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Hyperviscosity-related ischemic stroke in TOF with marked secondary erythrocytosis successfully managed with therapeutic phlebotomy

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Case Report

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Abstract

Background

Ischemic stroke is an uncommon but potentially devastating complication of cyanotic congenital heart disease [1,2]. Chronic hypoxia in Tetralogy of Fallot can result in secondary polycythemia and hyperviscosity, predisposing patients to thrombotic events [2,3]. The role of therapeutic phlebotomy in this setting remains controversial and is generally reserved for selected patients with symptomatic hyperviscosity [2,4]. We report a rare case of hyperviscosity-related ischemic stroke in an adult with Tetralogy of Fallot and pulmonary atresia successfully managed with therapeutic phlebotomy.

Case Presentation

A 43-year-old man with Tetralogy of Fallot and pulmonary atresia presented with acute right-sided hemiparesis, slurring of speech, and altered sensorium. He had a previous history suggestive of a transient ischemic event. Neuroimaging demonstrated a large left middle cerebral artery territory infarct with evidence of a prior right parietal infarct. Clinical examination revealed central cyanosis and grade 4 digital clubbing. Haematological evaluation showed marked secondary polycythemia with haemoglobin 18.9 g/dL, haematocrit 60%, and red blood cell count 7.85 × 10^6/μL. Serum erythropoietin was markedly elevated at 426 mIU/mL, consistent with chronic hypoxia-driven erythrocytosis. Iron studies demonstrated concomitant iron deficiency with microcytosis. Echocardiography confirmed Tetralogy of Fallot with pulmonary atresia, a large ventricular septal defect with bidirectional shunting, overriding aorta, and right ventricular hypertrophy. In view of symptomatic hyperviscosity associated with acute ischemic stroke, two sessions of therapeutic phlebotomy were performed with the removal of approximately 350 mL of blood during each session, accompanied by isotonic saline replacement and hemodynamic monitoring. Hematocrit decreased from 60% to 47.6% and haemoglobin from 18.9 g/dL to 14 g/dL, with clinical improvement and no procedure-related complications.

Conclusions

This case highlights hyperviscosity as a potentially modifiable contributor to ischemic stroke in adults with cyanotic congenital heart disease. Therapeutic phlebotomy, when used judiciously with adequate volume replacement and monitoring, may be an effective adjunctive intervention in selected patients with symptomatic secondary polycythemia. Early recognition of hyperviscosity-related neurological complications is essential for timely management and improved clinical outcomes.

Background

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease and consists of a ventricular septal defect, right ventricular outflow tract obstruction, overriding aorta, and right ventricular

hypertrophy [1]. Chronic right-to-left shunting results in persistent hypoxemia, which stimulates erythropoietin production and leads to secondary erythrocytosis [2,3]. Although erythrocytosis serves as a compensatory mechanism to improve oxygen delivery, excessive increases in red blood cell mass may result in hyperviscosity syndrome and predispose patients to thrombotic complications [2,3].

Neurological manifestations, including transient ischemic attacks and ischemic stroke, represent important causes of morbidity in adults with cyanotic congenital heart disease [4,5]. The pathogenesis is multifactorial and involves chronic hypoxia, hyperviscosity, endothelial dysfunction, coagulation abnormalities, and paradoxical embolisation through right-to-left shunts [2,5].

Therapeutic phlebotomy has traditionally been used to reduce blood viscosity in selected patients with symptomatic hyperviscosity. However, its role remains controversial because excessive phlebotomy may lead to iron deficiency and microcytosis, which can paradoxically worsen blood viscosity [2,6–8]. We report a rare case of hyperviscosity-related ischemic stroke in an adult with Tetralogy of Fallot and pulmonary atresia who demonstrated significant haematological improvement following therapeutic phlebotomy.

Case Presentation

A 43-year-old man with a known history of Tetralogy of Fallot with pulmonary atresia presented with sudden onset weakness of the right upper and lower limbs, slurring of speech, and altered sensorium of four days' duration. The symptoms began abruptly and progressively worsened. He also reported a previous episode of transient right-sided weakness approximately two years earlier that resolved spontaneously within a few hours, suggestive of a prior transient ischemic event.

The patient had undergone cardiac stenting in 2001, although procedural records were unavailable. At presentation, he was receiving aspirin, clopidogrel, and atorvastatin. There was no history of hypertension, diabetes mellitus, thyroid disease, tuberculosis, bronchial asthma, meningitis, smoking, alcohol consumption, or substance abuse.

On examination, central cyanosis and grade IV digital clubbing were present. Oxygen saturation was approximately 92% while receiving supplemental oxygen. Neurological examination revealed right hemiparesis and dysarthria. The National Institutes of Health Stroke Scale (NIHSS) score at presentation was 18, indicating severe neurological impairment, while the modified Rankin Scale (mRS) score was 5, reflecting severe disability and a bedridden state requiring constant assistance. Cardiovascular examination demonstrated findings consistent with cyanotic congenital heart disease.

Non-contrast computed tomography (CT) of the head demonstrated a large left middle cerebral artery territory infarction involving the fronto-parieto-temporal region and basal ganglia, along with evidence of a previous right parietal infarct (Fig. 1A–B). Follow-up CT imaging performed four days later demonstrated the expected evolution of the infarction with well-demarcated hypodensity and persistent but stable mass effect (Fig. 2A–B).

Transthoracic echocardiography confirmed Tetralogy of Fallot with pulmonary atresia, a large subaortic ventricular septal defect with bidirectional shunting, overriding aorta, right ventricular hypertrophy, mild aortic regurgitation, and preserved left ventricular systolic function (left ventricular ejection fraction 50%).

Laboratory investigations revealed marked secondary erythrocytosis with haemoglobin of 18.9 g/dL, hematocrit of 60%, and red blood cell count of 7.85 × 10^6/μL. Serum erythropoietin was markedly elevated at 426 mIU/mL, consistent with chronic hypoxia-driven erythropoiesis. Iron studies demonstrated iron deficiency with serum iron of 38 μg/dL, ferritin of 13.8 ng/mL, transferrin saturation of 9%, and total iron-binding capacity of 442 μg/dL. Thrombocytopenia was present with a platelet count of 45 × 10^3/μL. Serial haematological parameters, erythropoietin levels, iron profile, and laboratory trends are summarised in Fig. 3.

Considering symptomatic hyperviscosity associated with acute ischemic stroke in the setting of secondary erythrocytosis, therapeutic phlebotomy was performed on two occasions, on 4 May 2026 and 6 May 2026. Approximately 350 mL of blood was removed during each session with simultaneous isotonic saline replacement and continuous hemodynamic monitoring.

Following the procedures, haematological parameters improved significantly (Fig. 3). Haemoglobin decreased from 18.9 g/dL to 14.0 g/dL, hematocrit from 60% to 47.6%, and red blood cell count from 7.85 × 10^6/μL to 5.87 × 10^6/μL. The patient remained hemodynamically stable throughout both procedures and experienced no immediate procedure-related complications.

Discussion

Adults with cyanotic congenital heart disease are at increased risk of thromboembolic complications because of chronic hypoxia-induced secondary erythrocytosis, hyperviscosity, endothelial dysfunction, abnormal platelet function, and coagulation abnormalities [2,3,5]. Although secondary erythrocytosis initially serves as a compensatory physiological response to improve oxygen delivery, excessive elevations in hematocrit may impair microcirculatory blood flow and contribute to cerebral ischemia and thrombotic events [2,3].

Our patient demonstrated several factors that may have contributed to a prothrombotic state, including marked erythrocytosis, elevated erythropoietin levels, iron deficiency with microcytosis, thrombocytopenia, and a history suggestive of previous cerebrovascular events. The presence of an old infarct on neuroimaging suggested previous cerebrovascular involvement and may indicate an ongoing predisposition to thromboembolic events.

Perloff et al. emphasised that symptoms of hyperviscosity, rather than hematocrit values alone, should guide therapeutic phlebotomy in patients with cyanotic congenital heart disease [2]. Similarly, Kaemmerer et al. reported that excessive erythrocytosis is associated with increased thrombotic risk and highlighted the need for individualised management strategies in these patients [3]. Current

guidelines also recognise the complex balance between thrombosis and bleeding in adults with cyanotic congenital heart disease and recommend careful clinical assessment before intervention [4].

Iron deficiency represents an important but often overlooked contributor to hyperviscosity. Microcytic erythrocytes demonstrate reduced deformability and increased rigidity, which may paradoxically worsen blood viscosity despite a lower mean corpuscular volume [6]. Repeated or unnecessary phlebotomy may further exacerbate iron deficiency and should therefore be avoided. Our patient had biochemical evidence of iron deficiency, highlighting the importance of evaluating iron status when managing secondary erythrocytosis.

Current literature supports therapeutic phlebotomy primarily in patients with symptomatic hyperviscosity rather than solely based on elevated hematocrit values [2,7,8]. DeFilippis et al. and Thorne emphasised that phlebotomy should be reserved for carefully selected patients and performed with appropriate volume replacement to minimise adverse effects [7,8]. In our patient, carefully monitored phlebotomy with isotonic saline replacement resulted in a reduction of hematocrit from 60% to 47.6% without procedure-related complications and was associated with improvement in haematological parameters.

The uniqueness of the present case lies in the occurrence of a large ischemic stroke in an adult with Tetralogy of Fallot and pulmonary atresia in the setting of marked secondary erythrocytosis and hyperviscosity, supported by a markedly elevated serum erythropoietin level. Therapeutic phlebotomy with isotonic saline replacement resulted in substantial improvement in haematological parameters, including a reduction in haemoglobin and hematocrit levels. Although a direct causal effect of therapeutic phlebotomy on neurological recovery cannot be established in a single case report, the intervention may have contributed to reducing hyperviscosity and its associated thrombotic risk. These findings support the potential role of carefully selected, symptom-guided therapeutic phlebotomy in patients with cyanotic congenital heart disease and symptomatic hyperviscosity.

Given the multifactorial nature of ischemic stroke in cyanotic congenital heart disease, therapeutic phlebotomy should be viewed as part of an individualized management strategy rather than definitive treatment of the cerebrovascular event itself.

Conclusions

This case highlights the complex interplay between chronic hypoxia, secondary erythrocytosis, iron deficiency, and coagulation abnormalities in adults with cyanotic congenital heart disease. Although the precise mechanism of stroke in this patient cannot be definitively established and was classified as TOAST 5 (stroke of undetermined etiology), hyperviscosity and erythrocytosis were considered potential contributing factors. Therapeutic phlebotomy, when used judiciously with adequate hydration and close monitoring, may serve as a useful adjunctive intervention in selected patients with symptomatic hyperviscosity, while definitive management of the underlying cardiac disease is pursued.

Declarations

Ethics approval and consent to participate

Ethical approval was waived for this study because it is a single-patient case report and does not constitute human subjects research according to institutional policy.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Availability of data and materials

All data generated or analysed during this study are included in this published article. Additional information is available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SS contributed to patient management, data collection, literature review, and manuscript preparation and revision.

VL contributed to neurological evaluation, interpretation of clinical findings, and critical revision of the manuscript.

SK and AS supervised the study, reviewed the manuscript critically for important intellectual content, and approved the final version.

All authors read and approved the final manuscript.

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Figures

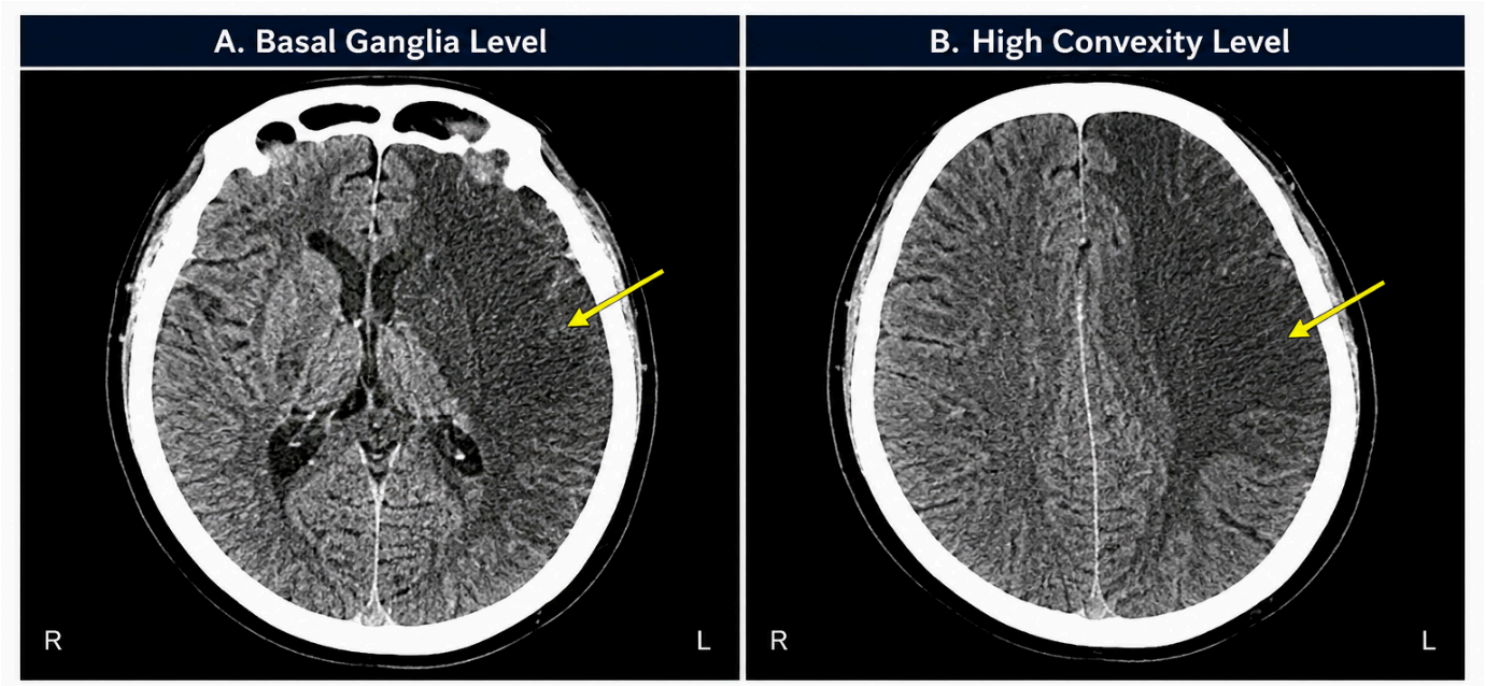


Figure 1

Baseline non-contrast CT head performed on 29 April 2026.

Legend: Axial images at the basal ganglia level (A) and high convexity level (B) showing a large hypodense area in the left middle cerebral artery (MCA) territory involving the basal ganglia and fronto-parieto-temporal regions with loss of gray-white matter differentiation and mass effect.

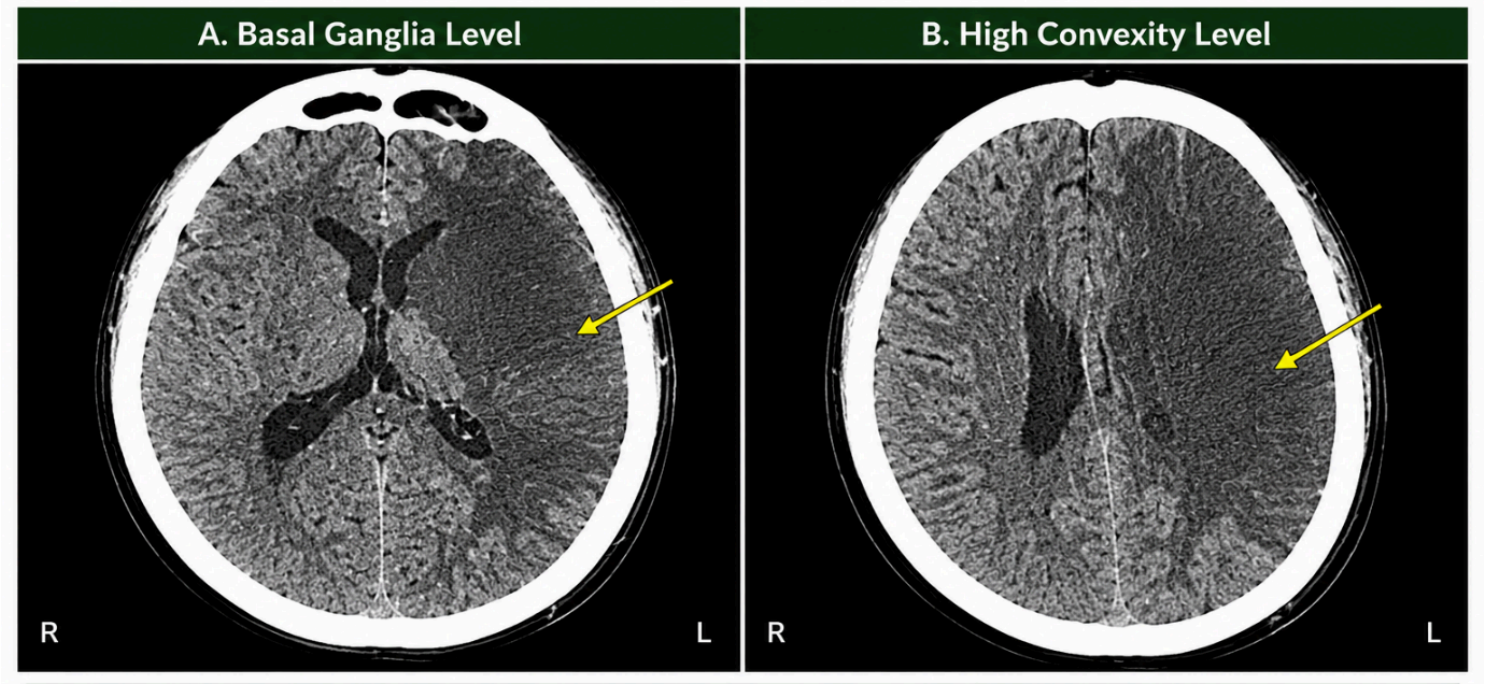


Figure 2

Follow-up non-contrast CT head performed on 03 May 2026.

Legend: Axial images at the basal ganglia level (A) and high convexity level(b) demonstrating expected evolution of the left middle cerebral artery (MCA) territory infarct with well- demarcated hypodensity involving the fronto-parieto-temporal regions and basal ganglia, with persistent mass effect. No evidence of hemorrahagic transformation.

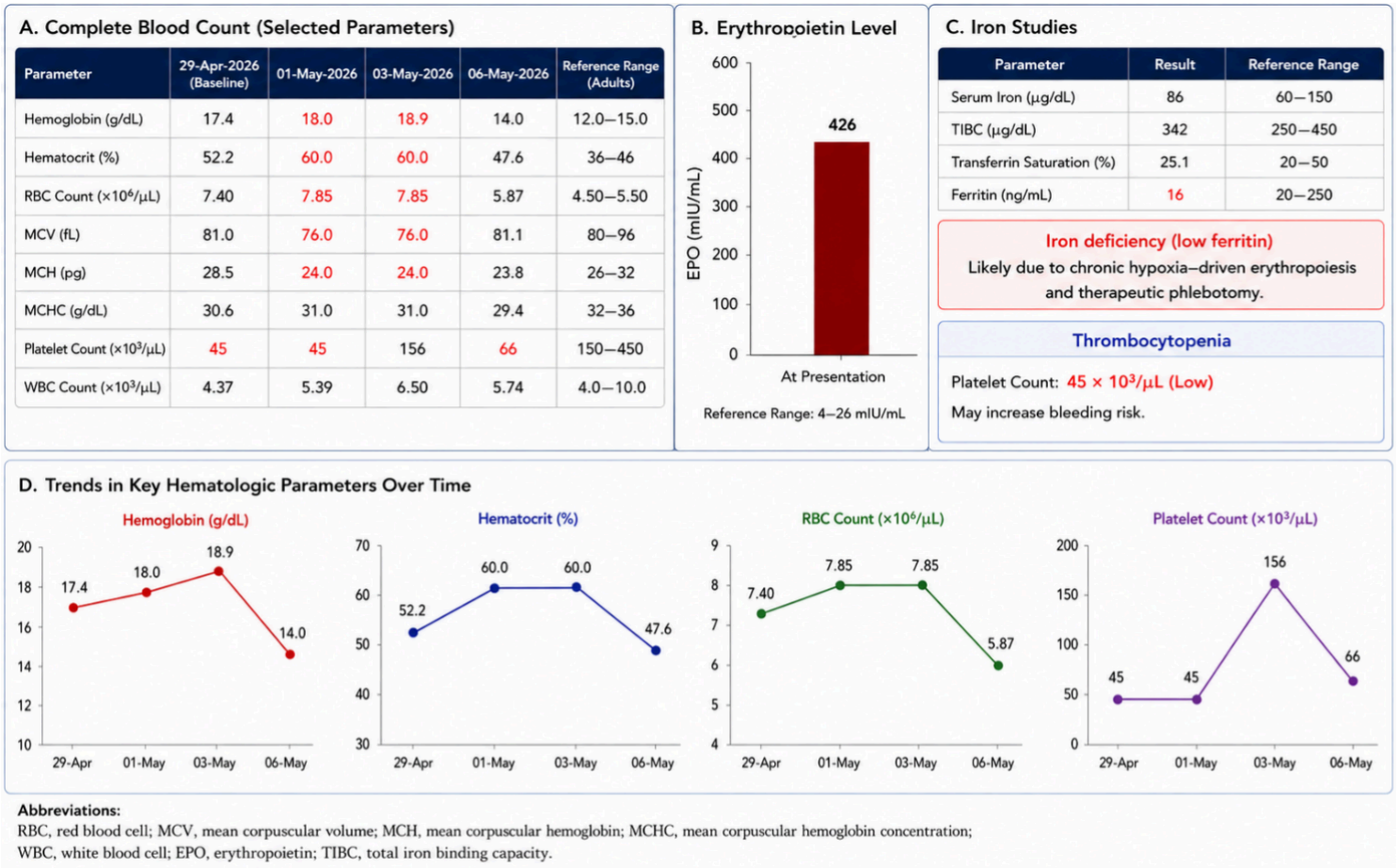


Figure 3

Hematologic Profile and Laboratory Findings

Legend: (A) Serial complete blood counts demonstrate elevated haemoglobin, hematocrit, and RBC count with microcytosis and low MCH/MCHC, consistent with secondary polycythemia. Thrombocytopenia is present. (B) Erythropoietin level is markedly elevated, appropriate for chronic hypoxia in tetralogy of Fallot. (C) Iron studies show low ferritin consistent with iron deficiency. (D) Trends in key hematologic parameters over time show a reduction following therapeutic phlebotomy.