International Journal of Science Academic Research
Vol. 03, Issue 06, pp.4012-4015, June, 2022
Available online at http://www.scienceijsar.com

ISSN: 2582-6425

Research Article

A CASE STUDY OF A FOUR YEAR HBSS CHILD DIAGNOSED WITH HIGH RISK FOR STROKE FROM MULTIPLE TRANSCRANIAL DOPPLER (TCD) SCAN WITH NO SIGN/SYMPTOM OF STROKE

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Received 25th April 2022; **Accepted** 14th May 2022; **Published online** 30th June 2022

Abstract

Transcranial Doppler (TCD) is a well-established predictor of the risk of ischemic stroke in Sickle Cell Disease (SCD) children aged 2-16 years. TCD measures the time-averaged maximal mean velocity (TAMMV) in distal intracranial portions of the internal carotid artery and the proximal middle cerebral artery (MCA). Stroke prevention for SCD trial proposed guidelines for the appropriate use of STOP TCD technique to achieve high sensitivity and specificity in the detection of high mean velocity TAMMV values for prediction of likely stroke events in children with sickle cell anaemia and recommended the use of chronic blood transfusion regime as preventive therapy. Stroke prevalence in untreated SCD children with abnormal TCD is poor (3%). However, the case study revealed a 4-year-old Hemoglobin SS, despite persistent results of high risk for stroke from multiple TCD scans has had no clinical symptoms. **Conclusion:** This young child will benefit from combined treatment with hydroxyurea and chronic transfusion therapy with continuous monitoring to reduce the probability of developing stroke in future without intervention. Magnetic Resonance Imaging (MRI) to detect Silent Cerebral Infarct (SCI) will be required to augment her risk for stroke. **Recommendation:** There's a need for a more sensitive and specific method of screening for stroke risk among SCD children as the sensitivity of TCD scan may be weak in specialist centres nationwide, early referral of SCD children to a paediatric haematologist for optimal care and incorporation of health care financing schemes for SCD children to increase adequate care and stroke prevention.

Keywords: Sickle Cell Disease, Transcranial Doppler Scan, Stroke, Chronic Blood Transfusion and Hydroxyurea.

INTRODUCTION

Sickle cell disease (SCD) and its variants are genetic disorders resulting from the presence of a mutated form of haemoglobin known as haemoglobin S (HbS). The most common form of SCD worldwide is homozygous HbS disease (HbSS), an autosomal recessive disorder formally described by Herrick in 1910, although In 1874, Dr Horton, a Sierra Leonian medical Doctor, reportedly gave the first description of clinical symptoms and signs which is now referred to as sickle cell disease. SCD causes significant morbidity and mortality, particularly in people of sub-Saharan African ancestry, especially in Nigeria. Stroke is a major neurological complication in SCD and a significant cause of morbidity and mortality.[7] It is also one of the most devastating complications of the disease. CVD or stroke refers to a sudden onset of focal or global neurologic deficit of vascular origin lasting more than 24 hours. It is usually ischaemic in young children but can also be haemorrhagic. Transient Ischaemic Attack (TIA) or stroke occurs in 25% of patients with sickle cell disease. Approximately 10%- 20% of children with SCD under the age of 10 years will develop a stroke, most often in the first decade of life. The peak incidence of stroke occurs in children between the ages of 2 and 9 years[6] and continues to accumulate through childhood but rarely occurs in the first 2 years of life. Studies have shown that "silent" lesions occur on MRI studies even in the absence of clinical signs. These silent lesions are known as Silent/Subclinical Cerebral Infarcts (SCI). Subclinical cerebral infarcts (SCI) are the most common cerebral injury in children with SCA[10] and occur in sickle cell disease patients 27% and 37% of patients before their 6th and 14th birthdays, respectively.

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Silent stroke or SCI is defined by an abnormal MRI in the absence of history and physical signs of an overt CVD. Risk factors for SCI include male gender, low steady-state haemoglobin levels, higher baseline systolic blood pressure, and previous seizures.[11] Subclinical strokes are associated with neurocognitive dysfunction in apparently healthy SCD patients and are a risk factor for overt stroke.[10] In children with SCA, SCI is prominent in infants and toddlers[11] which is detected in MRI in 22% of Hb-SS patients and 6% of SC disease. The prevalence of SCI in Nigerians with SCA is not known. However, the prevalence of overt stroke among SCA children in Nigeria ranges from 2.9% to 8.6%.[3,] TCD often detects flow abnormalities indicative of stroke risk before lesions in MRA become evident and most children with SCI do not have cerebral vasculopathy detected by MRA of the circle of Willis. More so, clinical useful risk factors that will be used to predict SCD children with SCI are yet to be fully established, thus the necessity for use of TCD in Nigeria. Chronic blood transfusion therapy (CTT) has been the mainstay of intervention for primary and secondary stroke prevention in children with SCD. Current guidelines recommend indefinite transfusion therapy for SCD children who have a stroke and those at high risk for stroke from abnormal TCD findings or MRI lesions of SCI. TCD screening is stated to be predictive of stroke risk in SCD children[14], this facility is almost non-existent in Nigeria as it is affordable in only two centres in Nigeria with adequate capacity to operate this diagnostic device[7]. Moreover, the availability of chronic blood transfusions is highly limited due to the shortage of regular and safe blood supply in health care facilities[20,]. Life expectancy for SCD persons is reduced in Nigeria compared to developed countries in which stroke is one of the major causes of death in them. This highlights the

importance of early prevention, detection and treatment of stroke in SCD children.

CASE STUDY

History

I present a 4-year-old female child in nursery two who presented at the Paediatric Clinic with a referral from Sickle Cell Foundation on account of persistent diagnosis of high risk for stroke from multiple (10) TCD scans done. She was diagnosed with Haemoglobin SS at the Mercy Children's Hospital 3 years earlier (2018) after being managed for complaints of distended abdomen with associated moderate to severe abdominal pain and constipation 3-4 days duration. Her phenotype HbSS was confirmed the same year at Sickle Cell Foundation with a High-performance liquid chromatography test.

She had been regular with her clinic visits at Mercy Children's Hospital and had 4 admissions at various times at the hospital, these were:

- 2018- Her first visit to mercy children's hospital was diagnosed with HbSS and treated on account of abdominal distention with constipation of 4 days duration.
- 2019- She was managed for dactylitis of feet and hands at the age of 3 years.
- 2020 - Early in the year had a fever and was managed for malaria.
- August 2020- She was managed for a respiratory infection.

She had Exchange Blood Transfusion (EBT) done 2 years earlier after the 5th TCD scan still showed a high risk for stroke in which subsequent TCD scans done since then were reported to be high risk for stroke. She was thus referred to the LUTH POP clinic for expert management and care after the last TCD scan was done.

Her mother commenced antenatal at 4 weeks gestation with booking parameters essentially normal. Pregnancy wasn't eventful and she was delivered via spontaneous vaginal delivery at term and weighed 3.5kg at birth. No history of Jaundice in the neonatal period. Immunisation was up to date according to the National Programme for Immunisation schedule. She was exclusively breastfed and attained milestones when due as no developmental delay was noted by her mother or paediatricians from referring hospital. Her daily medications include Tabs pallidrine, Penicillin V, Folic acid, Vitamin B Complex and Tabs Hydroxyurea 450mg daily.

On examination, a young female child in no form of distress, afebrile=36.8°C, acyanosed, anicteric, not dehydrated, not pale, nil finger clubbing, nil pedal oedema and no palpable lymph nodes. SPO_2= 98% in room air. Weight= 19kg, Height= 111cm, Mid upper arm circumference = 15cm. Parameters were all appropriate for age. She was conscious and alert, oriented in time, place and person. Her speech was spontaneous, of normal pitch and not pressured. Cranial nerves I-XII were assessed and normal. No obvious deformities, bulk was normal globally, tone was normal in both upper and lower limbs, power was 5 in both upper limbs and lower limbs. Reflexes were normal globally. Her neck was supple with no signs of meningeal irritation and cerebellar function was normal. No obvious chest wall abnormalities, precordium normative, capillary refill prompt, radial pulse was 112 bpm, regular, full volume not bounding. There was radio-femoral synchrony, blood pressure was 90/70mmHg. Apex beat located at 4th intercostal space, mid-clavicular line, No thrills, No heaves, 1st and 2nd heart sounds heard, no murmurs, No bi-basal crepitations. Chest symmetrical, moved with respiration, respiratory rate was 20 cpm, trachea was central, normal tactile fremitus, percussion notes resonant bilaterally, good air entry bilaterally with vesicular breath sounds, normal vocal fremitus. Good oral hygiene with erupted lower molar and upper incisor teeth, tonsils not enlarged, abdomen full, moved with respiration, umbilicus was inverted, no area of tenderness, liver was not palpable, spleen was clinically palpable, 3cm below the left costal margin, spleen span was 10-12cm, kidneys not palpable, bowel sounds heard and normoactive.

She was commenced on chronic blood transfusion regimen (This involves monthly EBT sessions for 6 months then a repeat of TCD scan).

Caps Hydroxyurea was increased to 500mg daily.
TCD Scan was scheduled to be repeated by experts.

DISCUSSION

The case study highlighted an asymptomatic female known HbSS child with a high risk for stroke from multiple TCD scans (~10) done in 2 years and referring hospital still requested repeat TCD Scans despite no change in result of the test nor clinical condition of the patient. The STOP TCD technique was used in studies done in Austria, Brazil, Gulf (Omar, Qatar, UAE) that achieved early detection of SCD children at risk for stroke. However, there is a disparity in results from two different studies in Nigeria, that utilized the STOP TCD technique, both studies suggested the necessity for the development of threshold velocities for TAMM in Nigeria with the use of strict guidelines as well as incorporating sufficient skilled manpower and routine TCD screening accessible to SCD children as to achieve optimal benefits in the utilisation of TCD scan in the prevention of stroke in Nigeria. Moreover, several studies Akingbola et al,[4] Ojewumi et al,[14] deduced the high sensitivity of parameters such as low hematocrit, high serum lactate dehydrogenase, high steady-state leukocyte count and oxygen saturation levels in detecting of high risk for ischaemic stroke in HbSS. This can be used in developing countries with limited access to TCD scans as most centres in Nigeria have limited access to TCD scans[21, 23]. Although rare, abnormal values from TCD scans with either no clinical correlation with SCD child or variance to MRI, as a study reported SCD children with stroke who had abnormal low TCD scan values. MRI used to detect SCI, can be combined with TCD findings to enhance specificity for SCD children at high risk for stroke. This may not be feasible in Nigeria due to the high cost of neuroimaging in the country and is a limitation in accessing SCI in SCD in developing countries.[13] MRI test will be useful in this child as she's in the age group (4years) at risk of SCI, although clinically there's no neurocognitive impairment as she has good academic performance. Recent studies have shown that hydroxyurea treatment at a high dose can substitute CTT in stroke prevention for children with abnormal TCD velocities, especially when CTT is not feasible.[22] More so, Chronic Transfusion Therapy (CTT) is beneficial both for the prevention and therapeutic management of SCD children at

risk for a stroke either from SCI or abnormal values from TCD scan, although progressive silent infarct occurs even with CTT. CTT can be combined with hydroxyurea to achieve optimal benefits in stroke.

Recommendations

Early referral of SCD children to a paediatric specialist hospital for appropriate care. This will combat the rising prevalence of SCD children with stroke and poor prognosis at presentation. Health care financing schemes for children with chronic medical conditions like SCD. This will help proper management and access to neuroimaging (MRI) increase the early detection of silent cerebral infarct. Research funding for SCI in SCD Nigerian children. This will help to understand the prognostic effect of SCI in SCD children in future.

Conclusion

The routine use of TCD screening for stroke prevention in SCD children is important but weak. Therefore, a more sensitive and specific method is needed. The combined use of chronic transfusion therapy and hydroxyurea is more beneficial in children with persistent high risk for stroke compared with a solitary use of either management with continuous monitoring to combat the risk of stroke in future.

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