Strokes in Childhood Sickle Cell Disease - case discussions

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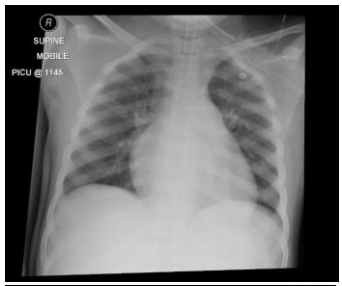
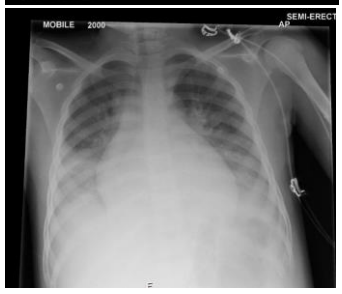
Case 1 AA 12y/o Female- HbSS

- Admitted to local hospital with Acute Chest Syndrome- transfused. Readmitted 2 days later with further pain and anaemia- more transfusion given
- Reacted to second transfusion- intravascular haemolysis and hyperkalaemia
- Ventilated and transferred to PICU- renal failure (on haemodialysis to reduce K+ levels
- High pyrexia, high CRP, bilateral basal consolidation on CXR- broad spectrum antibiotics

Day 1 of admission to PICU



Day 5 of admission to PICU



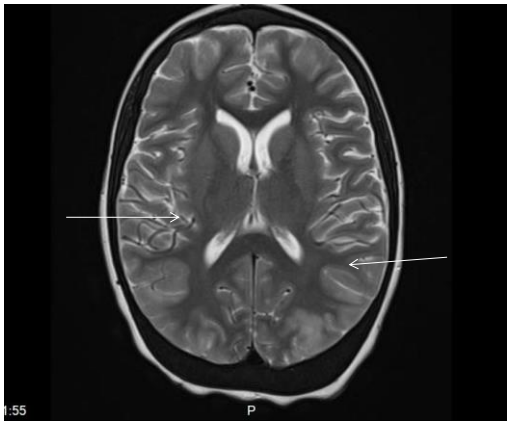
Case 1 AA continued

- Discharged to the wards on D14 (4 days of ventilation, renal support needed for 4 days).
- Anaemia corrected with methylprednisolone cover twice, but no further haemolysis, hence further transfusions given without any steroid cover
- Day 2 of transfer to general wards- transient visual loss and seizures associated with hypertension- , levetiracetam loading.

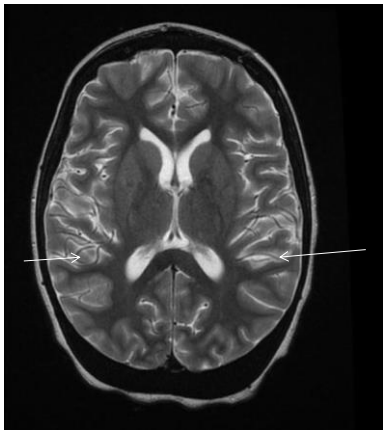
Case 1 Clinical progress

- Marked cognitive impairment, including confusion and delirium
- Further seizures- phenytoin + levetiracetam
- Treated for presumed infective encephalopathy
- CSF examination: no evidence of bacterial or viral sepsis or autoantibody associated neurological syndromes

Case 1 MRI/MRA scan



Day 2 after first neurological symptoms



Day 14 after first neurological symptoms

T2-weighted imaging shows cortical hyperintensity- features suggestive of atypical PRES- No vasculopathy associated with SCD

Case 1 Clinical progress

- Slow but definite radiological improvement
- Slow but steady clinical progress with intensive Speech and Language therapy, but continued to demonstrate significant receptive and expressive dysphasia
- Final diagnosis: Atypical PRES due to severe sickle – related symptoms- ACS, acute intravascular haemolysis and severe anaemia. Note steroid use.
- Hydroxycarbamide initiated prior to discharge
- Not on transfusion programme due to severe reaction
- No red cell allo antibody- cause of severe haemolysis at presentation not clear

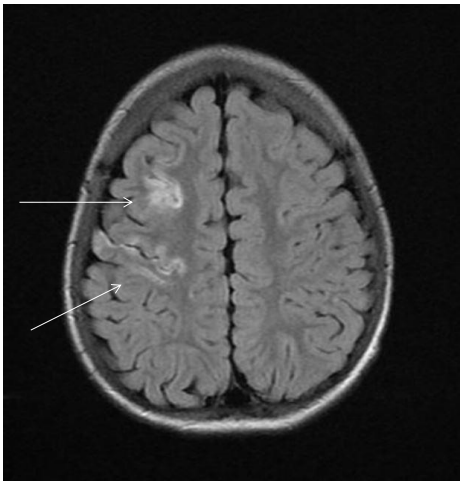
Case 2 RAQ 6 y/o male- HbSS

- Presented to ED with a sudden- onset left-sided weakness and left-sided focal seizure. Clinical examination was consistent with a diagnosis of an acute stroke
- On hydroxycarbamide for recurrent ACS, but recent DNA appointment, HC doses missed
- TCD normal until August 2015, but not done in Aug 2016 or Aug 2017 (not ordered)

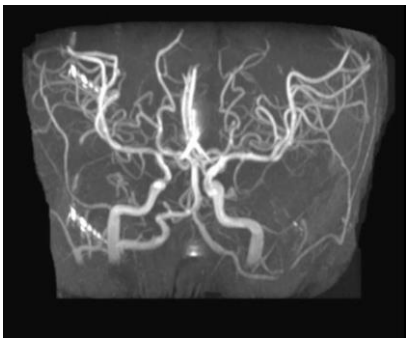
Case 2 Management

- Urgent red cell exchange transfusion in HDU
- Left-sided weakness, but rapidly improved over course of 48 hours
- TCD normal D3 of presentation
- CT scan on admission- no bleed
- MRI scan- movement artefact- right-sided infarction

Case 2 Repeat MRI under GA



Right MCA territory infarcts involving the right fronto-parietal cortex/subcortical white matter and right lentiform nucleus



No evidence of cerebral vasculopathy

Case 2 Further management

- Transfusion programme commenced for secondary stroke prevention- aiming to keep Sickle % <30
- Echocardiogram showed patent foramen ovale
- Dipyridamole started as antiplatelet agent until definitive PFO closure
- Stroke unlikely due to sickle vasculopathy

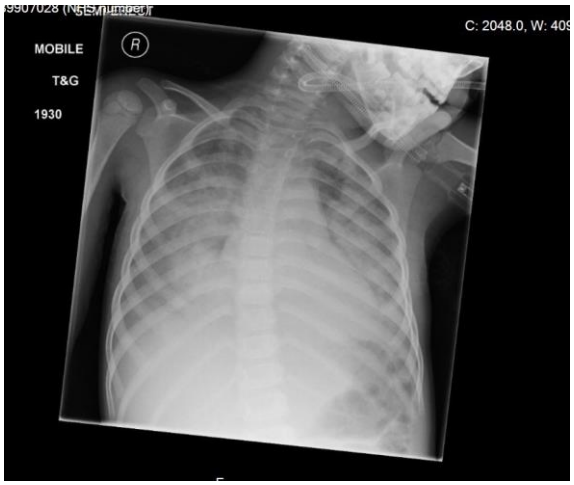
Case 3 AS-5y/o male- HbSS

- Past history of recurrent splenic sequestration- on RBC Tx December 2013-September 2016
- Splenectomy September 2016
- Port-a-cath removed December 2016
- Left hip washout early 2017
- 2 x admissions in June 2017 with painful episodes, on second admission also treated for LRTI- mother very strongly refused hydroxycarbamide.
- Known speech delay

Case 3 AS- continued

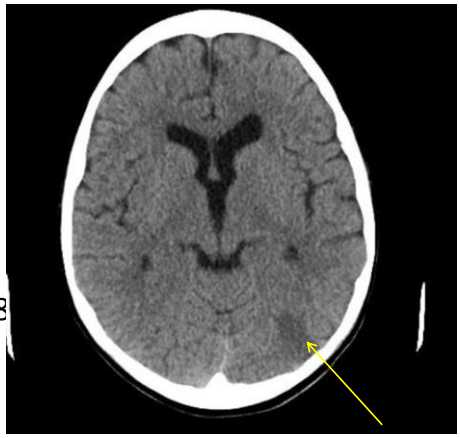
- Transferred to KCH PICU from local hospital with rapidly deteriorating respiratory status due to ACS
- Parainfluenza 1 isolated from NPA
- Ventilated for 5 days
- Manual partial exchange transfusion on admission

Case 3 AS- CXR on admission

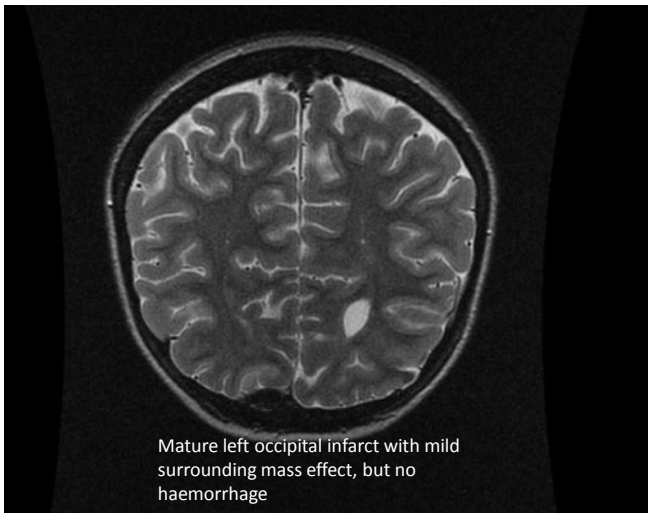


Case 3 Further progress

- Hypertensive and confused on extubation
- Urgent CT scan of brain showed occipital and parietal infarction
- Further exchange transfusion – S% 34 to 18
- Regular transfusion programme commenced



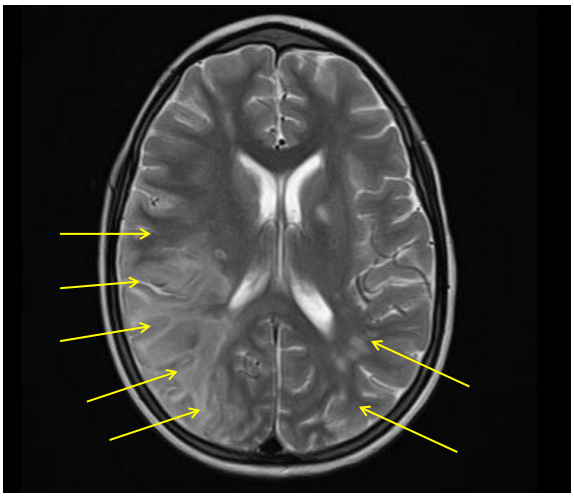
Case 3 MRI brain- one week later



Case 4 JO – 8 y/o male

- Routine TCD in early childhood revealed bilateral extracranial disease with severe 'stenosis' – absence of the internal carotids bilaterally, likely to be a congenital anomaly, rather than due to SCD
- He supplies his circle of Willis through the vertebral vessels with a left-sided dominance.
- Top up transfusions given 2014-2016- serial MRI –stable vascular ' anomalies' (although some recent evidence of progression of the 'stenosis'- MRI sequences indicated that the petrous segments of the vessels, which were previously visible were no longer visible)
- Hydroxycarbamide commenced at high dose in mid 2016, transfusions discontinued, as not clear whether transfusions are needed in a possible congenital malformation
- 9 months after cessation of transfusion- dizzy after a vigorous game of football

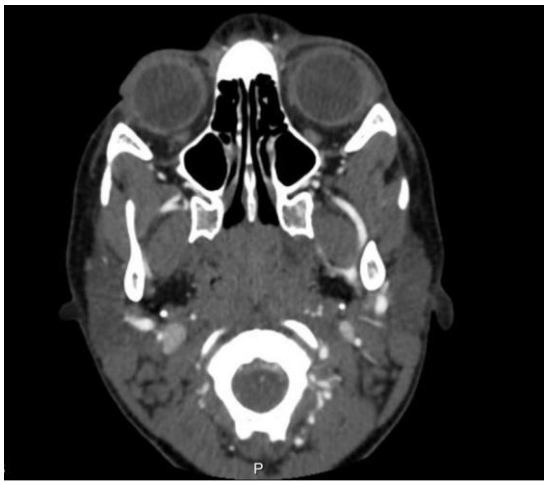
Case 4 JO- neuroimaging



Case 4 JO

- Acute severe bilateral damage; right middle cerebral artery distribution- extensive, and left-sided watershed changes
- Severely disability as a result of the acute event- intensive neuro-rehab
- Urgent exchange transfusion and subsequent top up transfusion programme to keep S% <30. Hydroxycarbamide stopped

Case 4 JO- neuroimaging



Bilateral ICA occlusion with patent posterior communicating arteries supplying the circle of Willis.

Summary

- 4 interesting recent cases of neurological events:
  - Atypical PRES following ACS and severe transfusion – associated intravascular haemolysis of unknown cause
  - AIS due to patent foramen ovale in the absence of vasculopathy
  - AIS following severe ACS- exchange transfusion, anaemia, ventilation and hypertension
  - Massive stroke in a child with severe bilateral vascular stenoses

Discussion

- Following the establishment of the TCD surveillance programme over a decade ago, sickle cell vasculopathy and stroke rates have reduced in many services in Europe and the US.
- We have seen a similar pattern in our centre
- These strokes are atypical and complex, needing intensive multi-disciplinary management