Catastrophic cerebral sinovenous thrombosis with haemorrhagic conversion in a new diagnosis of paediatric acute myelogenous leukaemia

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DESCRIPTION

A previously healthy 14-month-old boy with 5 days of cough, rhinorrhea, diarrhoea and fever to 38.9°C was admitted to an outside hospital with altered mental status, intermittent bradycardia and hypertension, but otherwise a normal physical examination. A complete blood count (CBC) revealed leucocytosis (33 k/ μ L), anaemia (10.4 g/dL), thrombocytopenia (48 k/ μ L) and peripheral blasts; flow cytometry showed an aberrant blast population positive for CD4, CD11b, CD11c, CD15, CD33, CD38, CD45, CD56, CD123, negative for TdT and cMPO, and cancer cytogenetics revealed KMT2A (MLL)-MLLT3 t(9;11)(p22;q23), consistent with acute myelogenous leukaemia (AML) with monocytic features (FAB M5). Coagulation studies revealed disseminated intravascular coagulopathy (DIC) with elevated international normalized ratio (INR) (1.6), decreased fibrinogen (107 mg/dL) and elevated D-dimer (7 286 ng/mL (normal <255 ng/mL); International Society of Thrombosis and Hemostasis DIC Score was 5. MRI of the brain demonstrated a bilateral thalamic mass lesion, with blood degradation products and restricted diffusion, extending to the left midbrain measuring 6 cm $\times$ 4 cm $\times$ 4 cm (figure 1).

Eighteen hours into his admission, he was transferred to our institution intubated, sedated and critically ill. On physical examination, there was no evidence of petechiae or bruising. However, he did have new anisocoria and sluggish pupillary reactivity with decorticate posturing, thus medical interventions for elevated intracranial pressure were initiated. Repeat CBC demonstrated leucocytosis (56 k/ μ L) and absolute blast count of 15.7 k/ μ L.

Interpretation of the outside MRI of the brain favoured bilateral thalamic haemorrhagic venous infarcts; follow-up CT of the head demonstrated extensive haemorrhagic infarcts in bilateral thalami and basal ganglia, growth of acute intraparenchymal haematoma with intraventricular extension and severe ventriculomegaly. CT venography confirmed extensive deep venous sinus thrombosis. The patient was taken emergently to the operating room by neurosurgery for bilateral frontal ventriculostomies. Despite surgical decompression, vasopressor support, rapid anticoagulation and chemotherapy administration, he succumbed to refractory intracranial hypertension several hours after the procedure. The family compassionately withdrew care the following day.

In patients with acute leukaemia and altered mental status, thrombotic or coagulopathic complications are associated with high mortality and require high suspicion in diagnosis to ensure timely management. The hypercoagulable state in acute leukaemia is attributed to a complex interaction of prothrombotic factors and cancer procoagulant produced by leukaemic cells, inflammatory cytokines, central venous catheter placement, chemotherapy and comorbid thrombophilia.¹ While haemorrhage is the most common manifestation of DIC in patients with paediatric cancer, thrombotic events (TEs) occur less frequently with varied incidence of 1.2%–16% and over half manifesting as central nervous system thrombosis.^{2–4} Patients with AML are three times more likely to have TE at the time of diagnosis compared with patients with acute lymphoblastic leukaemia, who are more likely to develop thrombosis during treatment.³ Although coagulopathy is classically associated with acute promyelocytic leukaemia (APML) (FAB M3), DIC is seen in one-third of non-APML subtypes such as M5 AML in our patient.⁵ Transfusion of platelets and fresh frozen plasma are the most frequently reported supportive measures, as well as anticoagulation when thrombosis is present.⁴

Cerebral sinovenous thrombosis (CSVT) is the most common type of central nervous system TE and most frequently diagnosed at presentation or early in therapy.^{2,6} Therapeutic anticoagulation is recommended by international guidelines in adults with CSVT with haemorrhagic transformation.⁷ Anticoagulation in paediatric CSVT with haemorrhagic conversion has shown reduction in mortality and improvement in long-term morbidity, although institutional practices may vary.⁸

Figure 1 MRI, brain. Axial T2-weighted image demonstrates a bilateral thalamic heterogeneous lesion, with abnormal increased T2 signal representing oedema. Sagittal T1-weighted postgadolinium image demonstrates a filling defect, representing thrombosis, along the straight sinus and confluence of sinuses.

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Learning points

- Diagnosis of thrombotic events (TEs) require a high degree of suspicion.
- Cerebral sinovenous thrombosis (CSVT) is the most common central nervous system TE in acute myelogenous leukaemia (AML).
- TEs occur more frequently at time of diagnosis in AML compared with ALL.

Contributors CNN and ACW conceptualised the report, and planned the data and information needed to emphasise the learning points. CNN performed data collection, performed literature and chart review, wrote the initial draft, assisted in interpretation of data, and assisted in editing. FR-R assisted in report conceptualisation, interpreted the diagnostic imaging, determined and selected the most impactful MR images, edited and formatted the images, provided interpretation of imaging in the report, and assisted in editing. ACW assisted in literature and chart review, assisted in interpretation of data, edited the manuscript, and oversaw conduct of the report.

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