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CONCURRENT ARTERIAL ISCHAEMIC STROKE AND CEREBRAL VENOUS SINUS THROMBOSIS COMPLICATING A HYPERCYANOTIC SPELL IN AN ADOLESCENT WITH UNREPAIRED TETRALOGY OF FALLOT

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ABSTRACT

Introduction: Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease and is now almost universally corrected in infancy; survival without repair into adolescence is, therefore, rare and predisposes to cumulative hypoxaemia-related morbidity.

Case description: We report a 16-year-11-month-old girl with unrepaired TOF who developed a severe hypercyanotic spell (peripheral oxygen saturation 40%) triggered by vomiting and dehydration, with associated left-sided headache. Investigations revealed profound secondary erythrocytosis (haemoglobin 19.6 g/dl, haematocrit 66.7%) and a markedly elevated D-dimer level. Echocardiography confirmed severe TOF physiology, with pulmonary arteries anatomically adequate for total repair (McGoon ratio 2.3). Brain magnetic resonance imaging and angiography demonstrated a hyperacute left temporo-parieto-occipital cortical borderzone infarction together with thrombosis of the left transverse and sigmoid sinuses, subsequently confirmed on transfemoral cerebral angiography. The patient improved clinically and biochemically with oxygen therapy, intravenous hydration, propranolol, empirical antimicrobial prophylaxis, therapeutic low-molecular-weight heparin, and subsequent low-dose aspirin.

Conclusion: This case illustrates a rare dual arterial-venous cerebrovascular phenotype arising from the interaction between chronic hypoxaemia-driven hyperviscosity and an acute hypovolaemic trigger in unrepaired TOF and highlights the importance of timely definitive surgical correction and proactive thrombotic risk stratification in adolescents with long-standing cyanotic congenital heart disease.

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Tetralogy of Fallot (TOF), cyanotic congenital heart disease, hypercyanotic spell, cerebral venous sinus thrombosis, ischaemic stroke

LEARNING POINTS

- Survival into adolescence without surgical correction is uncommon in Tetralogy of Fallot and predisposes to cumulative hypoxaemia-related complications, including cerebrovascular events. Timely definitive repair and continuous cardiology follow-up remain essential.
- A hypercyanotic spell precipitated by vomiting or dehydration can produce a combined arterial (watershed) infarction and cerebral venous sinus thrombosis through a shared mechanism of chronic hyperviscosity, hypercoagulability, and acute hypoperfusion.
- Marked D-dimer elevation and new neurological symptoms in a patient with cyanotic congenital heart disease should prompt urgent brain magnetic resonance imaging/ magnetic resonance angiography, since arterial and venous cerebrovascular events may coexist and both require distinct, timely management.

INTRODUCTION

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease and it accounts for approximately 7-10% of all congenital heart disease cases[1]. It is anatomically defined by a ventricular septal defect, aortic override, right ventricular outflow tract obstruction, and right ventricular hypertrophy-a combination that produces a right-to-left shunt and chronic systemic hypoxaemia if the lesion is left uncorrected[2].

A hypercyanotic ("Tet") spell is a sudden, severe hypoxaemic episode caused by dynamic worsening of right ventricular outflow tract obstruction with an abrupt increase in right-to-left shunting[3]. Spells are typically precipitated by agitation, fever, exertion, or dehydration-factors that reduce pulmonary blood flow and acutely compromise cerebral perfusion-and recurrent episodes have been linked to hypoxic neurological injury[2].

Chronic hypoxaemia stimulates renal erythropoietin production and secondary erythrocytosis[3]; once haematocrit exceeds 65%, the resulting rise in blood viscosity impairs microcirculatory flow and paradoxically reduces effective tissue oxygen delivery[4]. Hyperviscosity is further associated with endothelial dysfunction, platelet activation, and coagulation-cascade activation, creating a prothrombotic state that confers a higher risk of systemic thromboembolism in cyanotic congenital heart disease than in patients without chronic hypoxia[3,4].

Ischaemic stroke occurs more frequently in children with cyanotic congenital heart disease than in the general paediatric population, through a multifactorial mechanism encompassing cerebral hypoperfusion, hyperviscosity-related stasis, and coagulation activation reflected by elevated D-dimer[5]. Cerebral venous sinus thrombosis (CVST) may arise under similarly procoagulant conditions, particularly dehydration or haemoconcentration[4], yet reports of simultaneous arterial and venous cerebral thrombosis in TOF remain scarce[6]. Non-invasive perfusion techniques such as arterial spin labelling are increasingly used to characterise the haemodynamic mechanisms underlying paediatric stroke[6]. We describe an adolescent with unrepaired TOF who developed a severe hypercyanotic spell, complicated by concurrent cortical borderzone infarction and ipsilateral cerebral venous sinus thrombosis-a rare neurovascular phenotype that illustrates the interplay between chronic hypoxia, haemoconcentration, and coagulation abnormalities in this population.

CASE DESCRIPTION

A 16-year-11-month-old girl was referred to the paediatric cardiology clinic from a secondary-care hospital with a known diagnosis of unrepaired TOF and suspected cerebral infarction. She presented with acute dyspnoea and marked oxygen desaturation; on arrival, peripheral oxygen saturation (SpO_2) was 40%, with central and peripheral cyanosis of the lips and fingers. Oxygen was administered via a simple face mask at 5 l/min, with partial improvement in saturation.

The episode was accompanied by a left-sided headache and a single episode of non-bilious, non-bloody vomiting in the emergency department. TOF had been diagnosed at 3 months of age, but the patient had not undergone regular cardiology follow-up or definitive surgical correction; her mother had underestimated the severity of the disease and believed the child could recover without hospital treatment. She reported recurrent cyanotic episodes and exertional dyspnoea since early childhood, particularly during strenuous activity. Two weeks before this admission she had been hospitalised elsewhere for a stabbing left-sided headache and three episodes of vomiting. There was no history of trauma, seizures, or loss of consciousness; growth and developmental milestones were age appropriate, nutritional status was adequate, and there was no family history of congenital heart disease.

On examination she weighed 56 kg and measured 165 cm in height. Vital signs were: blood pressure 120/70



Figure 1. Clinical photographs demonstrating A) digital clubbing and B) central and peripheral cyanosis with supplemental oxygen support.

mmHg, heart rate 118 beats/min (regular), respiratory rate 35 breaths/min, temperature 36.6°C, warm extremities, and capillary refill time under 2 seconds. She was fully conscious (Glasgow Coma Scale 15, E4V5M6) but appeared weak, dyspnoeic, and tachypnoeic, with chest-wall retractions. Cardiac auscultation revealed a grade 3/6 ejection systolic murmur at the left upper-to-mid sternal border, single S1 and S2, and no gallop rhythm. Digital clubbing and generalised cyanosis were present *(Fig. 1)*. Oxygen saturation was 45% on room air, improving to 72% with 5 l/min supplemental oxygen via simple face mask. Neurological examination showed no neck stiffness and a negative Brudzinski sign; cranial nerves III-IV and VI-VIII were intact with no facial asymmetry, dysarthria, or hearing impairment, and there was no motor lateralisation. Muscle strength was 5/5 in all four limbs, deep tendon reflexes were +2 and symmetrical, and no pathological reflexes were elicited. Anthropometric assessment indicated an underweight status relative to height age.

Laboratory investigations demonstrated marked secondary polycythaemia, with haemoglobin 19.6 g/dl and haematocrit 66.7%. White blood cell count was 6,180/µl and platelet count was 156,000/µl. D-dimer was markedly elevated at 4,620 ng/ml. Prothrombin time was 13.8 seconds (reference range 9-12 seconds) and activated partial thromboplastin time was 25.9 seconds (reference range 23-33 seconds), indicating no clinically significant abnormality in standard coagulation parameters. Other routine haematological findings were unremarkable.

Transthoracic echocardiography demonstrated situs solitus with atrioventricular and ventriculoarterial concordance and normal pulmonary venous drainage. The right atrium and right ventricle were dilated; the mitral and aortic valves were normal, and tricuspid regurgitation was trivial. Severe infundibular pulmonary stenosis was present, with a pressure gradient of 90 mmHg, and major aortopulmonary collateral arteries were identified. The right and left pulmonary artery diameters measured 1.4 cm and 1.6 cm, respectively, and the abdominal aortic diameter was 1.3 cm. A large perimembranous ventricular septal defect (2.0-2.7 cm) with 50% aortic override was observed, together with a patent foramen ovale. The aortic arch was left-sided and normal, and left ventricular ejection fraction was 78%. The McGoon ratio (sum of right and left pulmonary artery diameters divided by abdominal aortic diameter) was 2.3, and the Nakata index was 221.7 mm^2/m^2 *(Fig. 2)*. These findings confirmed the diagnosis of TOF and indicated anatomical suitability for definitive total surgical correction.

Brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) revealed a hyperacute ischaemic infarction in the cortical borderzone of the left temporo-parieto-occipital region, together with thrombosis of the left transverse and sigmoid sinuses extending to the proximal left internal jugular vein *(Fig. 3)*. Transfemoral cerebral angiography, performed on 10 February 2026, confirmed a contrast filling defect in the left transverse sinus consistent with sinus thrombosis *(Fig. 4)*.

Based on the clinical history, physical examination, and supporting investigations, the patient was diagnosed with TOF (McGoon ratio 2.3), post-hypercyanotic spell, ischaemic stroke due to thrombosis of the left transverse sinus, and cephalgia secondary to hyperviscosity.

Management comprised continued supplemental

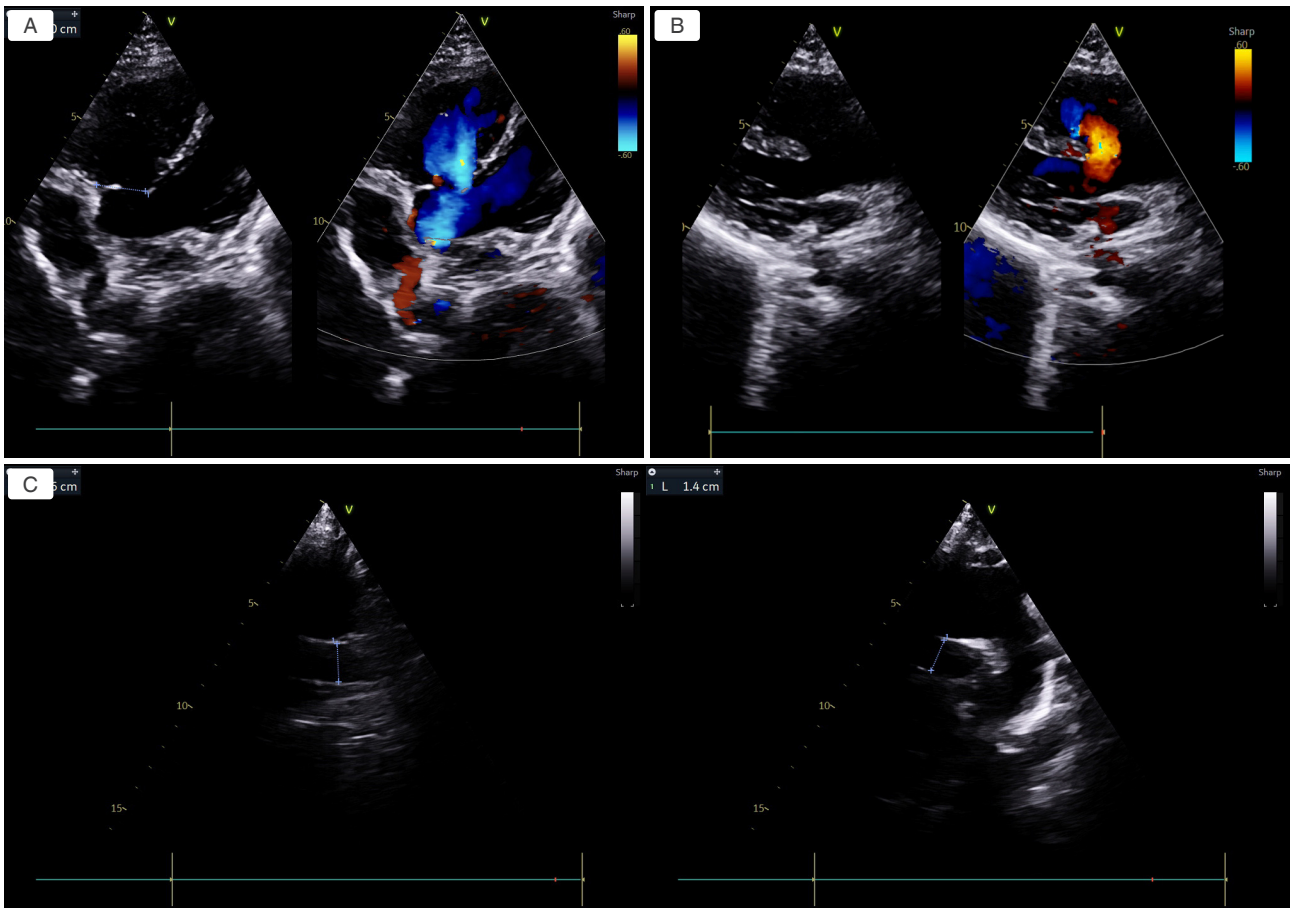


Figure 2. Representative transthoracic echocardiographic images: A) color and continuous-wave Doppler demonstrating shunt flow across the ventricular septal defect with a peak right ventricular outflow tract gradient of 90 mmHg; B) parasternal long-axis view showing the overriding aorta and perimembranous ventricular septal defect; C) two-dimensional measurement of great-vessel diameters used to derive the McGoon ratio (2.3) and Nakata index (221.7 mm²/m²).

oxygen (6 l/min via simple face mask) and intravenous hydration with 5% dextrose in half-normal saline (D5 1/2 NS), 1,500 ml over 24 hours, to correct dehydration and haemoconcentration and thereby reduce the risk of recurrent cyanotic spells. Oral propranolol 10 mg every 8 hours was given as a beta-adrenergic blocker to reduce cardiac workload and prevent recurrent hypercyanotic spells. Empirical intravenous ceftriaxone 1.5 g every 12 hours and metronidazole 500 mg every 8 hours were initiated, planned for 4-8 weeks, as prophylaxis against brain abscess given the recognised risk of intracranial infection in cyanotic congenital heart disease. Following confirmation of cerebral venous sinus thrombosis on angiography, therapeutic anticoagulation was started with subcutaneous enoxaparin (0.6 ml loading dose, then 0.3 ml every 12 hours for 3 days).

Follow-up laboratory evaluation after adequate intravenous hydration, symptomatic management, and anticoagulation therapy showed a decline in haemoglobin (16.2 g/dl), haematocrit (56.3%), and D-dimer (2,570 ng/ml). The patient was discharged after 5 days on oral cefixime 100 mg every 12 hours and metronidazole 500 mg every 8 hours to complete the antimicrobial course, together with low-dose aspirin 60 mg once daily for 3-6 months as antithrombotic therapy, propranolol 10 mg every 8 hours, iron supplementation once daily, omeprazole 20 mg once daily, and paracetamol 500 mg every 8 hours, as needed, for headache.

DISCUSSION

TOF is typically corrected electively at 3-6 months of age in contemporary practice; survival without repair into adolescence is, therefore, uncommon. This is consistent with historical natural-history data showing that only around 24% of unoperated patients survive beyond 10 years and approximately 10% beyond 20 years[1,2]. The annual incidence of arterial ischaemic stroke in children outside the neonatal period is 1-2 per 100,000, and a 2024 meta-analysis found that congenital heart disease confers a significantly increased, predominantly ischaemic, stroke risk (hazard ratio 3.25)[2]. Although TOF-specific incidence data are limited, this risk is plausibly amplified by recurrent hypercyanotic spells, dehydration, severe erythrocytosis with hyperviscosity, and persistent right-to-left shunting-all of which favour cerebral hypoperfusion and thrombosis[4]. By comparison, pooled paediatric estimates place haemorrhagic stroke incidence at approximately 1.45 per 100,000 person-years, while brain abscess is rarer (0.3-0.9 per 100,000 per year) but clinically relevant in cyanotic congenital heart disease[3,4]. The presentation

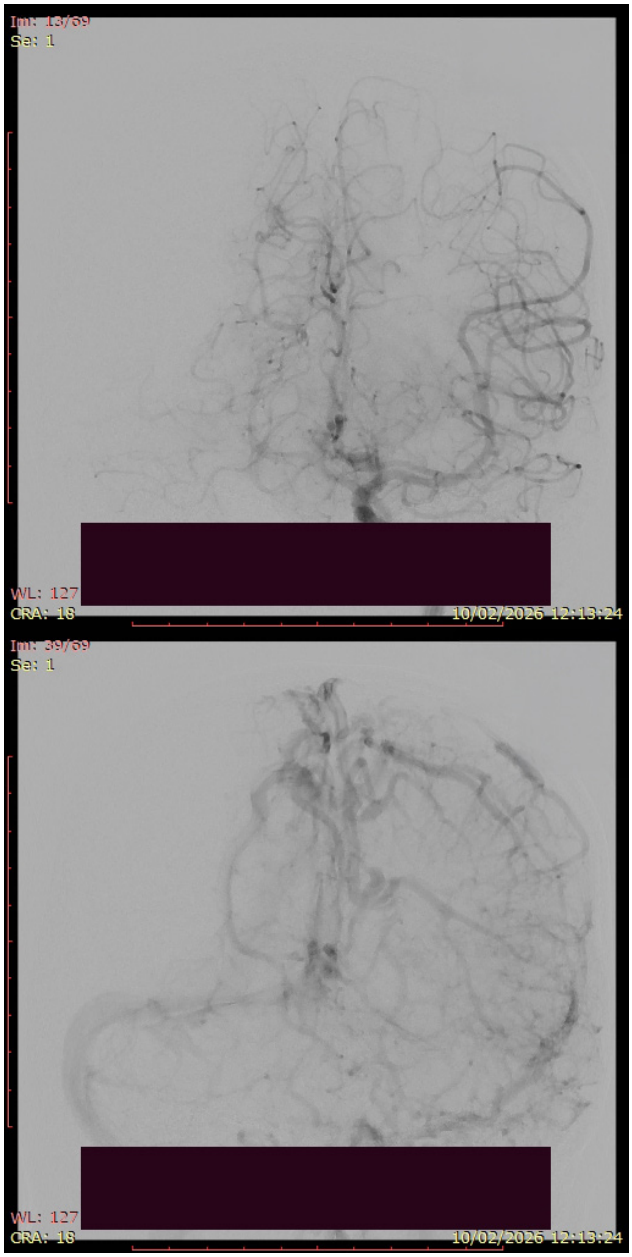


Figure 3. *Transfemoral cerebral angiography demonstrating a contrast filling defect in the left transverse sinus, consistent with thrombosis.*

described here, therefore, reflects cumulative end-organ morbidity rather than an incidental event, consistent with systematic reviews implicating cardioembolic mechanisms, haemodynamic instability, and disease-associated coagulopathy across the wider congenital heart disease population[6].

This case also underscores that social and health-system factors can be as pathogenetically relevant as cardiac anatomy itself. Parental underestimation of disease severity, discontinuity of cardiology follow-up, and the absence of definitive repair together perpetuated recurrent hypercyanotic spells and cumulative hypoxaemic burden, ultimately heightening the risk of neurological and infectious complications.

Clinically, profound desaturation (initial SpO^2 approximately 40%), central and peripheral cyanosis, tachypnoea with retractions, and partial response to supplemental oxygen were consistent with a hypercyanotic spell. Right ventricular outflow tract obstruction in TOF is not purely fixed; dynamic infundibular spasm can acutely worsen obstruction, reduce pulmonary blood flow, increase right-to-left shunting, and precipitate rapid systemic hypoxaemia[7]. Typical triggers include sympathetic stimulation (agitation, crying, pain), while hypovolaemic states, such as vomiting or diarrhoea, can also provoke spells by reducing preload and altering the systemic-to-pulmonary vascular resistance ratio[8]. In this patient, vomiting should therefore be regarded not as an incidental symptom but as a physiologically relevant precipitant of systemic and cerebral hypoperfusion; headache in this setting may reflect hypoxaemia, hyperviscosity, raised intracranial pressure from venous sinus thrombosis, or early intracranial infection, and warrants parallel vascular and infectious evaluation[6,9].

Echocardiography confirmed severe TOF physiology—significant infundibular stenosis with a high pressure gradient, a large perimembranous ventricular septal defect, aortic override, and right-heart dilation—reflecting chronic right ventricular pressure overload and a predisposition to recurrent spells. Pulmonary artery size, expressed through the Nakata index and McGoon ratio, is a key determinant of surgical suitability; total repair is generally feasible above a McGoon ratio of 1.2 and a Nakata index of 150 mm^2/m^2, with a ratio near 2 considered normal and values below 0.8 inadequate for complete repair[3]. With a McGoon ratio of 2.3, this patient's pulmonary vasculature was anatomically adequate for total correction, making the prolonged delay to intervention a critical concern given that primary repair at 3-6 months of age is now performed safely in most centres with favourable outcomes[3,4].

A haemoglobin of 19.6 g/dl and haematocrit of 66.7% indicated marked secondary erythrocytosis, predisposing to hyperviscosity, impaired microcirculatory flow, and thrombogenesis; contemporary management prioritises hydration and iron-status optimisation, reserving therapeutic phlebotomy for refractory hyperviscosity symptoms[8]. The markedly elevated D-dimer level was consistent with active thrombosis and secondary fibrinolysis, though this marker cannot replace neuroimaging in confirming cerebral venous sinus thrombosis[8]. MRI/MRA demonstrated a hyperacute infarction in the left temporo-parieto-occipital cortical borderzone together with thrombosis of the left transverse and sigmoid sinuses extending to the proximal internal jugular vein, later confirmed on transfemoral cerebral angiography.

The most coherent explanation for this presentation is a dual cerebrovascular phenotype arising within a single spell-triggered episode. Acute dynamic right ventricular outflow tract obstruction reduces pulmonary blood flow and increases right-to-left shunting, producing systemic hypoxaemia and metabolic acidosis that further exacerbate shunting and reduce cerebral oxygen delivery ; watershed

territories are especially vulnerable during systemic hypoperfusion owing to their intrinsically lower perfusion pressure, and the coexistence of a hypovolaemic trigger with a borderzone infarct pattern supports a predominantly haemodynamic, rather than embolic, mechanism[3]. Chronic hypoxaemia, in turn, primes the system through erythrocytosis and hyperviscosity, which slow flow, impair microvascular perfusion, and promote endothelial dysfunction and activation of haemostatic pathways[9,10]. The resulting cerebral venous sinus thrombosis fits within Virchow's triad of stasis, hypercoagulability, and endothelial injury, further exacerbated by dehydration and acute hypoxaemia; arterial hypoperfusion and venous congestion may then interact bidirectionally to amplify tissue injury, as arterial insufficiency predisposes to watershed ischaemia while venous thrombosis raises back-pressure and further impairs perfusion gradients[8]. Although no radiologically confirmed brain abscess was documented, unrepaired cyanotic congenital heart disease predisposes to intracranial infection because right-to-left shunting bypasses the pulmonary capillary filter, allowing septic microemboli to reach the cerebral circulation[8,9].

Initial management of recurrent spells focuses on interrupting the hypercyanotic cycle: high-flow oxygen, knee-to-chest positioning, sedation to reduce sympathetic drive, volume resuscitation in hypovolaemia, and measures to increase systemic vascular resistance all help restore systemic perfusion by reducing right-to-left shunting[9]. In patients with significant erythrocytosis, maintaining hydration and iron status is essential for both thrombosis prevention and reduction of spell recurrence[4], and adolescents with unrepaired TOF and cerebrovascular complications should undergo expedited evaluation for definitive surgical correction to mitigate long-term neurological sequelae[5]. Propranolol reduces infundibular spasm and stabilises right ventricular outflow tract dynamics[3]. Confirmed cerebral venous sinus thrombosis generally warrants therapeutic anticoagulation with heparin (unfractionated or low-molecular-weight) as first-line acute therapy, even in selected cases with intracranial haemorrhage, under individualised assessment[9]; the enoxaparin regimen used here represented appropriate acute-phase therapy, though continued anticoagulation with clinical and radiological monitoring is typically required to guide duration and recurrence risk[8,9]. Low-dose aspirin may be rationalised as secondary prevention of arterial ischaemic stroke given the clinically dominant watershed infarct, with aetiological stratification guiding the choice between antiplatelet and anticoagulant therapy where CVST coexists[10]. Empirical ceftriaxone and metronidazole are reasonable when brain abscess is suspected, but prolonged prophylactic antibiotics in the absence of confirmed infection should be individualised and reassessed with close follow-up and repeat neuroimaging[9].

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