

# Evans Syndrome as the Initial Presentation of Systemic Lupus Erythromatosus in a Rural Kenyan Hospital: A Case Report

\*<sup>1</sup>Vonwicks C. Onyango; MBChB, MMed, FCP(SA),

<sup>2</sup>Kenneth H. Makokha; MBChB,

<sup>3</sup>Samuel M. Gachie; BSc. Clinical Medicine, Higher Diploma (Cardiology),

<sup>4</sup>Boniface Mutiso; Diploma Clinical Medicine, MBChB (ongoing),

<sup>5</sup>Nicholas Auma; Diploma Clinical Medicine, MBChB,

<sup>6</sup>William C. Fryda; MD.

<sup>1</sup>Consultant Physician, Department of Medicine, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, KENYA

<sup>2</sup>Medical Officer, Department of Endoscopy, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, KENYA

<sup>3,4</sup>Senior Clinical Officers, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, KENYA

<sup>5</sup>Medical Officer(intern), St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, KENYA

<sup>6</sup>Chief Physician Haemato-Oncologist, St. Joseph Rift Valley Hospital, Gilgil, Nakuru County, KENYA

\*Corresponding author: Vonwicks C. Onyango,

ORCID ID: <https://orcid.org/0009-0004-6791-8809>

DOI: <https://doi.org/10.5281/zenodo.8174103>

Published Date: 22-July-2023

---

**Abstract:** Evans syndrome is a rare autoimmune disorder characterized by the occurrence of autoimmune hemolytic anemia and immune thrombocytopenic purpura with or without immune neutropenia. The syndrome may be idiopathic, but in typical clinical settings, secondary causes, predominantly autoimmune diseases, may be the underlying etiology. We present a case of lupus presenting initially as Evans syndrome.

**Keywords:** Evans syndrome, autoimmune hemolytic anemia, immune thrombocytopenic purpura, systemic lupus erythromatosus, Coombs test.

---

## 1. CASE SUMMARY

### *Presenting illness and physical examination*

A 22-year-old nulliparous lady from Kisii, Kenya, presented to us with severe bleeding diathesis (epistaxis, bleeding gums, coffee-ground emesis, melena stool), profound lethargy, and fevers. This was on a background of 4-6 months of recurrent polyarthritis (of small and medium joints of upper and lower limbs), progressive alopecia, oral ulcers, a hyperpigmented rash in the malar region, and a recent onset of twitching of both upper and lower limbs followed by drowsiness. She had been treated elsewhere for "arthritis" without significant improvement.

Clinically, she was in extremis: markedly wasted with conjunctival pallor, scleral jaundice, with a blood pressure of 72/46 mmHg, a heart rate of 128bpm, a respiratory rate of 28 breaths/minute, oxygen saturation by pulse oximetry of 85% in room air, a temperature of 40°C, random blood glucose of 64mg/dl, and a low Glasgow Coma Scale (GCS) of 12/15. She was

actively nose-bleeding and had blood oozing from her gums. During admission, she had two consecutive generalized tonic-clonic seizures. She underwent a successful comprehensive initial resuscitation. Her other significant physical examination findings included: alopecia *totalis*, malar rash sparing the nasolabial folds, bilateral exudative conjunctivitis, multiple oral ulcers (some septic), and generalized petechial and ecchymotic rashes, especially over bony prominences. She had asymmetrical polysynovitis of the wrists, elbows, and ankles without joint deformation. She had coarse bilateral lung crepitations, was in mild fluid overload with normal S1 and S2 heart sounds, and had an S3 gallop and hemic murmur in the apex (consistent with high-output heart failure). Other than the low GCS and the convulsions, she had no focal neurology. A digital rectal exam showed melena stool.

#### **Diagnostic workup**

Her basic work-up included a complete blood count showing bicytopenia with hemoglobin 5.8 g/dl, mean corpuscular volume 103 fl, platelets  $42 \times 10^3/\mu\text{L}$ , white blood cells  $5.4 \times 10^3/\mu\text{L}$ , and a blood smear showing markedly decreased platelets in number, decreased erythrocytes with rouleaux formation, 2+ spherocytes and 2+ fragmented red cells, and normal leucocytes with no toxic granulations. She had a positive direct Coombs test, a negative indirect Coombs test, elevated total bilirubin of 3.6 mg/dl, direct bilirubin of 1.8mg/dl, an ESR of 50mm/hr (these are consistent with features of autoimmune hemolytic anemia). She had a positive rheumatoid factor, a strongly positive antinuclear antibody (ANA) with estimated titer 1:1000, a strongly positive anti-double stranded-DNA with titer  $>1:100$  (consistent with a SLE diagnosis), normal creatinine of 0.5mg/dl, urinalysis showed many WBC/hpf but no proteinuria or hematuria, a negative HIV test, a negative syphilis screening test, negative malaria, and a negative Hepatitis B and C screen. Abdomino-pelvic ultrasound showed free fluid in the pelvis but grossly normal visceral organs. A chest x-ray showed bilateral lung infiltrates with right mid-lung zone consolidation consistent with pneumonia. A CT scan of the brain showed features of cerebral edema with mild atrophic changes but no space-occupying lesions, intracranial hemorrhage, or leptomeningeal enhancement. A lumbar puncture and CSF analysis were normal. Interval upper GI endoscopy showed marked pangastritis with fundal and pre-pyloric punctate hemorrhages, with gastric biopsy showing chronic non-atrophic superficial *H. pylori*-negative gastritis.

#### **Management and follow-up**

The patient was clinically diagnosed with Evans syndrome (features of autoimmune hemolytic anemia with immune thrombocytopenic purpura) in systemic lupus erythematosus (SLE). Following successful resuscitation, she was started on high-dose steroids using intravenous dexamethasone at 8mg thrice daily and subsequently oral prednisone at 1mg/kg/day (with gastro-protection using oral omeprazole and osteo-protection using oral calcium and vitamin D supplements), oral methotrexate starting at 10mg/week with daily (rather than weekly) oral folic acid at 5mg in view of the anemia, and hydroxychloroquine 200mg twice daily. She was transfused with 4 units of whole blood, and the active bleeding diatheses subsided within 24 hours following administration of intravenous tranexamic acid at 1gm thrice daily. The seizures were deemed to be due to neurolupus and were aborted with intravenous diazepam and a loading dose of intravenous phenytoin at 750mg in normal saline, followed by a maintenance dose. The pneumonia, urinary tract infection, and septic oral ulcers were treated with intravenous, and subsequently, oral antibiotics. She was given concomitant comprehensive supportive therapy and discharged ambulating by a wheelchair after two weeks of inpatient management. At the time of discharge, the complete blood count was completely normal, the jaundice had resolved, liver functions were normal, and the seizures were well controlled.

It has now been nine months since the diagnosis. She is on follow-up at the medical clinic, ambulant without any support, fully functionally independent, and compliant with medical therapy, principally methotrexate and hydroxychloroquine (the steroids have since been stopped). Her hair has since almost all grown back, but the malar rash has persisted (See images 1 and 2 below). There has been no evidence of lupus nephritis so far, and the disease has only had mild flare-ups on occasion based on the SLE Disease Activity Index (SLEDAI) scores.



**Image 1:** 9 months later, the *alopecia totalis* has subsided with the hair almost all grown back. (Photos taken and posted with full consent of the patient)



**Image 2:** Malar rash sparing the nasolabial folds. The rash is hyperpigmented in dark skin. Notice the associated skin exfoliation on the nasal bridge. (Photos taken and posted with full consent of the patient)

## 2. DISCUSSION

Systemic lupus erythematosus (SLE) is an autoimmune disease with multiple systemic involvements and protean manifestations. One of such potential manifestations is the occurrence of autoimmune hemolytic anemia (AIHA), immune thrombocytopenic purpura (ITP) with or without immune neutropenia. This entity is Evans syndrome (1). The AIHA and ITP may occur concurrently or sequentially. The AIHA is due to IgG autoantibodies reacting to red blood cell (RBC) surface antigens at normal body temperature (37°C) (i.e., warm AIHA, present in 60-70% of cases (2)), thus causing intravascular hemolysis and the ensuing anemia and jaundice (3). This is in contradistinction to cold AIHA, in which autoantibodies (usually IgM) exhibit maximal affinity to RBC antigens at temperatures below body temperature. The presence of autoantibodies against autologous RBC surface antigens is demonstrated by a positive direct antiglobulin (DAT) test, also called the Coombs test (4). The ITP occurs when autoantibodies bind the surface glycoprotein receptors GPIIb/IIIa on the platelets and megakaryocytes, thereby inducing their degradation or destruction in the spleen and liver. This leads to thrombocytopenia and defective thrombopoiesis and megakaryopoiesis (5). Evans syndrome may be primary (idiopathic) or secondary (associated with an underlying disorder). Secondary causes include SLE (most commonly associated with up to 50% of cases), non-Hodgkin lymphoma, chronic lymphocytic leukemia, Sjogren syndrome, etc. (3). The management of Evans syndrome depends on the underlying causes, if any, and generally includes steroids (the mainstay of treatment), immunosuppressants, intravenous immunoglobulins, and monoclonal antibodies (3). Idiopathic Evans syndrome may relapse after initial therapy and may be associated with refractory AIHA and ITP warranting splenectomy (6).

Our patient presented with severe symptomatic macrocytic anemia complicated by features of high-output heart failure. This was largely due to the AIHA (as evidenced by pallor, jaundice, reticulocytosis, and schistocytes on the blood smear and a positive Coombs test), as well as the bleeding disorders caused by the thrombocytopenia. She had no leucopenia and has maintained normal leucocyte and neutrophil counts all through. In her case, she had multiple clinical findings that fulfilled the diagnostic criteria for SLE as per the American College of Rheumatology and the European League Against Rheumatic diseases (7). The convulsions with associated CT scan brain findings are consistent with neurolupus, which is a potentially fatal presentation in SLE without prompt and effective management (8). It is remarkable how quickly she's responded to therapy. Her initial presentation of Evans syndrome has completely resolved on steroids and immunosuppressants, and she's remained in hematological remission to date with ongoing multidisciplinary follow-up.

### 3. CONCLUSION

The concomitant or sequential occurrence of AIHA and ITP with or without autoimmune neutropenia should prompt a diagnosis of Evans syndrome. While up to 50% of cases may be idiopathic, the remainder are mainly associated with hematological and autoimmune diseases, of which SLE is the most common. The management is directed at searching for and treating underlying causes in the context of a multidisciplinary team.

### ACKNOWLEDGEMENT

The authors acknowledge the following staff at St. Joseph Rift Valley Hospital, Gilgil, Kenya, who attended to the patient: Nursing staff: Pauline Nyagah, Beatrice Elegwa, Agnes Akumu, Christine Baraza, and Stephen Kiarie; Laboratory staff: Paul Njuguna, Peter Kibet, and Zebedeo Machuka; Sonographer: Thomas Kamau; Physiotherapist: Daniel Kahinga; Patient attendants: Silas Odhiambo, Zipporah Kahenza; and Mrs. Sharon Agina for proofreading the manuscript.

### Informed consent

Written informed consent was obtained from the patient to publish this case report, including the images.

### Funding

The authors have no source of funding or support to declare.

### REFERENCES

- [1] Shaikh H, Mewawalla P. Evans Syndrome. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC.; 2023.
- [2] Barcellini W, Fattizzo B. The Changing Landscape of Autoimmune Hemolytic Anemia. *Front Immunol.* 2020;11:946.
- [3] Audia S, Grienay N, Mounier M, Michel M, Bonnotte B. Evans' Syndrome: From Diagnosis to Treatment. *J Clin Med.* 2020;9(12).
- [4] Packman CH. The Clinical Pictures of Autoimmune Hemolytic Anemia. *Transfus Med Hemother.* 2015;42(5):317-24.
- [5] Zufferey A, Kapur R, Semple JW. Pathogenesis and Therapeutic Mechanisms in Immune Thrombocytopenia (ITP). *J Clin Med.* 2017;6(2).
- [6] Chaturvedi S, Arnold DM, McCrae KR. Splenectomy for immune thrombocytopenia: down but not out. *Blood.* 2018;131(11):1172-82.
- [7] Aringer M. EULAR/ACR classification criteria for SLE. *Semin Arthritis Rheum.* 2019;49(3s):S14-s7.
- [8] McGlasson S, Wiseman S, Wardlaw J, Dhaun N, Hunt DPJ. Neurological Disease in Lupus: Toward a Personalized Medicine Approach. *Front Immunol.* 2018;9:1146.