Unmet Need in Diagnosis of Iron Deficiency anemia: a case scenario

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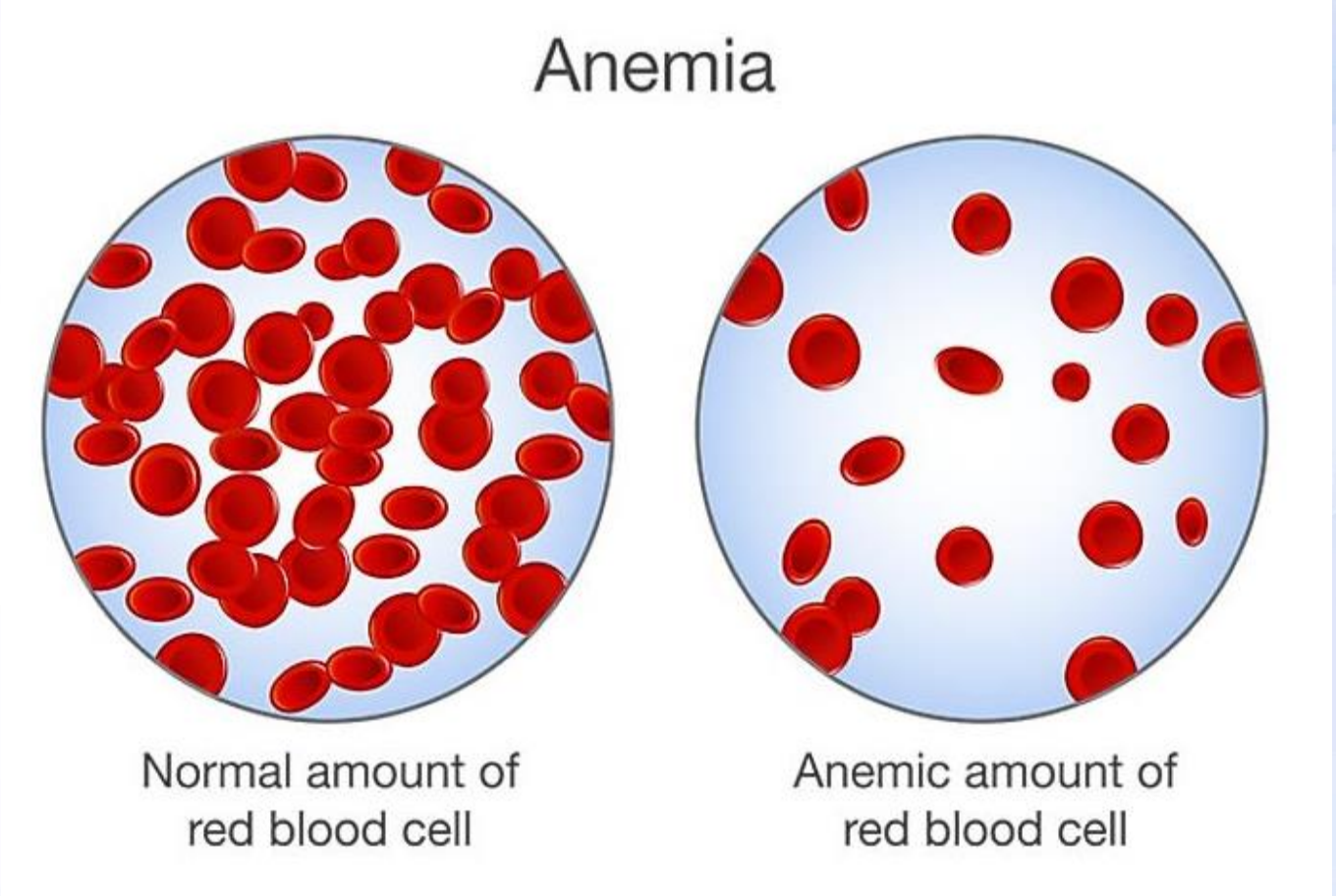
Fars Pediatric Association

Disclosure

- ✓ I have nothing to disclose for this conference
- ✓ But my commitment to patients:
  - ✓ Treatment for all
  - ✓ Support patients
  - ✓ Access to treatment for poor people



- Background
- Case study
- Take home message
- Discussion: How to diagnose and manage iron deficiency anemia (IDA)

Learning Objective

- We will learn how to diagnose iron deficiency anemia based on a case scenario
- We will discuss current evidence on the association of iron deficiency anemia and thrombosis
- We will learn to increase the awareness of iron deficiency as a risk factor for thrombosis in the pediatric population

Background

- Iron deficiency is the most common micronutrient deficiency worldwide and one main cause of anemia, affecting one third of the world population

- Iron deficiency anemia (IDA) is a prevalent condition among infant and children, affects ~40% of children under 5 years of age often leading to severe health complications

- Anemia, and specifically IDA, has long been implicated as a risk factor for arterial and venous thrombosis

Case study:

- History
  - A 2-year-old boy presented with complaints of excruciating headaches for 5 days and an episode of vomiting the day before admission
  - He had no signs of upper respiratory tract infection or a history of head trauma
  - The mother stated that the baby had the daily consumption of cow's milk ranged from five to seven full cups per day.
  - No iron supplement given during infancy while he was on breast-fed
- Physical Exam
  - He was quite pale but clinically stable, No fever, an awake, alert, interactive toddler
  - Pale conjunctiva, no yellow sclera, no hepatosplenomegaly, no lymphadenopathy
  - Neurological examination was normal, with no cranial nerve or focal neurological deficits
  - No clinical signs of increased intracranial pressure detected.

What is the best next approach?

1-CBC

2-Brain MRI/CT scan

3-EEG

4-Endoscopy

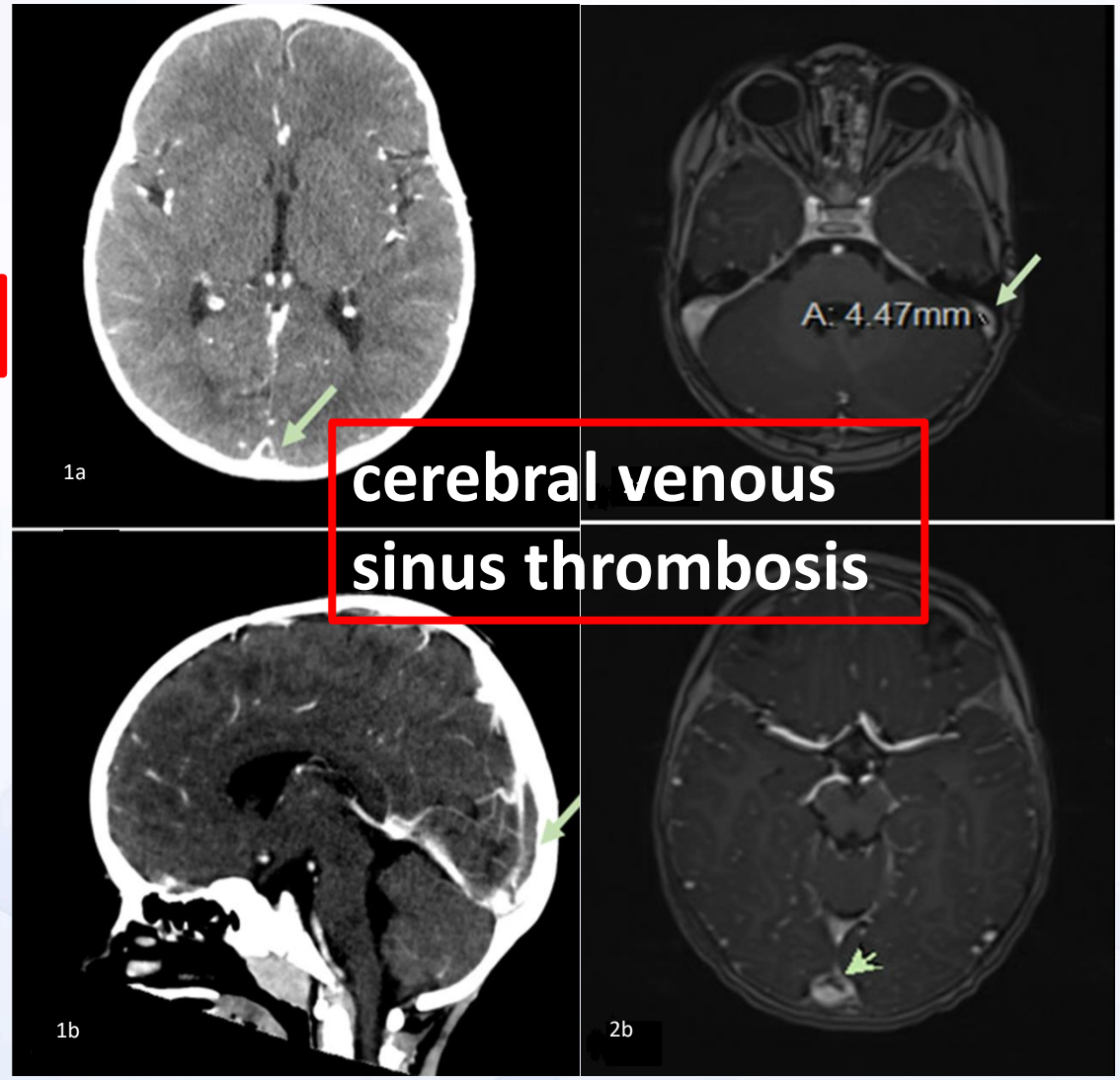


Fig. 1: CT scan of the brain without and with IV contrast
1a Contrast-enhanced CT scan demonstrates empty delta sign indicating thrombosis of the SSS, where contrast outlines a triangular filling defect this represents thrombus (Arrow).
1b Sagittal view for the same patient demonstrates sagittal extent of the thrombus (Arrow)

Fig.2: MRI examination of the brain
2a Corresponding to the CT finding, there is a residual thrombus measuring 4.47mm demonstrated in SSS (Arrow).
2b Demonstrates a small residual thrombus seen in the upper part of the left sigmoid sinus (Arrow).

What another laboratory test is recommended before MRI under general anesthesia?

1-Coombs test and CRP

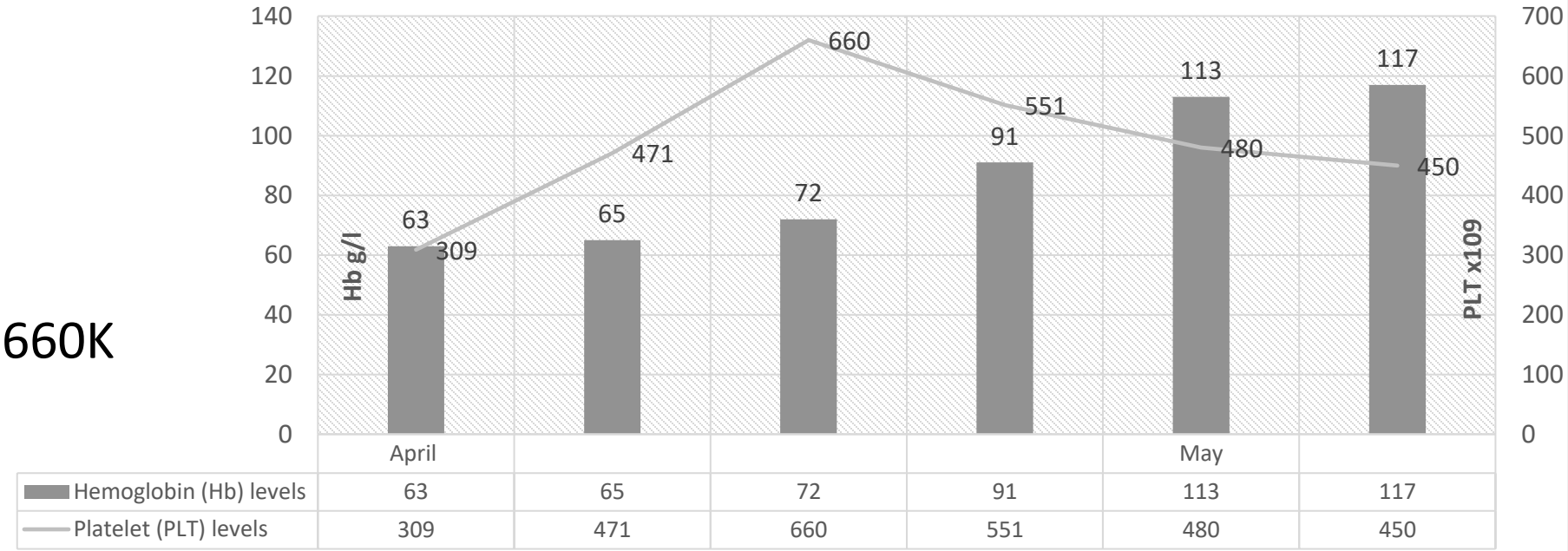
2-Bone marrow aspiration

3-CBC and reticulocyte count → Pre MRI scan CBC was done as per routine work up

4-Iron/TIBC, Ferritin

Investigations: CBC

- Hb: 6.3 gr/dl
- MCV: 50
- MCH: 12
- RBC count: 2.1 million
- RDW: 26.7
- Platelet count: 309K ➡ 660K
- WBC: 5000



Hemoglobin (Hb) levels	63	65	72	91	113	117
Platelet (PLT) levels	309	471	660	551	480	450

Fig. Trends of hemoglobin and platelets during his admission and follow-up.

What other blood test is suggested to confirm the diagnosis?

1-Iron/TIBC and ferritin

Fe: 2.3 umol/L
TIBC: 71.5
Ferritin: 6.7 ng/ml

2-Hemoglobin electrophoresis

3-Urine copper

4-Blood lead levels

What Kind of treatment is recommended?

1-Blood transfusion and Enoxaparin ➡ Blood transfusion may be given if a patient has active bleeds or has chest pain/shortness of breath and recent observational study of 125 children aged 6-36 months, a Hb of **3.9 gr/dl** had sensitivity 92% and specificity 72% for transfusion (Dou Lin Rose Sun et al. J Pediatr. 2024 March)

2-IV Iron infusion and Enoxaparin ➡ IV iron infusion is indicated once patients have IBD, intolerance to oral iron with Hb less than 10 gr/dl

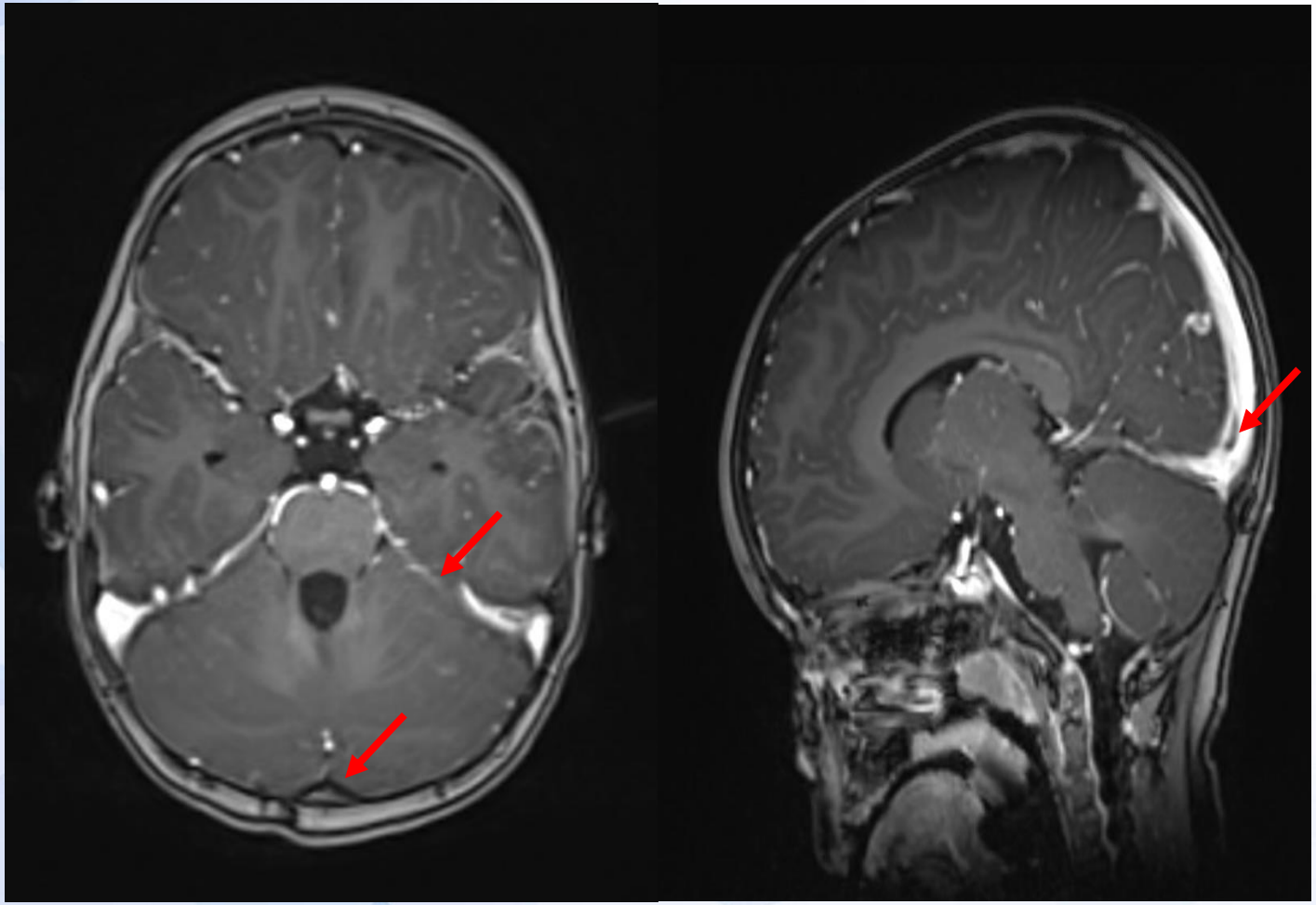
3-Oral iron intake and warfarin

4-Folic acid supplement and warfarin

Follow-up: cerebral venous sinus thrombosis secondary to severe iron-deficiency anemia

- The patient underwent IV iron infusion followed by oral iron intake along with enoxaparin for three months
- Blood work was improving gradually
  - Exhibits Hemoglobin levels improvement after correction of his iron deficiency,
  - An obvious improvement in his hemoglobin levels after IV iron infusion is noted
  - Simultaneously, platelets levels were gradually decreasing
- Other values yield insignificant including celiac serology calprotectin, Gastrointestinal PCR panel, and liver function tests all were satisfactory, and stool occult blood was negative
- Ultrasound of the abdomen was unremarkable; no evidence of hepatosplenomegaly, particularly no superadded mass identified.

Follow-up brain MRI and blood work: 3 months S/P CVST



- There is further resolution of previously shown cerebral venous sinus thrombosis of the superior sagittal sinus and left-sides transverse with a small residual thrombosis seen
- There is complete resolution of previously shown residual thrombosis in the superior aspect of the left internal jugular vein and superior aspect of the left sigmoid sinus

- Hb: 11.7 gr/dl
- MCV: 75
- MCH: 25
- RBC count: 4.8 million
- RDW: 12.1
- Platelet count: 399000

Ferritin: 13
Iron: 16.7
TIBC: 66

Diagnostic Approach

1

History:

History of excessive milk intake
Symptoms of altered mental status
Papilledema, headaches and seizure

2

Neuroimaging:

Brain CT and MRI are essential for the diagnosis. Doppler ultrasound has been used in neonates with open fontanels for the diagnosis of CVST; however, it requires a skilled radiographer to localize thrombosis within the SSS

3

Thrombophilia Screening

Comprehensive thrombophilia screening tests are crucial including Protein C, S, Antithrombin III, Homocysteine, Factor V Leiden, and Factor II prothrombin mutation

Ideal treatment for CVST Secondary to IDA

Low-molecular-weight heparin

Timely initiation of anticoagulant therapy, such as low-molecular-weight heparin (LMWH): Enoxaparin:1 mg/kg/dose/sc twice daily for 3 months and extended therapy in case of a continuing increased thrombosis risk profile

Iron supplementation

Intravenous iron infusion is recommended over oral supplementation in severe iron deficiency anemia to prevent prevent the risk of thrombosis in in small pediatric patients followed followed by oral iron supplement (3 supplement (3 mg/kg/day)

Follow-Up Care

Regular monitoring within 3 months
The combination of MRI and magnetic resonance venography (MRV) is crucial for precise localization of thrombi in pediatric patients with CVST.

Discussion: CVST Secondary to IDA

1 Prevalence

Cerebral venous sinus thrombosis secondary to iron deficiency anemia is a rare occurrence in the pediatric population, with limited reported cases.

2 Challenges

Establishing a definitive causal relationship between IDA and CVST remains a challenge →

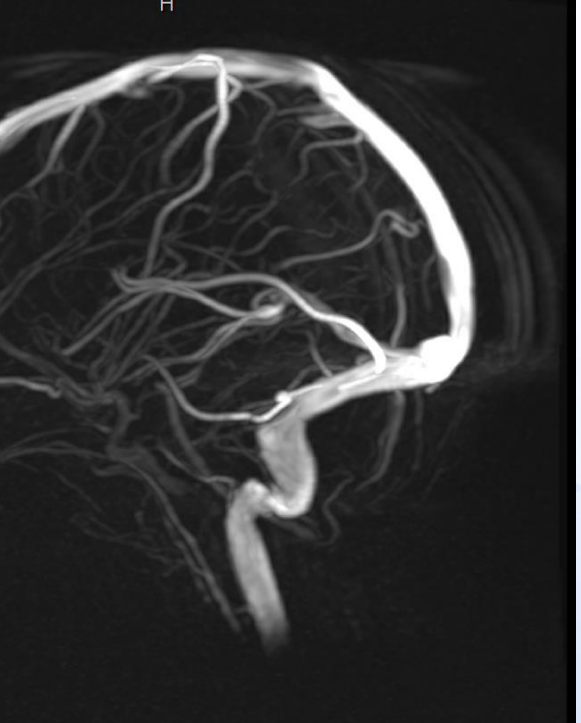
1-Microcytosis decreases the cell deformability and increase the viscosity, causing abnormal (turbulence) flow patterns and predispose to venous thrombosis
2-Serum iron is an important regulator of thrombopoiesis. Normal iron levels are required to prevent thrombocytosis by acting as an inhibitor

3 Prognosis:

Cerebro-vascular diseases are one of the top 10 causes of mortality and morbidity in children
Early interventions and targeted treatment are associated with favorable clinical outcomes

4 Research:

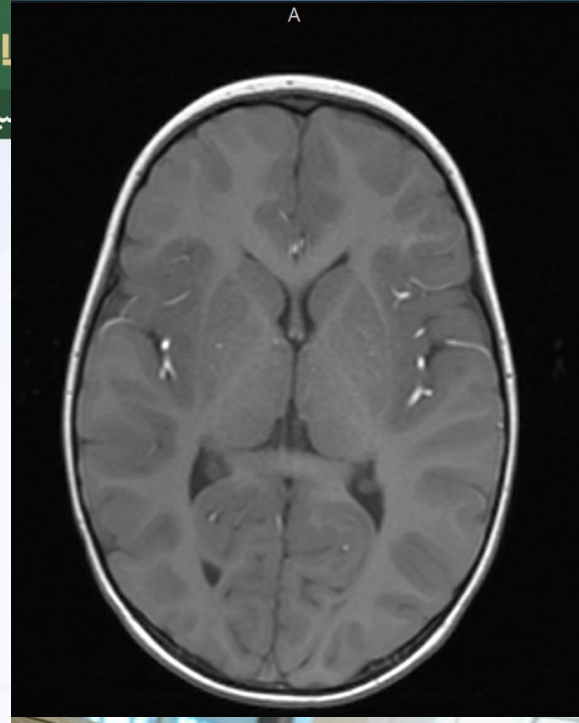
Further research is crucial to understand the frequency and underlying mechanisms of CVST secondary to iron deficiency anemia in pediatric patients.



Take home message:
Anemia is often considered to be a risk factor for cerebral venous thrombosis

- After 6 months a repeated MRI brain venogram without contrast, showed complete resolution of the thrombus.

- **Thanks for your Attention**



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