

A CASE REPORT ON EVANS SYNDROME

¹*Dr. Malathi Balamurugan and ²Dr. Balamurugan,

¹Associate Professor, Department of Physiology, Karuna Medical College, Palakkad.

²Cardio-Diabetesity Consultant, Department of Cardiology, Vadavalli Medical Centre, Coimbatore.

*Corresponding Author: Dr. Malathi Balamurugan

Associate Professor, Department of Physiology, Karuna Medical College, Palakkad.

Article Received on 09/02/2018

Article Revised on 02/03/2018

Article Accepted on 23/03/2018

ABSTRACT

Evans syndrome is a very rare autoimmune disorder in which the immune system destroys the body's red blood cells, white blood cells and/or platelets. These patients experience thrombocytopenia (too few platelets) and Coombs' positive haemolytic anaemia (premature destruction of red blood cells due to auto immunity). The best treatment options for Evans syndrome depend on many factors, including the severity of the condition; the signs and symptoms present; and each person's response to certain therapies. Here we describe a case of Evans syndrome in a 29 year old female.

KEYWORDS: Evans syndrome, Autoimmune disorder, Haemolytic anaemia, Thrombocytopenia.

INTRODUCTION

Evans syndrome is a very rare autoimmune disorder in which the immune system destroys the body's red blood cells, white blood cells and/or platelets. The syndrome was first described in 1951 by Robert Evans and colleagues.^[1] The incidence and prevalence of Evans Syndrome is not clearly known.^[1] One study gives the disease is disorder diagnosed only in 0.8 to 3.7 % of patients with Idiopathic thrombocytopenic purpura (ITP) or Autoimmune haemolytic anaemia (AIHA) at onset.^[2] These patients experience thrombocytopenia (too few platelets) and Coombs' positive hemolytic anemia (premature destruction of red blood cells due to auto immunity). The best treatment options for Evans syndrome depend on many factors, including the severity of the condition; the signs and symptoms present; and each person's response to certain therapies.^[2] Evans syndrome occurs in individuals of all ages.^[3] In a 1997 survey of North American pediatric hematologists, the median reported age at diagnosis was 7.7 years (range, 0.2-26.6 years).^[3] No sexual predilection and no racial predilection are known in Evans syndrome.^[4] Here we describe a case of 29 year old female with autoimmune haemolytic anaemia and thrombocytopenia successfully treated. She had positive Coombs test and neutropenia.

CASE REPORT

29 years old female patient was admitted with complains of bleeding per vagina since 2 months. History of severe lower abdominal pain, difficulty in breathing, guiddiness was present. She was apparently normal before 2

months. She is not a known diabetic, hypertensive, asthmatic or epileptic. No H/O thyroid disorders, blood transfusion or surgeries. Her menstrual history was normal 5/30 cycles, regular cycles. She attained menarche at 14 years and was unmarried. O/E had purpuric spots all over the body. She was conscious, orientated, Obese, afebrile and dehydrated. Examination revealed pallor, no lymphadenopathy, abdomen: soft, no hepatomegaly and/or splenomegaly.

On admission her right upper limb blood pressure was 140/90 mmHg. Pulse rate: 98 /minute. Investigations were sent and patient was given Inj vit K 1 amp IM, Inj streptovit 1amp IM. IV fluids were started. Her investigations showed Total WBC count: 2,800/ mm³, Differential count : N- 28%, E-2%, L- 68%, M-2% .Erythrocyte sedimentation rate (ESR): 100 mm / hr ,RBC count: 1.12 million/mm³, Haemoglobin: 2.2 g/dl, PCV: 11.6%, MCV:103fL, MCH:29.5 pg, MCHC: 28.4 g/dl, Platelet count: 12,000/mm³, Reticulocytosis + PS: dimorphic anaemia with neutropnia and thrombocytopenia, Microcytic hypochromic anaemia with few macrocytes, elongated red cells, tear drop cells, and target cells. WBCs normal, Neutrophils were matured with prominent lobes. Platelets decreased in count. Blood sugar (fasting): 97.59mgs%, Post prandial blood sugar: 128 mgs%. Her urine examination showed Pale yellow cloudy urine with PH: 6; proteins: +; sugar: trace; RBCs: plenty; pus cells: 20-25; RBC cast and bacteraia: +.

On the second day patients was given Inj Imfer (iron dextrose 1amp in 100 ml NS ,Tab: Milical 1000 mg TID, Tab: Regesterone 10 mg TID, Tab: Folvite 5mg BD,

SypPotchlor 2 tsp TID, Inj Avil: 05 ml IM, Inj dexamethasone:0.5 ml IM was given. Patient was evaluated as a case of haemolytic anaemia with Idiopathic thrombocytopenic purpura/ viral infection/ anaemia / acid peptic disease. . Patient continued to bleed and further investigations showed, renal function tests: Serum urea: 20 mg, Serum creatinine: 0.6, Serum. Uric acid: 5.6 and others showed Serum. LDL: 1037, Serum sodium: 127 mEq/L, Serum potassium: 2.3 m Eq/L. Her liver function tests showed Serum bilirubin (Total): 1.3, Serum bilirubin (Direct): 0.5, SGOT: 79u/L, SGT: 140 U/L, Serum alkaline phosphatase: 95.6 U/L. Her serum proteins were Serum proteins (total): 5.7, Serum albumin: 3.2, Serum globulin: 2.5. She was CPR: positive. Her PT: 21 sec, ap TT: 41 sec, INR: 1.5. Her thyroid function test showed fT3: 1.34 pg/nl, fT4: 1.13 mg/dl, TSH: 2.40 Miu/ml. 2 units of packed cell concentrate and 1 unit of whole blood was arranged and transfused.

On the third day patient continued to bleed PV though better and afebrile. CV Sand RS- NAD; BP stable .Her blood parameter were improving. Scan abdomen was done Abdominal scan showed: no hepatosplenomegaly; cystitis: + X ray chest showed cardiomegaly; lung field – normal. She was again transfused with 1 unit of packed cell concentrate. On the the fifth day patient still bleeding pv other investigations were done. She was Direct coombs: positive, Indirect: negative, ANA:-negative, Anti DS DNA – negative And autoimmune haemolytic anaemia was diagnosed with thrombocytopenia Started on tab. Wysolone 20 mg TID and Tab: traphic MF TID. Her bone marrow aspiration excluded lymphoproliferative diseases and malignancies. She was diagnosed as “Evans syndrome”. She was given Tab. Wysolone 20 mg, Tab Rantac 150 mg .Tab Ovaral – G, Tab traptic MF. Her vitals were stable, blood parameters improving and was discharged. She was asked to come for review after 2 weeks.

DISCUSSION

Evans syndrome is a rare disease. It is listed in the Office of rare diseases (ORD) of National institute of health (NIH). While Evans syndrome is not thought to be inherited in most cases and rarely occurs in more than one person in a family, there are a few cases in the medical literature describing "familial Evans syndrome."^[5,6,7] The aetiology and exact pathophysiology is unknown . Immune dysregulation may be involved in the pathogenesis of the disease. Constitutive production of IL-10 and INF α may lead to activation of autoreactive, antibody-producing B cells,^[8] although these abnormalities of immune response are seen in other autoimmune disorders. These auto antibodies are directed against the antigens specific to red cells, platelets or neutrophils. These antibodies do not cross react. Wang et al demonstrated decreased serum levels of immunoglobulin G (IgG), immunoglobulin M (IgM), and immunoglobulin A (IgA) in these patients.^[9,10] The cytopenias that occur with

Evans syndrome may be related to T-cell abnormalities; decreases in helper T cells and increases in suppressor T cells were noted in these patients.

These patients do not have enough healthy red blood cells (anaemia), they may experience weakness, fatigue, paleness, light-headedness, and shortness of breath. Low platelets can cause easy or unexplained bruising; prolonged bleeding from small cuts; and purpura. People with low white blood cells may be more susceptible to infections.^[2] Many people with Evans syndrome go through periods of remission in which the signs and symptoms of the condition temporarily disappear or become less severe.^[2]

The characteristic clinical course includes periods of remissions and exacerbations. Recurrences of thrombocytopenia and anemia are common, as are episodes of hemorrhage and serious infections. A full blood count will confirm the presence of cytopenias and a blood film should be examined for features of AIHA (polychromasia, spherocytes) and to exclude other underlying diagnoses (malignancies, microangiopathic haemolytic anaemia, congenital haemolytic and thrombocytopenic conditions). Features of haemolysis should be sought including a raised reticulocyte count, unconjugated hyperbilirubinaemia and decreased haptoglobins.^[3,10,11,12,13] The indirect antiglobulin test may also be positive (52–83%) patients,^[3,12]

Assays for antiplatelet and antigranulocyte antibodies have shown varied results.,^[14] in a report of 32 adult patients with AIHA, showed antiplatelet antibodies in 91% (demonstrated by thromboagglutination and indirect antiglobulin consumption tests) and leucocyte antibodies in 81% (demonstrated by a cytotoxicity test). It is advisable to measure serum immunoglobulins and immunoglobulin subclasses in all patients; not only to exclude differential diagnoses, such as common variable immunodeficiency (CVID) and IgA deficiency, which have been reported to develop acquired cytopenias,^[15,16] and also as a baseline prior to immunomodulatory therapy.

Bone marrow investigation may be of use in evaluation of Evans syndrome where it is necessary to exclude infiltrative processes in patients who present with pancytopenia. Otherwise it is not usually helpful as the findings are non-specific and may be normal or show trilineage increased cellularity,^[3,11] Evans syndrome is a diagnosis of exclusion and by definition other confounding disorders should not be present.^[1]

Patients rarely do well without treatment and responses to treatment are variable and often disappointing .On occasions it can be fatal. The best treatment options for Evans syndrome depend on many factors, including the severity of the condition; the signs and symptoms present; and each person's response to certain therapies. For example, people who need to be hospitalized due to

severe anaemia or thrombocytopenia are often treated with blood transfusions followed by therapy with corticosteroids or intravenous (IV) immune globulin. Other treatment options include immunosuppressive drugs. Most affected individuals respond to these treatments; however, relapse is frequent. In patients who are not responding to standard treatments, rituximab or splenectomy may be considered. Some patients respond well to rituximab treatment and experience an extended period of remission, while others have little to no response.^[2] For cases that are very severe and difficult to treat, stem cell transplantation may be used to provide a long-term cure. Autologous and allogeneic stem cell transplantation have been used in a small number of patients (14 patients aged 5-52 years), with mixed results.^[2]

Splenectomy traditionally used as initial second-line therapy in patients with autoimmune cytopenias (ITP or AIHA) who have failed to respond or relapsed following standard therapy with steroids +/- IVIG, the role of splenectomy in the management of Evans syndrome is not clearly established. In general, the response rate to splenectomy in Evans syndrome is poorer than the 70–75% response rates reported in chronic ITP although there are so few data that accurate response rates cannot be quoted for Evans syndrome.^[17] Splenectomy should be avoided in children <6 years of age but can be considered in older children and adults as an

Long-term survival data are limited. In patients followed for a median range of 3-8 years, mortality ranged from 7-36%.^[3,11,13] The main causes of death were hemorrhage and sepsis. None of these patients developed any malignancy.

CONCLUSION

Patients and their families must be educated about the chronic nature of Evans syndrome, which can include periods of remission and exacerbation. It is important that the clinician explain potential adverse effects of medications, especially long-term steroids, whenever a steroid is administered to treat an exacerbation

REFERENCES

1. Evans RS, Takahashi K, Duane RT. Primary thrombocytopenic purpura and acquired hemolytic anemia. *Arch Intern Med*, 1951; 87: 48-65.
2. Norton A, Roberts I. Management of Evans syndrome. *Br J Hematol*. January 2006; 132(2): 125-137.
3. Mathew, P., Chen, G. & Wang, W. Evans syndrome: results of a national survey. *J Pediatr Hematol Oncol*, 1997; 19(5): 433-7.
4. Genty I, Michel M, Hermine O, Schaeffer A, Godeau B, Rochant H. Characteristics of autoimmune hemolytic anemia in adults: retrospective analysis of 83 cases. *Rev Med Interne*, 2002; 23(11): 901-9.
5. Ahmed FE, Albakrah MS. Neonatal familial Evans syndrome associated with joint hypermobility and mitral valve regurgitation in three siblings in a Saudi Arab family. *Ann Saudi Med*, 2009; 29(3): 227-230.
6. Ahmed FE, Qureshi IM, Wooldridge MA, Pejaver RK. Hereditary spastic paraplegia and Evans's syndrome. *Acta Paediatr*, 1996; 85(7): 879-881.
7. McLeod AG, Pai M, Carter RF, Squire J, Barr RD. Familial Evans syndrome: a report of an affected sibship. *J Pediatr Hematol Oncol*, 1999; 21(3): 244-247.
8. Karakantza M, Moukaki A, Theodoropoulou M, Bussel JB, Maniatis A. Th1 and Th2 cytokines in a patient with Evans' syndrome and profound lymphopenia. *British Journal of Haematology*, 2000; 110: 968-970.
9. Wang W, Herrod H, Pui CH. Immunoregulatory abnormalities in Evans syndrome. *Am J Hematol*, 1983; 15(4): 381-90.
10. Wang WC. Evans syndrome in childhood: pathophysiology, clinical course, and treatment. *Am J Pediatr Hematol Oncol*, 1988; 10(4): 330-8.
11. Pui C., Williams, J & Wang, W. Evans syndrome in childhood. *Journal of Pediatrics*, 1980; 97: 754-758.
12. Pegels, J.G., Helmerhorst, F.M., Van Leuwen, E.F., de Plasvan Dalen, C., Engelfriet, C. P. & Von dem Borne, A.E.G.K.R. The Evans syndrome: characterisation of the responsible autoantibodies. *British Journal of Haematology*, 1982; 83: 343-345.
13. Savasan, S., Warrier, I. & Ravindranath, Y. *Archives of Disease in Childhood*, 1997; 77: 245-248.
14. Fagiolo E. Platelet and leucocyte antibodies in autoimmune haemolytic anaemia. *Acta Haematologica*, 1976; 56: 97-106.
15. Hansen, O.P., Sørensen, C.H. & Astrup, L. Evans' syndrome in IgA deficiency. Episodic autoimmune haemolytic anaemia and thrombocytopenia during a 10 years observation period. *Scandinavian Journal of Haematology*, 1982; 29: 265-270.
16. Sneller, M.C., Strober, W., Einstein, E., Jaffe, J.S. & Cunningham-Rundles, C. New insights into common variable immunodeficiency. *Annals of Internal Medicine*, 1993; 118: 720-730.
17. Blanchette, V.S. & Price, V. Childhood chronic immune cytopenic purpura: unresolved issues. *Journal of Pediatric hematology/ Oncology*, 2004; 25(1): S28- S33.