Scottish Paediatric & Adult Haemoglobinopathy Network

Paediatric Guideline: Stroke and Other CNS Manifestations in Sickle Cell Disease

Comprehensive RCPCH guidance on the diagnosis, management and rehabilitation of children and young people with stroke and specifically secondary to sickle cell disease is available and should be consulted.
https://www.rcpch.ac.uk/resources/stroke-childhood-clinical-guideline-diagnosis-management-rehabilitation

ACUTE ISCHAEMIC STROKE (AIS)
Stroke is a potentially devastating complication of sickle cell disease. It is commonest in individuals with HbSS when it occurs in up to 10% of patients without primary prevention. Vaso-occlusion of the cerebral vessels leads to infarction, generally in the territory of the middle cerebral artery, and untreated the majority will have a recurrence. Assessment using the FAST criteria (below) identifies 88% of anterior circulation strokes in children.

Predictive factors for stroke include those with a history of transient ischaemic attacks, chest syndrome, hypertension, a family history of sickle related stroke, or those with a low Hb F and/or low total haemoglobin.

The Stroke Prevention Trial (STOP) showed that children with transcranial Doppler (TCD) velocities of >200cm/sec are also at significant risk and should be offered primary prevention with chronic transfusion.

Presentation
Acute onset focal neurological deficit
- Assess using the FAST criteria: >= 1 of facial weakness, arm weakness or speech disturbance
- Altered level of consciousness or behaviour
- Assess using AVPU less than V or GCS less than 12

The following symptoms may also be indicative of stroke
- New onset seizures
- Severe new onset headache
- New onset ataxia, vertigo or dizziness
- Sudden onset of neck pain or stiffness
- Witnessed acute focal neurological deficit which has since resolved

Investigations

Imaging for all suspected stroke in patients with sickle cell disease.
N.B The availability and timing of some resources may depend on local services, agreement and expertise. Local protocols and policies should be developed for clarification.

- Ensure that urgent cranial computerised tomography (CT) scan is performed within one hour of arrival at hospital in every child with a suspected stroke.

Guidance recommends:

- computerised tomography angiography (CTA) (covering aortic arch to vertex), if the CT scan does not show haemorrhage.
  OR
  CTA, limited to intracranial vascular imaging, if haemorrhagic stroke (HS) is demonstrated
- Consider primary imaging using magnetic resonance imaging (MRI) in suspected stroke only if it is available within one hour of arrival at hospital.
- Provide MRI in a clinically timely manner for both AIS and HS patients for improved diagnostic resolution, if not obtained in/at the initial imaging investigation.
- Provide MRI within 24 hours if initial CT is negative and stroke is still suspected.
- Consider adding magnetic resonance angiogram (MRA) at the time of undertaking MRI; this should cover the aortic arch to vertex in arterial ischaemic stroke (AIS) and can be limited to the intracranial circulation in HS.

Other Investigations

- Pre-exchange investigations as per exchange transfusion protocol
- Glucose level
- Lumbar puncture may be necessary to exclude infection or subarachnoid haemorrhage.

Management

Immediate:

- Urgent neurological assessment in conjunction with neurology team
- Regular monitoring of conscious level by GCS or AVPU and neurological status by PedNIHSS assessment tool.
- Monitor temperature, heart rate, BP, RR, SaO_2 and aim to keep SaO_2>94%,
- Withhold oral feeding until safe swallow has been established
- Maintain normal fluid and electrolyte balance
- Exchange transfusion urgently, aiming to achieve HbS below 20%, with target Hb 100-110g/l, ideally by automated red cell apheresis.
- Provide top up transfusion to Hb100g/l to improve oxygenation if exchange is likely to be delayed by >6 hours or if stroke occurs in the context of acute anaemia
- For patients in centres where automated exchange is not available consideration should be given to stabilisation and transfer
- Seizures may occur and require anticonvulsant therapy

- Early multidisciplinary functional assessment (as soon as possible and within 72 hours) by physiotherapy, occupational therapy and speech and language therapy (PT/OT/SLT)
- Aspirin should be avoided routinely and exchange transfusion should be prioritised over thrombolysis
- If initial CT is negative and stroke is still suspected but MRI is not immediately available or contraindicated then consider treatment based on clinical assessment.

Long term:

- Liaison with multidisciplinary community allied health professionals to support discharge and rehabilitation
- A regular transfusion programme as secondary stroke prevention should be instituted with target pre-transfusion Hb >90g/l and HbS level <30%
- Monitor children with regular neurocognitive testing, MRI/A and TCD.
- Intensify therapy if monitoring identifies progressive cerebrovascular disease
    - Options include lower HbS target, addition of hydroxycarbamide or antiplatelet agents, surgical revascularisation or HSCT. All children and their siblings should be tissue typed.
    - Those with recurrent stroke or worsening vasculopathy despite optimum haematological management should be considered for stem cell transplant or surgery and discussed at an appropriate MDT.
    - Hydroxycarbamide can be considered when transfusion is not possible

TRANSIENT ISCHAEMIC ATTACKS

Initiate prompt evaluation, including neurologic consultation and neuroimaging studies (following the imaging guidance above), in people with SCD who have a recent history of signs or symptoms consistent with transient ischemic attack. TIA is a strong risk factor for subsequent stroke; if history and investigations are consistent with TIA then consider acute management as per stroke guidance.

SILENT CEREBRAL INFARCTIONS (SCI)

The possible benefits of transfusion should be discussed with young people and their families if SCI are identified on MRI. Additional factors favouring a transfusion programme are:

- impaired cognitive performance or progressive deterioration
- evidence of increase in the size or number of SCI on serial MRI
- evidence of intracranial or extracranial vasculopathy on MRA
- other co-morbidities exist which may benefit from regular transfusion

Consider hydroxycarbamide if transfusions are declined or contra-indicated
These patients should be discussed at an MDT and HSCT may be considered.

HAEMORRHAGIC STROKE (HS)

Sickle cell disease is associated with an increased risk for haemorrhagic stroke including subarachnoid haemorrhage and recurrence of HS.
Subdural and extradural haemorrhage are under recognised complications in sickle cell disease and can occur in the absence of trauma related to hypervascular bone, bone infarction or venous thrombosis

Investigations

Follow the imaging guidance above (section on acute ischaemic stroke)
Pre-exchange transfusion investigations as per exchange transfusion protocol

Management

- Urgent neurosurgical input is indicated
- Management and supportive care as for acute ischaemic stroke including exchange transfusion
- To prevent recurrence, neuroimaging as for acute HS in children and young people without sickle cell disease is indicated (see RCPCH guideline). Consider exchange transfusion prior to direct intra-arterial contrast injection.
- Refer to RCPCH guideline for further information on prevention of recurrence

CONVULSIONS

Febrile convulsions may occur with high fevers, including after vaccination, however it is important to distinguish these from convulsions due to acute stroke.

Investigations

- Follow the imaging guidance for acute ischaemic stroke to exclude acute haemorrhage or ischaemia if stroke is suspected. A self-limiting single seizure with no clinical suspicion of stroke does not require acute imaging
- Blood cultures and other infection screen including LP as clinically indicated
- Consider EEG or imaging in consultation with neurology team

Management

Immediate:

- Anticonvulsant, as per local hospital protocol
- Antipyretic, such as paracetamol

Definitive:

- If no abnormality on EEG and CT/MRI and MRA, and no recurrence, watch and wait.
- If EEG abnormal, but CT/MRI and MRA are both normal, consider anticonvulsants.
- If silent infarction is detected on scanning, or vessel stenosis/occlusion on angiogram then see management for silent cerebral infarction above.

MENINGITIS

Presentation

Fever, headache, neck stiffness, photophobia

Investigations

Urgent imaging is not part of the assessment for meningitis unless there is focal neurology or reduction in GCS
Lumbar puncture and blood culture

Management

As per local antibiotic policy

REFERENCES

Stroke in Childhood: Clinical guideline for diagnosis, management and rehabilitation (2017), RCPCH

SICKLE CELL DISEASE IN CHILDHOOD: STANDARDS AND GUIDELINES FOR CLINICAL CARE 2nd edition October 2019

Central nervous system complications and management in sickle cell disease Michael R. DeBaun and Fenella J. Kirkham, Blood 2016 127:829-838

https://www.rcpch.ac.uk/resources/stroke-in-childhood-clinical-guideline

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NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.