in only 0.8% to 3.7% of all patients with either ITP or AIHA at onset.

1 Defined by Robert Evans in 1951 when he studied the relationship between autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP).

1 CASE REPORT

A 43 years old female presented to gynecology outpatient department in a private hospital with complaints of bleeding per vaginal bleeding since 4 days. Her last menstrual period was 15 days prior to the current episode. Her menstrual cycles were regular in duration in past but she complained of excessive flow and generalized weakness for last 3 months. She had history of uneventful pregnancy 14 years back. No obvious gynecological cause for bleeding was identified during examination and investigations. Her routine blood examination detected anemia, Hb- 4.5 gm/dl and low platelet count (12000 cells/cu mm). Later she was referred to our centre. On examination she was pale, mild hepatosplenomegaly with palpable lymph nodes. Three days later she developed ecchymotic patches on right forearm and abdomen. Her haemoglobin was 4.5 g/ dl, white blood cell count 9800 cells / cu mm, reticulocyte count 4% and platelet count was 15000 cells/ cumm. Her peripheral smear showed microcytic hypochromic anemia with thrombocytopenia with no giant cells. Iron studies were 36 micro gm/dl (41 - 141 micro gm / dl), serum ferritin 12 micro gm/dl (10-150 micro gm/ dl) and serum iron binding capacity was slightly high. (251 - 406 micro gm/dl).

Bone marrow examination showed erythroid hyperplasia with crowding of megakaryocytes. Her unconjugated bilirubin was 2.8 mg/dl, coagulation profile was in normal range. Her VDRL, HBV, HIV, HCV, ANA, dSDNA, APLA (antiphospholipid antibody) and dengue was found to be negative.

Haptoglobin was found to be 26 mg/dl (30-200mg/dl) and serum lactate dehydrogenase LDH was 433 U/L. Haemoglobin electrophoresis and DAT (Direct anti globulin test) was positive. Thyroid function test and IgA, IgG was negative. USG abdomen showed mild hepatosplenomegaly.

She underwent four units of blood and six units of platelets. Her platelet count was 32000 cells /cumm and Hb – 7.2 g/ dl. Her vaginal bleeding complaint was gradually reduced to normal. Treatment with supportive antibiotics with prednisolone was initiated. On fifth day patient developed left sided hemiparesis. Her left plantar was extensor on examination. Her repeat platelet count dropped to 90000 cells/ cumm with haemoglobin of 5.9 g / dl. Repeat PT, INR, APTT were normal. Fundal examination showed retinal hemorrhages. She got deteriorated and she subsequently died within 2 hours. CT brain showed massive right sided intra cerebral hemorrhage with mid line shift.

To sum up the case - Gynecological etiology for the per vaginal bleeding this patient had thrombocytopenia which was immune (Idiopathic) in nature. Her thrombocytopenia appeared to be idiopathic in nature as there was no evidence of collagenosis, infection or liver disease. Splenic sequestration was unlikely as there was only mild splenomegaly on
USG. Platelet production was not reduced as bone marrow examination evidenced - crowding of mega karyocytes and absence of neutropenia. Her anemia was haemolytic in nature (unconjugated bilirubin and high LDH, high reticulocyte count with reduced haptoglobins) and lastly iron deficiency anemia was secondary to menorrhagia. With both the picture of ITP and AIHA the patient was diagnosed to with Evans syndrome. [1]

2 DISCUSSION
In ES, the AIHA is largely the warm-agglutinin subtype. This subtype represents almost 80% of all cases of AIHA and is characterized by autoimmune destruction of red blood cells (RBCs) [2]. More recent data suggest the spectrum of the disease has broadened specially in children and there is increasing evidence of Evans syndrome reflecting the state of profound immune disregulation as opposed to coincidental combination of immune cytopenias [3] Evans Syndrome is classified as primary (Idiopathic) or secondary (Associated with some other disease) and it has been demonstrated that secondary disease responds better than primary variable [4]. There are case reports of Evan’s Syndrome with SLE, incomplete lupus [5], primary antiphospholipid syndrome, Sjogren’s syndrome common variable immuno deficiency, non hodgkin’s malignant lymphomas and chronic lymphocytic leukaemia [3]. In our case we were not able to detect the cause or association of any disease in our patient. In a study of Michael etal. sixty eight patients of Evans Syndrome mortality was seen in 23.4 % cases. The possible causes being septic shock, associated cancers, stroke, acute myocardial infarction, refractory anaemia with lymphomas. Importantly one of two patients of stroke was suspected to have intracerebral haemorrhage like in our patient [4]. The management of Evan’s Syndrome is difficult and challenging. Blood and platelets transfusion is the treatment given to improve symptoms and gain time but its use should be minimized. The first line of treatment is prednisolone and intravenous immunoglobulins (IVIG). Second line of treatment consists of immuno suppressants (mycophenolate mofitil, cyclosporine, danazol) the monoclonal antibody rituximab and chemotherapy (vincristine). Splenectomy may also be considered a second-line treatment and even splenectomy. More recently small number of patients have been treated by stem cell transplantation. [1, 3, 4]

3 CONCLUSION
Evans’s Syndrome is a rare, chronic, refractory disease but sometimes may present acutely. In patients presenting with immune thrombocytopenia and anemia with haemolytic factor, DAT is mandatory test. Instead of monotherapy with corticosteroids, combination of steroids with newer modalities like immunsuppressant’s and rituximab should be instituted as early as possible in order to prevent or delay life threatening complications.

REFERENCES