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# EBSTEIN'S ANOMALY WITH SECONDARY ERYTHROCYTOSIS AND SEVERE PULMONARY HYPERTENSION PRESENTING AS ACUTE ISCHEMIC STROKE: A CASE REPORT

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## ABSTRACT

Ebstein's anomaly is a rare congenital cardiac malformation characterised by apical displacement of the tricuspid valve leaflets. When complicated by secondary erythrocytosis, severe pulmonary hypertension, and a hypercoagulable state, it carries an exceptionally high risk of paradoxical embolism and cerebrovascular events. We report a 55-year-old female with a 15-year history of Ebstein's anomaly and severe pulmonary hypertension who presented with acute altered sensorium, low-grade fever, and passage of loose stools. Clinical examination revealed cyanosis, Grade III pandigital clubbing, pallor, and left hemiparesis. Investigations confirmed secondary erythrocytosis (Hb 22.9 g/dL, HCT 67.6%), a markedly elevated serum erythropoietin of 66 mIU/mL, and a D-dimer of 1500 ng/mL. The platelet count was $1.61 \times 10^5$/µL (161,000/µL). Echocardiography demonstrated apical displacement of the tricuspid septal leaflet with a preserved ejection fraction of 51%. MRI Brain revealed multifocal acute and chronic infarcts in bilateral frontoparietal regions, bilateral thalamus, and bilateral cerebellum. The patient was managed with anticoagulation, antiplatelet agents, and supportive therapy, and was successfully discharged following completion of treatment. This case underscores the importance of recognising erythrocytosis-driven hypercoagulability as a precipitant of multifocal ischemic stroke in patients with cyanotic congenital heart disease.

**KEYWORDS:** Ebstein's anomaly; Secondary erythrocytosis; Erythropoietin; Pulmonary hypertension; Ischemic stroke; Paradoxical embolism; Hemiparesis; Congenital heart disease.

## INTRODUCTION

Ebstein's anomaly is a rare congenital cardiac defect accounting for less than 1% of all congenital heart diseases, characterised by apical displacement of the tricuspid valve leaflets into the right ventricle, resulting in a variably sized "atrialized" right ventricle and functional right ventricular outflow obstruction. The malformation predisposes to right-to-left shunting, progressive cyanosis, and secondary erythrocytosis driven by chronic hypoxia-induced erythropoietin secretion.

Secondary erythrocytosis in cyanotic congenital heart disease is a compensatory but double-edged physiological response. While the increase in red cell mass partially offsets arterial oxygen desaturation, the resultant hyperviscosity, thrombocytopenia, and coagulopathy create a markedly hypercoagulable state. Paradoxical embolism — the passage of venous thrombi through an intracardiac shunt into the systemic circulation — is a well-recognised but under-appreciated mechanism of stroke in this population.

Pulmonary arterial hypertension secondary to Ebstein's anomaly further compounds the haemodynamic burden, perpetuating hypoxia and erythropoietin-driven erythrocytosis. The confluence of these derangements in a single patient presenting with acute multifocal ischemic stroke represents an exceptionally complex clinical scenario with limited documented precedent. We present this case to highlight the pathophysiological interplay

and the multidisciplinary management required in such patients.

## CASE PRESENTATION

A 55-year-old woman from Tuticorin presented to the Emergency Department of Tirunelveli Medical College Hospital with a 2-day history of altered sensorium, associated with one day of low-grade fever and a single episode of loose stools. She had a known history of Ebstein's anomaly diagnosed 15 years earlier and was on regular cardiology follow-up for severe pulmonary hypertension.

There was no history of seizure, headache, vomiting, chest pain, palpitations, loss of consciousness, recent trauma, or previous cerebrovascular events. There was no documented history of diabetes mellitus, systemic hypertension, smoking, or alcohol consumption.

On examination, the patient was conscious but drowsy and inconsistently obeyed verbal commands. Vital signs were as follows: blood pressure 160/100 mmHg, pulse rate 86 beats/minute and regular, respiratory rate 20 breaths/minute, and oxygen saturation 84% on room air, which improved to 94% with supplemental oxygen at 2 L/min via nasal cannula.

General examination revealed pallor, central cyanosis, Grade III pandigital clubbing, and moderate dehydration. No lymphadenopathy, pedal oedema, or elevated jugular venous pressure was noted.

Cardiovascular examination revealed apex beat was localised to the fifth left intercostal space, 1 cm lateral to the midclavicular line. Cardiac auscultation was performed over the aortic, pulmonary, Erb's, tricuspid, and mitral areas, as well as along the left parasternal border and epigastrium. A loud P2 was noted. A grade III pansystolic murmur was maximal at the left lower sternal border with inspiratory accentuation, consistent with tricuspid regurgitation. An early diastolic decrescendo murmur at the left upper sternal border suggested pulmonary regurgitation secondary to severe pulmonary hypertension.

Respiratory system examination was unremarkable with normal vesicular breath sounds and no adventitious sounds. Abdominal examination showed no hepatosplenomegaly or ascites.

Neurological examination revealed left-sided upper motor neuron weakness. Tone was increased in the left upper and lower limbs with exaggerated deep tendon reflexes. Plantar response was extensor on the left side. Cranial nerve examination was normal. Sensory examination was grossly preserved. The overall clinical picture suggested an acute right hemispheric cerebrovascular event.

## INVESTIGATIONS

### Haematological and Biochemical Evaluation

Initial laboratory investigations demonstrated marked erythrocytosis with significant haemoconcentration:

- Haemoglobin: 22.9 g/dL
- Haematocrit: 67.6%
- RBC count: $7.2 \times 10^6/\mu L$
- Total leukocyte count: 14,600 cells/µL
- Platelet count: $1.61 \times 10^5/\mu L$ (161,000/µL)

**Renal function and metabolic parameters were within normal limits**

- Blood urea: 34.5 mg/dL
- Serum creatinine: 0.7 mg/dL
- Serum sodium: 136 mEq/L
- Serum potassium: 3.6 mEq/L
- Random blood glucose: 85 mg/dL

**Markers of coagulation and thrombosis revealed**

- D-dimer: 1500 ng/mL
- Prothrombin time (PT): 23.6 seconds
- Activated partial thromboplastin time (aPTT): 41.7 seconds
- INR: 1.93

Serum erythropoietin level was markedly elevated at 66 mIU/mL, strongly supporting secondary erythrocytosis due to chronic hypoxaemia rather than a primary myeloproliferative disorder. Antinuclear antibody testing was negative. JAK2 V617F mutation testing was not performed during this admission; however, the markedly elevated erythropoietin level in conjunction with longstanding cyanotic congenital heart disease makes a primary myeloproliferative neoplasm unlikely.

### Electrocardiography

Electrocardiogram demonstrated sinus rhythm without evidence of acute ischaemia or significant arrhythmia.

### Echocardiography

Transthoracic echocardiography confirmed Ebstein's anomaly with apical displacement of the septal tricuspid leaflet by approximately 4 cm from the annular plane. Severe pulmonary hypertension was present. Left ventricular systolic function was preserved with an ejection fraction of 51%. No intracardiac thrombus or valvular vegetations were identified. Although an interatrial communication was not visualised on transthoracic imaging, the possibility of a patent foramen ovale or small atrial septal defect could not be definitively excluded. Bubble contrast echocardiography and transoesophageal echocardiography were not performed during this admission.

### Neuroimaging

Non-contrast computed tomography of the brain demonstrated hyperdense vascular structures suggestive of underlying thrombotic pathology. Subsequent magnetic resonance imaging of the brain revealed multiple acute and chronic infarcts involving the bilateral

frontoparietal regions, bilateral thalami, and bilateral cerebellar hemispheres. The multifocal and multi-territorial distribution strongly favoured an embolic aetiology rather than isolated large-vessel atherosclerotic disease. In the setting of Ebstein's anomaly, severe pulmonary hypertension, and marked secondary erythrocytosis, these findings were highly suggestive of a cardioembolic or paradoxical embolic mechanism associated with hyperviscosity-related thrombogenesis.

## DIFFERENTIAL DIAGNOSIS

**The following differential diagnoses were considered**

- Cardioembolic or paradoxical embolism secondary to Ebstein's anomaly and erythrocytosis-driven hypercoagulability — Primary diagnosis, supported by multifocal infarct pattern on MRI consistent with an embolic source.
- Thrombotic stroke secondary to hyperviscosity syndrome — Supported by Hb 22.9 g/dL and HCT 67.6%; however, the multi-territorial MRI pattern favoured a cardioembolic or paradoxical embolic mechanism.
- Systemic Lupus Erythematosus (SLE) with cerebral vasculitis — Considered given age and sex; excluded by negative ANA.
- Antiphospholipid Antibody Syndrome — Elevated INR and D-dimer raised this possibility; however, the clinical context and imaging pattern were consistent with the primary diagnosis.
- Infective Endocarditis with septic emboli — Considered given fever; excluded by echocardiographic absence of vegetations and clinical course.
- Polycythemia Vera — Excluded by markedly elevated serum erythropoietin (66 mIU/mL), which is characteristically suppressed in primary myeloproliferative disorders, and by the longstanding history of cyanotic congenital heart disease providing a clear physiological basis for secondary erythrocytosis.

## TREATMENT AND CLINICAL COURSE

The patient was admitted for multidisciplinary management involving internal medicine, neurology, cardiology, and haematology teams. Initial treatment focused on stabilisation of airway, breathing, and circulation, correction of dehydration, optimisation of oxygenation, and prevention of further thromboembolic events.

Supplemental oxygen was administered, resulting in improvement of oxygen saturation from 84% on room air to 94% on low-flow oxygen therapy. Careful intravenous hydration was instituted to correct dehydration and reduce blood viscosity associated with severe secondary erythrocytosis. Antithrombotic therapy was initiated with aspirin and clopidogrel for secondary stroke prevention. Anticoagulation with unfractionated heparin was administered under close clinical monitoring because of the strong suspicion of a cardioembolic or paradoxical embolic mechanism.

The patient continued treatment for underlying cardiac disease with enalapril and spironolactone. Atorvastatin was prescribed for vascular protection. Supportive measures included maintenance of adequate hydration, prevention of venous stasis, nutritional optimisation, and physiotherapy.

Given the markedly elevated haemoglobin (22.9 g/dL) and haematocrit (67.6%), hyperviscosity syndrome was considered. Current evidence in cyanotic congenital heart disease favours correction of dehydration and avoidance of iron deficiency as first-line measures. Therapeutic phlebotomy is generally reserved for patients with symptomatic hyperviscosity and should be performed cautiously, as repeated venesection may induce iron deficiency and paradoxically worsen blood viscosity.

During hospitalisation, the patient demonstrated gradual neurological improvement with resolution of altered sensorium and partial recovery of left-sided motor deficits. She remained haemodynamically stable throughout her hospital stay and was discharged with advice for regular follow-up with cardiology, neurology, and haematology services.

## DISCUSSION

Ebstein's anomaly is a rare congenital cardiac malformation characterized by apical displacement of the septal and posterior tricuspid valve leaflets into the right ventricle, resulting in atrialization of a variable portion of the right ventricle. The condition accounts for less than 1% of all congenital heart diseases and is frequently associated with interatrial communications such as atrial septal defects or patent foramen ovale, predisposing affected individuals to right-to-left shunting, cyanosis, and paradoxical embolization.

The present case demonstrates the complex interplay between chronic hypoxemia, secondary erythrocytosis, severe pulmonary hypertension, and ischemic stroke. Chronic arterial desaturation stimulates renal erythropoietin production, resulting in compensatory erythrocytosis aimed at improving systemic oxygen transport. The markedly elevated serum erythropoietin level of 66 mIU/mL observed in our patient supports an appropriate physiological response to chronic hypoxia and effectively distinguishes secondary erythrocytosis from primary erythrocytosis such as polycythemia vera, in which erythropoietin levels are typically suppressed.

Mc Mullin MF, in *Harrison's Principles of Internal Medicine*, states that secondary erythrocytosis associated with chronic hypoxemia in cyanotic congenital heart disease represents a physiologic compensatory response mediated by increased erythropoietin production. However, excessive elevation of haematocrit may result in hyperviscosity syndrome, manifesting as headache,

dizziness, visual disturbances, thrombotic complications, and cerebrovascular events. Routine phlebotomy is not recommended and should be reserved for patients with symptomatic hyperviscosity because repeated venesection may induce iron deficiency, produce microcytic erythrocytes, increase blood viscosity, and impair tissue oxygen delivery.[8] The haematocrit of 67.6% documented in our patient placed her at substantial risk for viscosity-related complications and thromboembolic phenomena.

The neuroimaging findings were particularly noteworthy. MRI of the brain demonstrated multifocal acute and chronic infarctions involving bilateral frontoparietal regions, bilateral thalami, and bilateral cerebellar hemispheres. Such a multi-territorial distribution strongly suggests an embolic mechanism rather than atherosclerotic large-vessel disease. In patients with Ebstein's anomaly, several mechanisms contribute to thromboembolic risk, including right atrial enlargement, blood stasis, tricuspid regurgitation, endothelial dysfunction, arrhythmias, and the potential presence of right-to-left intracardiac shunting through an atrial septal defect or patent foramen ovale. Although an interatrial communication was not directly demonstrated on echocardiography in this case, its presence cannot be excluded, and the elevated D-dimer level together with the extensive multi-territory infarct distribution support a cardioembolic or paradoxical embolic pathogenesis.

Severe pulmonary hypertension likely played an important contributory role by perpetuating right-to-left shunting and chronic hypoxemia. Sustained hypoxemia further stimulates erythropoietin production and erythrocytosis, thereby creating a vicious cycle of increased blood viscosity, impaired microvascular flow, and enhanced thrombotic risk.

An important therapeutic consideration in cyanotic congenital heart disease is the cautious use of phlebotomy. Contemporary evidence suggests that routine phlebotomy should be avoided in the absence of symptomatic hyperviscosity because repeated venesection may induce iron deficiency, resulting in microcytic erythrocytes that paradoxically increase blood viscosity and impair oxygen delivery. Therefore, maintenance of adequate hydration, correction of iron deficiency when present, optimisation of oxygenation, and individualised antithrombotic therapy remain essential components of management.

The elevated erythropoietin concentration together with longstanding cyanotic congenital heart disease strongly supports secondary erythrocytosis as the underlying haematologic abnormality, making a primary myeloproliferative neoplasm such as polycythemia vera unlikely. In polycythemia vera, erythropoietin levels are characteristically suppressed due to autonomous erythroid proliferation, whereas the elevated erythropoietin of 66 mIU/mL recorded in this patient is consistent with an appropriate hypoxia-driven erythropoietic response.[8]

Reports describing the coexistence of Ebstein's anomaly, severe pulmonary hypertension, erythropoietin-driven secondary erythrocytosis, and multifocal ischemic stroke remain exceedingly uncommon. This case highlights the need for heightened clinical vigilance for cerebrovascular complications in adults with cyanotic congenital heart disease, particularly in the presence of marked erythrocytosis and pulmonary hypertension. Early recognition and multidisciplinary management are critical for improving neurological and cardiovascular outcomes.

## CONCLUSION

This case represents a rare convergence of Ebstein's anomaly, secondary erythrocytosis confirmed by elevated serum erythropoietin (66 mIU/mL), severe pulmonary hypertension, and acute multifocal ischemic stroke with left hemiparesis. The erythropoietin-driven erythrocytosis created a profoundly hypercoagulable state, likely contributing to a cardioembolic or paradoxical embolic mechanism resulting in the observed multi-territory cerebral infarction. Prompt recognition of this rare but catastrophic complication, combined with targeted anticoagulation and multidisciplinary care, enabled successful patient recovery and discharge.

This case serves as a vital reminder that clinicians managing patients with cyanotic congenital heart disease must maintain vigilance for cerebrovascular events, particularly in the presence of secondary erythrocytosis and pulmonary hypertension. Serum erythropoietin estimation is a valuable tool in confirming the secondary nature of erythrocytosis, distinguishing it from primary myeloproliferative disorders, and guiding management. A source-control philosophy — addressing the haematological derangement and the cardiac substrate alongside acute stroke care — is essential for optimising outcomes in this complex patient population.

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