

## Case Report

# A patient with cerebral venous thrombosis associated with severe anaemia – a case report

M Hasitha Madusanka Dilruk, Michael Jansz

Lady Ridgeway Hospital, Colombo, Sri Lanka

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Corresponding Author M Hasitha Madusanka Dilruk, E-mail: <m31998@pgim.cmb.ac.lk>  <https://orcid.org/0000-0003-2840-9724>

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## Introduction

Cerebral venous thrombosis (CVT) is a rare form of stroke, particularly in paediatrics. Young females (median age 38) are the most commonly affected population (70%). CVT is a result of clot formation within a major cerebral vein. These veins include dural sinuses, cortical veins, vein of Galen and jugular veins [1]. Cases of CVT have a good prognosis with anticoagulation. However, there is a mortality of 5% [2] and some patients may have residual neurological weakness [3].

## Case presentation

A13-year-old girl was brought by her parents to the preliminary care unit (PCU) complaining of drowsiness since midnight. She had complained of weakness of her lower limbs with a limp and headache for 2 days. Her mother had noticed abnormal jerky movements of the left side of her body along with rolling up of the eyes for a few seconds while she was in bed, after which she had been drowsy and unresponsive to commands. A few minutes after the event she had had urinary incontinence. Due to persistent unresponsiveness, the parents had decided to seek medical care nearly nine hours after the acute event.

She had attained menarche at the age of 12 years and since then she has had regular menstrual cycles with menstruation lasting for nearly one week. Her mother was unable to detail the volume of bleeding. There was no history of poisoning or snake bite. She was not on any regular medications (including contraceptive pills). There was no history of recurrent headaches, bleeding diathesis, strokes or seizures. She had been active and well till her recent symptoms. Her growth and development were age appropriate. Birth history and neonatal period had been uneventful. She did not have fever, earache or ear discharge recently. There was no surgery done in the past. No contact history of COVID-19 was found.

On admission, she was not responding to verbal commands. Her Glasgow coma scale (GCS) was 7/15 (E2, V1, M4). Her airway was patent; breathing spontaneously; chest expansion normal; breath sounds equal with no added lung sounds.; respiratory rate of 30; no recessions; SpO<sub>2</sub> 98% on room air; pulse rate of regular 88 bpm; good pulse volume; capillary refilling time of 1 second; blood pressure 116/80 mmHg (between 50th and 90th

centiles); no radio femoral delays; no cardiac murmurs. There was no dehydration, rashes or evidence of trauma. Her capillary blood sugar was 98 mg/dl and she was normothermic. Abdomen was soft while liver and spleen were not palpable. Lower limbs were not oedematous and did not show evidence of thrombophlebitis. There were no external features suggestive of congenital syndromes.

She was restless, intermittently, and had 4/5 muscle power of all four limbs with normal muscle tone (accurate assessment could not be done due to altered consciousness). Her deep tendon and superficial reflexes were normal including a downward Babinski sign. There was no neck stiffness and Kernig's sign was negative. Gaze palsy and nystagmus could not be elicited. Optic fundi assessment was not done as it was considered an unnecessarily risky procedure during the COVID-19 pandemic.

An intravenous cannula was inserted to the right proximal arm and blood was taken for venous blood gas (VBG) which showed, a pH of 7.47, pCO<sub>2</sub> 28.3 mmHg, HCO<sub>3</sub><sup>-</sup> 20.9 mmol/L, BE -2.9 lactate 1.5 mmol/L, which was consistent with respiratory alkalosis with metabolic compensation. Blood for full blood count (FBC), serum electrolytes, blood culture and coagulation profile were also taken at this time. As the patient's GCS was 7 and there was concern over the patency of airway it was decided that she should be intubated. Rapid sequence induction using intravenous midazolam 4 mg and suxamethonium 100 mg was followed by successful intubation. Intravenous cefotaxime 2.5g and intravenous acyclovir 500mg was administered followed by intravenous maintenance fluids.

After securing the airway, investigations were traced. FBC revealed a severe hypochromic microcytic anaemia with a neutrophil leucocytosis and thrombocytosis. Hb 6.3 g/dL, HCT 23.3%, MCV 53.1 fL, WBC 14,850/mm<sup>3</sup>, neutrophils 85%, platelet 625x10<sup>3</sup>/mm<sup>3</sup>. The other blood investigations were normal.

As this patient presented with unexplained reduced level of consciousness an urgent non-contrast CT brain was arranged. The CT revealed hyper-density in bilateral spatial veins, bilateral cerebral veins, vein of Galen, right basal vein of Rosenthal and straight sinus. There was associated subtle hypo-density in bilateral thalami indicative of venous sinus thrombosis with possible venous infarcts of bilateral thalami. The rest of the venous sinuses were normal. There was no haemorrhage, space occupying lesion or midline shift. Ventricular system and extra axial cerebrospinal fluid (CSF) spaces were normal (Figure 1).

After the initial investigations, including imaging, a tentative diagnosis of cerebral venous sinus thrombosis with thalami venous infarct was made.

Urgent haematology referral was done and subcutaneous enoxaparin (low molecular weight heparin) 1mg/kg twice daily was started. Following initial management, the patient was transferred to the intensive care unit. Within two days of treatment there was clinical improvement including increased conscious level. Further management was carried out by the paediatric and haematology team.

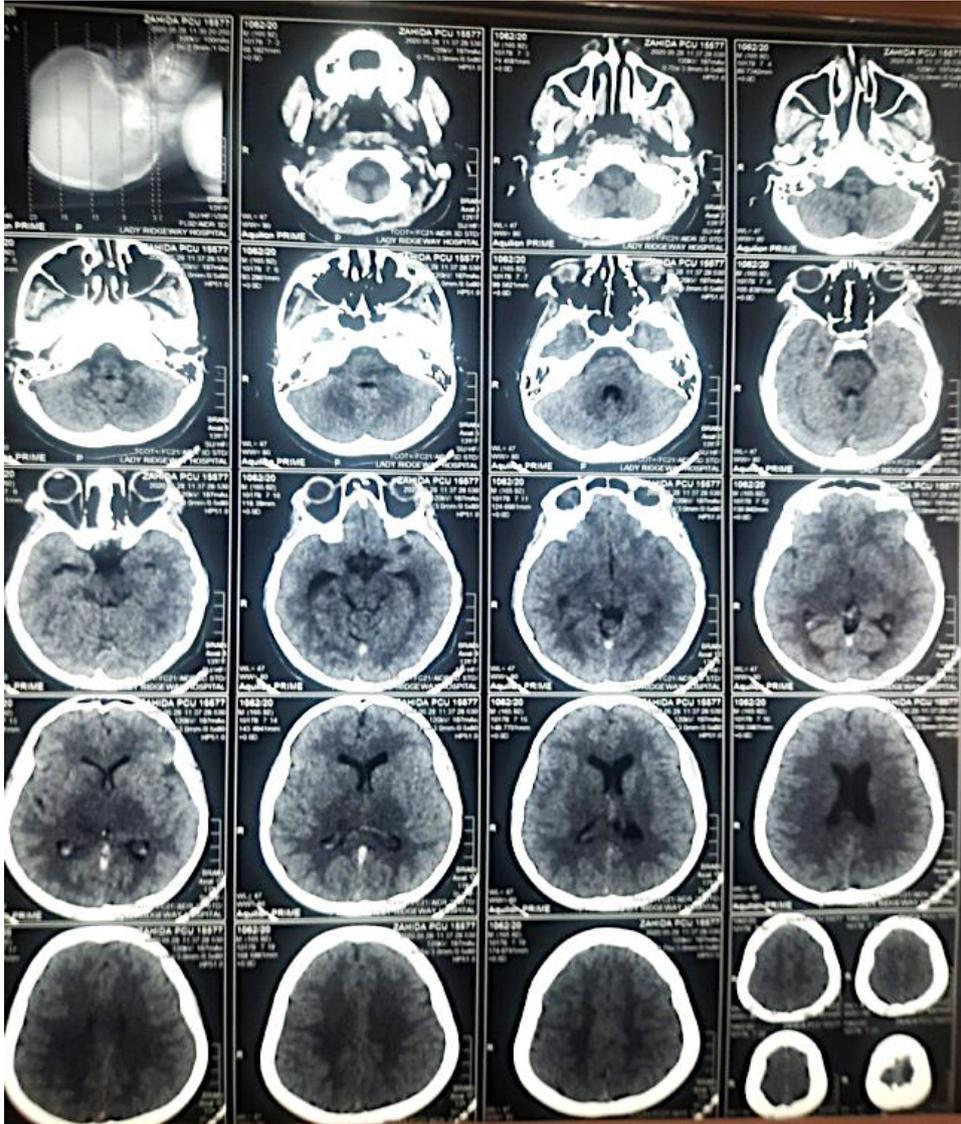


Figure 1: non-contrast CT brain

## Discussion

The patient's symptoms favoured a diagnosis of an intra cranial pathology due to the presence of headache followed by limb weakness and unconsciousness. Headache is the most common clinical feature of CVT (in 90% of cases) [3]. Headache has been classified by the International Headache Society into primary headache, secondary headache (secondary to an identifiable cause) and painful cranial neuropathies, facial pain and other headaches [4].

Since she had "reg flags" of headache (Table 1) including a focal neurological and altered conscious state, further evaluation with imaging was required. Management algorithm of headaches in the emergency department is shown in Figure 2.

**Table 1: Red flags or warning signs in children with headache** (Raucci et al. [4])

- Changes in mood or personality over days or weeks
- Severe vomiting, especially early morning
- Worsening of pain with cough or Valsalva manoeuvre
- Altered conscious state
- Papilloedema
- Focal neurologic deficit or meningismus
- Seizures or fever
- High-risk population (patients with sickle cell anaemia., malignancy, recent head trauma, ventricular-peritoneal shunt, others)
- Pain that wakes the child from sleep or occurs on waking
- Change of the character of headache in patients diagnosed with primary headache
- Poor general condition
- Increased head circumference
- Cranial nerve palsies
- Abnormal ocular movements, squint, pathologic pupillary responses
- Visual field defects
- Ataxia, gait abnormalities, impaired coordination
- Sudden onset of headache (first or worst ever)
- Increase in severity or characteristics of the headache
- Occipital headache
- Age < 5 years

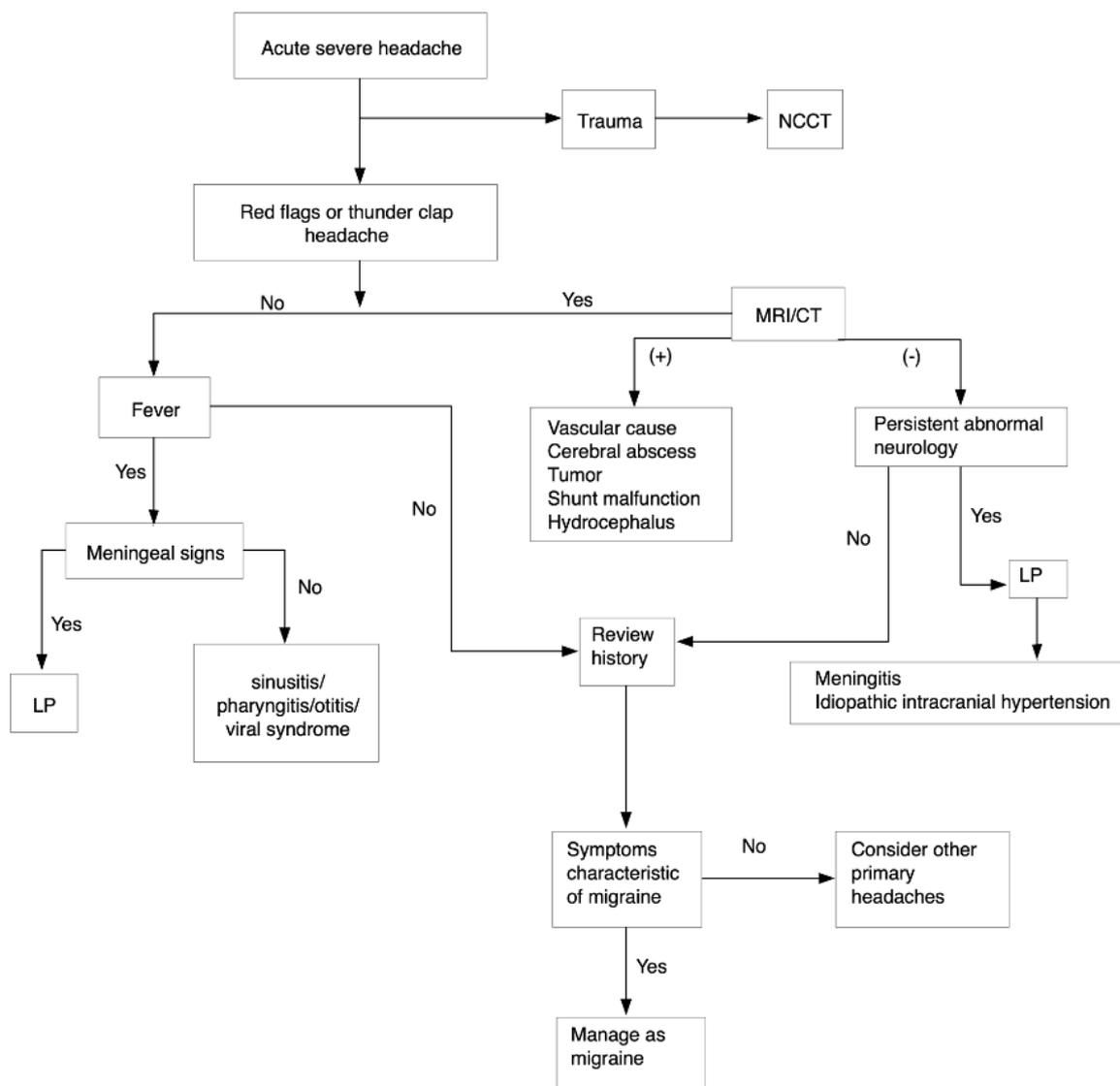


Figure 2: Management algorithm of headache in emergency department (Raucci et al. [4])

LP: lumbar puncture, NCCT: non-contrast CT

### Pathophysiology

CVT occurs in the cerebral veins and dural sinuses. The superior sagittal sinus is the most commonly affected sinus (62%) [2]. Virchow's triad, i.e. stasis of blood flow, hypercoagulability and endothelial injury are the risk factors for the development CVT [5]. Anaemia causes thrombosis by several mechanisms. Hypoxia, caused by anaemia, alters gene expression which enhances adherence between erythrocytes and the endothelium. Iron deficiency anaemia, itself, reduces inhibition of thrombopoiesis and may cause reactive thrombocytosis. Anaemia due to sickle cell disease is a prothrombotic state due to altered cell morphology causing increased viscosity, haemolysis causing enhanced platelet activation and aggregation [6,7].

Venous pressure rises due to the thrombosis. Subsequently, CSF absorption is reduced, leading to a rise in intra cranial pressure (ICP). Rise in venular and capillary pressure also occurs due to venous obstruction. It causes disruption of the blood brain barrier leading to vasogenic oedema; reduction of capillary perfusion leading to ischaemic injury; and venous and capillary rupture leading to parenchymal haemorrhage [8,9]. The most common cause of death is high ICP leading to trans-tentorial herniation [3].

### Clinical features

Symptoms and signs vary according to the site of thrombosis. Patients with thrombosis of cortical veins present with motor and sensory deficits or seizures; thrombosis of the sagittal sinus presents with bilateral lower motor deficit or seizure; thrombosis of the lateral sinus presents with intracranial hypertension and headache; thrombosis of the left transverse sinus presents with aphasia; thrombosis of the deep venous sinus presents with behavioural changes due to involvement of the thalamus; cavernous sinus thrombosis presents with ocular pain, chemosis, proptosis and ocular palsies [10,11]. This patient had thrombosis of the deep cerebral veins causing thalamus infarcts which explains the presence of unresponsiveness. In addition, there was thrombosis of the left straight sinus and basal vein of Rosenthal which explains the limb weakness with limp and the left focal seizure.

### Imaging in suspected cerebral venous thrombosis

Non-contrast CT would be the initial imaging modality in clinical practice in a patient with acute life-threatening neurological complaints. The classic feature in CVT is a hyperdense region in the venous sinus but it is present only in one third of cases. Posterior aspect of the superior sagittal sinus appears as a hyperdense triangle called "filled delta sign". Indirect signs of CVT are diffuse cerebral oedema (occurs in 50% of cases), more specifically venous oedema, or intra cranial haemorrhage. Venous infarcts are hypodense areas that involve more than one arterial territory or subcortical region sparing the cortex. Thrombosed cortical veins may rarely be visualised as cord-like linear hyper densities called the "cord sign". If CVT is detected in initial imaging, it should be confirmed with either a CT venogram or MRI with MR venogram which is the gold standard imaging for CVT. Both CT venogram and contrast-enhanced CT (CECT) will show direct and indirect signs. The most common direct sign is a filling defect of the dural sinus called "empty delta sign". However, 30% of CECT will be falsely negative. Therefore, it is not recommended as an imaging modality for CVT. Ultrasound scan may be used in neonates with an open fontanelle [2,5].

Only the initial non-contrast CT was used in this patient to diagnose CVT due to the highly suspicious clinical presentation and with consideration of radiation exposure.

### Treatment

Treatment is anticoagulation in order to prevent propagation of the thrombus and to prevent complications. Both the American Heart Association and the European Federation of Neurological Societies guidelines recommend anticoagulation even in the presence of haemorrhage. Two small randomised clinical trials (RCT) have shown better clinical outcomes, without increased incidence of haemorrhage, in the anticoagulated group. The current recommendation is to start immediate therapeutic low-molecular weight heparin (LMWH) or unfractionated heparin (UH). However, a single RCT showed a significantly lower mortality rate in the group that received LMWH than in the group that received UH. In the meantime, reversible risk factors should be eliminated immediately. Measures should be

taken to reduce ICP. If anticoagulation is contraindicated or if CVT is refractory to anticoagulation, endovascular thrombolysis or mechanical thrombectomy are the next available therapeutic options. Steroids are not recommended unless there is meningitis. Antiepileptics are indicated only if there is a seizure. Vitamin K antagonists (warfarin) should be initiated targeting an INR between 2-3 and it should be continued for 3-6 months in provoked CVT, 6-12 months in unprovoked CVT and lifelong if recurrent or complicated CVT. Direct oral anticoagulants are not recommended as the first line in CVT [2,3].

## Conclusion

Although headache is a common ED presentation, it needs to be further evaluated in a patient with red flag features in order to identify or exclude severe pathology. Cerebral venous thrombosis is a rare cause for headache with neurological deficit but is treatable, with good prognosis, in most cases. Although initial imaging with non-contrast CT may show thrombus and indirect signs of thrombosis, false negative results are common. Further assessment is required if there is a suspicion. The provoking factor, such as anaemia, dehydration and other prothrombotic states, should be identified and eliminated. Immediate treatment is anticoagulation along with supportive care.

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