ISSN: 2782-7550 (Print)
ISSN: 2782-7542 (Online)

ABMS

ANNALS OF BASIC AND MEDICAL SCIENCES

A Scientific Peer Reviewed Publication of The Faculties of Basic Medical and Basic Clinical Sciences,Usmanu Danfodiyo University Sokoto, Nigeria

https://www.abms.udusok.org
doi.org/10.51658/ABMS.202441.5

Case Report

Case Report: Evans Syndrome Coexisting with Sickle Cell Anaemia

Baba Jibrin[1]*, Fatima I. Abubakar[1], Nma M. Jiya[1], Murtala M Ahmad[1], Muhammad A. Ndakotsu[2], Abubakar U. Musa[2], Fati B. Jiya[1], Asma'u Adamu[1], Khadija O. Isezuo[1]

[1]Department of Paediatrics, Usmanu Danfodiyo University, Sokoto
[2]Department of Haematology & Blood transfusion, Usmanu Danfodiyo University, Sokoto

Abstract

Introduction: Evans syndrome is a chronic disorder of immune regulation whose aetiology is unclear. It is characterized by a combination of autoantibodies directed against red blood cells, platelets and/or neutrophils, with typical presentation of chronic and relapsing autoimmune haemolytic anaemia, immune thrombocytopaenia with few cases of neutropenia. It affects all age groups and gender, response to therapy varies' but is often poor. Coexistence with comorbidities like SCA presents with difficulty in diagnosis due to their similarities in clinical features, hence diagnosis may be delayed, sometimes complicating each other's clinical presentation and often making management more challenging.

Case Report: 11-year-old female, F.A known SCA patient who presented with fever, cough, jaundice, passage of dark brown coloured urine, epistaxis, petechia rashes and clinical features of anaemic heart failure. She had 6 blood transfusions and one exchange blood transfusion within 4 weeks of admission with worsening of symptoms. Subsequently developed right sided weakness and blindness. Serial FBC and, peripheral blood film showed severe cytopaenia (anaemia and thrombocytopenia), spherocytosis and, reticulocytosis. Direct coomb's test was positive while indirect coomb's test was negative. Bone marrow examination showed spherocytosis, LFT showed normal levels of enzymes with increased total and direct bilirubin. Brain CT revealed left occipital lobe infarcts with moderate cerebral atrophy. Prednisolone was commenced, patient responded well with improvement in the general health condition, resolution of motor weakness and cortical blindness. Follow up serial FBC showed increasing haematocrit, neutrophils, but with mild persistent thrombocytopenia which remained asymptomatic.

Conclusion: Evans syndrome is a rare disease with a diagnostic challenge and variable response to treatment. High index of suspicion should be the key in SCA patients whose clinical presentations may be confused with the disorder, thus likely to delay management and cause more complications.

Keywords: Autoimmune, anaemia, thrombocytopenia, sickle cell anaemia

Corresponding author:
Dr Baba Jibrin,

Department of Paediatrics,
Usmanu Danfodiyo University, Sokoto.
e-mail: jibrinbaba38@gmail.com,
phone no. 08036782914

Introduction

Evans syndrome is a rare condition with unknown worldwide frequency, however, a documented incidence of 0.5 – 1.2 per 1 000 000 persons-years in children < 13 years was reported (1). It is a complex autoimmune disease which is characterized by chronic and relapsing autoimmune hemolytic anemia, immune thrombocytopenic purpura with or without immune neutropenia and a positive coombs test in the absence of an underlying etiology (2,3). Autoantibodies are directed against antigens specific to red blood cells, platelets, or neutrophils, but these autoantibodies do not cross-react. It has no no age, gender and racial predilection. This syndrome shows a variable complicated clinical course with remissions, exacerbations and treatment is usually progressive with poor outcome, often associated with significant morbidity and mortality (3,4). Evans syndrome can be primary (idiopathic) when it occurs alone or classified as secondary when associated with an underlying disorder such as Systemic Lupus Erythromatosis, chronic lymphocytic leukaemia and viral infections (2). Coexistence with other diseases like sickle cell anaemia presents with difficulty in diagnosis due to their similarities in clinical features, hence diagnosis may take longer time, sometimes complicates each other's clinical presentation and often times make management challenging. No study to our knowledge has previously been reported on co-existence of Evans syndrome and Sickle Cell Anaemia in our environment.

Case Report:

An 11-year-old female known SCA patient who presented with fever, cough, jaundice, passage of dark brown urine, epistaxis with clinical signs of severe anaemic heart failure, petechia rashes and hepatosplenomegaly. She had 6 blood transfusions and one exchange blood transfusion within 4 weeks of admission with worsening of symptoms.

https://www.abms.udusok.org
doi.org/10.51658/ABMS.202441.5

Additionally, she developed right sided motor weakness and cortical blindness.
The laboratory results of the patient were the following:

1. Serial Full blood counts (FBC) showed cytopaenia

Table I: FBC Results before treatment with steroid

No.	Total Leucocyte Count Reference range 4 -11 x10 ^{9}/L	Haematocrit(%) Reference range 35 -45%	Platelet (x10 ^{9}/L) Reference range 150 -400 x10 ^{9}/L
1.	6.9 x10 ^{9}/L	7.3%	45 x10 ^{9}/L
2.	5.7 x10 ^{9}/L	10.3%	7 x10 ^{9}/L
3	3.7 x10 ^{9}/L	14.8%	43 x10 ^{9}/L
4	9.7 x10 ^{9}/L	13.5%	38 x10 ^{9}/L
5	6.6 x10 ^{9}/L	15.8%	28 x10 ^{9}/L

2. Post therapy (steroid) follow up FBC

Table II: FBC results after treatment with steroid

No.	Total Leucocyte Count Reference range (4 -11 x10 ^{9}/L)	Haematocrit(%) Reference range (4 -11 x10 ^{9}/L)	Platelet Reference range (150 -400 x10 ^{9}/L)
1	2.0 x10 ^{9}/L	28.4%	130 x10 ^{9}/L
2.	5.2 x10 ^{9}/L	30.9%	148 x10 ^{9}/L
3.	10.6 x10 ^{9}/L	32.5%	210 x10 ^{9}/L

3. Hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (Anti-HCV), Retroviral screening (RVS) (all non-reactive)
4. Raised reticulocyte count – 2%
5. Urinalysis- normal parameters
6. Abdominopelvic USS – hepatosplenomegaly
7. Peripheral blood film (PBF) showed severe pancytopaenia, spherocytosis and reticulocytosis, thrombocytopenia
8. Bone marrow showed hematinic deficiency and hyper proliferative anaemia, spherocytosis
9. Liver function test showed normal levels of enzymes with increased total and direct bilirubin.

Aspartate transferase (AST) -19U/L
Alanine transferase (ALT) -17U/L
Bilirubin Total- 1.89mg/dL ↑
Bilirubin direct – 0.73mg/dL ↑
Total protein – 6.8g/dL
Albumin- 3.9g/dL

10. Direct coomb's test -positive, and indirect coomb's test -negative
11. Brain CT revealed left occipital lobe infarcts with moderate cerebral atrophy.

On the basis of clinical and laboratory findings, the diagnosis of Evans syndrome was made. The patient was commenced on oral prednisolone at the dose of 1mg/kg/day in 2 divided doses for 6 weeks and responded well with improvement in the general health condition, resolution of motor weakness and cortical blindness. Follow up serial FBC tests done on the 4th, 5th and 6th week of treatment showed increasing haematocrit and neutrophils, but with mild persistent thrombocytopenia which remained asymptomatic. The patient was discharged, steroid was tail off and to be follow up at paediatric sickle cell clinic of the same hospital.

Discussion

Evans syndrome is an autoimmune disorder manifesting with two or more cytopenias, which commonly present as coexistence of simultaneous or sequential autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP), with or without immune neutropenia (only in 15% of cases) (2,3,4). The pathophysiology is unclear; however, it is characterized by auto-antibodies targeting own cells, in this case, red blood cells, platelets, and white blood cells. This condition has been speculated to be as a result of excessive immune dysregulation occurring sporadically (2).
Clinical manifestations are variable depending on the cell lineage affected which include signs and symptoms of AIHA (pallor, jaundice, lethargy), neutropenia (fever, recurrent severe infections), thrombocytopenia (petechiae, bruising, mucocutaneous and intracranial bleeding). ITP may lead to a life-threatening hemorrhage often associated with increased risk of ischemic complications such as acute coronary syndrome or cerebrovascular accidents which may also be due to AIHA. Physical findings may also reveal signs of severe anaemic heart failure, hepatosplenomegaly (5).
Evans syndrome has a chronic clinical course which includes periods of remission and exacerbation. The condition may be self-limiting but most patients rarely do well without treatment, and responses to therapy are transient, variable, often frustrating, and sometimes fatal (2). Generally, management of Evans syndrome is challenging and depends on several factors like severity and presence of other comorbidities (2,6). Coexistence of Evans syndrome with sickle cell anaemia like in the index patient may present with diagnostic challenge and dilemma especially with the later which can present with clinical manifestations and complications including anaemia,

jaundice, severe anaemic heart failure requiring frequent blood transfusions, cerebrovascular accidents, and hepatosplenomegaly. Thus, in this instances, diagnosis of Evans syndrome may take longer time, sometimes complicates each other's clinical presentation and often times make management challenging. Hence, high index of suspicion is key in diagnosis more so that it is often a diagnosis of exclusion. However, presence of cytopaenia on full blood count and differential, positive direct coomb's test and spherocytosis, few thrombocytes on peripheral smear are hallmark of laboratory abnormalities suggesting AIHA and ITP, which are diagnostic of Evans syndrome (7). Additionally, bone marrow examination is an important tool of investigation for the diagnosis of Evans syndrome as it is necessary to exclude infiltrative process in patients with pancytopenia, especially before starting steroid therapy (2).

Management includes blood transfusions, steroids and intravenous immunoglobulin (IVIG) therapy (6,8). Steroids are given at 1 to 2 mg/kg per day tapered over weeks. Majority of patients responds to steroids initially, the duration of response differs, although some relapse, prompting the use of additional or other treatment modalities (5).

The index case had several blood transfusions (add-on and exchange), was subsequently commenced on oral prednisone at 1mg/kg/day in 2 divided doses and she responded well with increasing levels of haematocrit and neutrophils. She however had mild persisting thrombocytopenia but remained asymptomatic. Thus, follow up and regular monitoring of clinical condition and investigations such as FBC, PBF should detect therapy.

Immunosuppressive drugs such as rituximab, cyclosporin and splenectomy may be considered in conditions refractory to the standard treatment or in cases of steroid-dependent (8,10). Hematopoietic stem cell transplant has been used in few presentations that were not responsive to all medical treatments. Both autologous and allogeneic stem cell transplantation has been tried in patients, with varied outcome (8-10).

Conclusion

Evans syndrome is a rare disease with a diagnostic challenge and variable response to treatment. Therefore, high index of suspicion should be the key in any patient especially in those with sickle cell anaemia whose clinical presentations may be confused with the disorder, thus likely to delay management and cause more complications.

References

1. Nikolaj Mannering, Dennis Lund Hansen, Hendrik Frederiksen. Evans Syndrome in Children below 13 years of age – A nationwide population-based cohort study. PLOS ONE. 2020; 15(4): e0231284
2. Shaikh H, Mewawalla P. Evans Syndrome. [Updated 2023 Apr 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519015/ (assessed 11th July, 2023)
3. Seidel MG. Autoimmune and other cytopenias in primary immunodeficiencies: Patho mechanisms, novel differential diagnoses, and treatment. Blood. 2014 Oct 9. 124 (15):2337-44.
4. Jaime-Perez JC, Aguilar-Calderon PE, Salazar-Cavazos L, Gomez-Almaguer D. Evans syndrome: clinical perspectives, biological insights and treatment modalities. Journal of Blood Medicine. 2018. 9:171-84
5. Michel M, Chanet V, Dechartres A, Morin AS, Piette JC, 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 Oct 08;114(15):3167-72
6. Mathew P, Chen G, Wang W. Evans syndrome: results of a national survey. Journal of Pediatric Hematology/Oncology. 1997 Sep-Oct;19(5):433-7
7. Norton A, Roberts I. Management of Evans syndrome. British Journal of Haematology. 2006;132(2):125-37.
8. Mantadakis E, Farmaki E. Natural History, Pathogenesis, and Treatment of Evans Syndrome in Children. Journal of Pediatric Hematology/Oncology. 2017;39(6):413–9. Epub 2017/06/28.
9. Miano M. How I manage Evans Syndrome and AIHA cases in children. British Journal of Hematology. 2016;172(4):524–34. Epub 2015/12/03. 10.1111/bjh.13866
10. Farruggia P, Macaluso A, Tropia S, Genova S, Paolicchi O, Di Marco F.et al. Effectiveness of cyclosporine and mycophenolate mofetil in a child with refractory Evans syndrome. Pediatric Reports.2011; 3 (2): e15.