Evaluation of strokes in children

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Introduction

Childhood stroke is perceived to be relatively rare. Epidemiological studies have revealed an annual incidence of approximately 3 per 100,000 paediatric strokes in children above one month of age [1]. Most of the strokes are ischaemic in origin while about 40-50% childhood strokes are of hemorrhagic in origin (ICH, Subarachnoid haemorrhages), although these figures vary in different studies [2]. Arterial ischaemic strokes (AIS) and venous ischaemia are the types of ischaemic strokes that occur in children. Some studies suggest that venous ischaemia is more common.

Clinical presentation

The signs and symptoms depend on the location and size of the occluded vessel as well as the patient's age. Anterior circulation strokes are much more common than posterior circulation strokes 1. Two-thirds of children will present with an acute face-arm-leg weakness [1]. Seizures or altered level of consciousness may complicate presentation. Preceding self-limited episodes of hemiparesis are experienced in 20% of patients [1].

Infants may have no clinical manifestations or delayed clinical presentation with initially flaccid paralysis in one side and later becoming spastic. Pathologic early hand preference is commonly a presenting complaint in infants. Firstly it may be that the occlusion is gradual, allowing adequate arterial anastomotic channels to develop. In addition, the potential for recovery is so great that children may be seen without major deficit for months or years after an ischemic event, despite large areas of brain infarction. A third reason for the delay in clinical presentation in infants is that identification of clinical signs may not occur until brain maturation reaches a stage allowing expression of the deficit [3].

Aetiology of stroke in children

In adults, the common underlying risk factors for stroke include hypertension, diabetes mellitus, atherosclerosis, cardiac arrhythmias and valvular abnormalities [4]. In childhood, however, the potential aetiologies are many which create a greater diagnostic challenge to the clinician.

Cardio-embolic causes are the most frequent cause of paediatric strokes. Potential mechanisms of stroke in cyanotic congenital heart disease include hyperviscosity and diminished oxygenation of blood, paradoxical emboli from right-to-left shunting and emboli from vegetations secondary to valvular disease. In the context of developing countries as in Sri Lanka, valvular lesions from acquired rheumatic heart disease play a major role. Other abnormal structural defects predisposing to emboli include atrial myxoma, cardiac rhabdomyoma, cardiomyopathies, bacterial endocarditis, and prosthetic valves. Cardiac arrhythmias, particularly atrial fibrillation, as in adults, predispose to emboli.

A variety of haematological causes will lead to arterial ischemic disease in children, though venous occlusion and hemorrhagic events may also occur in the same disease processes. Hyperviscosity syndromes (polycythemia, hyper-leukocytosis as in leukaemias, and thrombocytosis) can lead to occlusion of vessels [5]. Haemoglobinopathies, the prototype of which is sickle cell disease, are often complicated by stroke. The incidence of stroke in sickle cell disease is between 5% and 10%, with the median age of the first stroke being seven years of age. Recurrence without treatment occurs in up to 90% of patients, most within three years [6].

There has been a recent recognition of the importance of hypercoagulable states. These may be genetically acquired, associated with autoimmune and other systemic disorders, or found independent of an underlying disease. Anti Thrombin III, protein C, and protein S are

naturally occurring anticoagulants whose deficiencies are inherited as autosomal recessive traits[7]. Autoimmune disorders may lead to cerebrovascular disease through a vasculitis or by inducing a hypercoagulable state. A hypercoagulable state is created by antiphospholipid antibodies, which includes the lupus anticoagulant and the anti-cardiolipin antibody[8]. In systemic lupus erythematosis, neurologic involvement is seen in over 50% of patients. Prothombin gene mutation (G20210A), factor V laiden mutation and hyperhomocystinaemia have also been attributed to the causation of childhood stroke[9]. Homocystinuria, due to defect of methionine metabolism, may present as a thrombotic syndrome. High levels of homocystine lead to endothelial damage and increased platelet aggregation. Young adults heterozygous for homocystinuria are also felt to be at increased risk [10].

Polyarteritis nodosa, Wegener's granulomatosis, Henoch-Schonlein purpura, ulcerative colitis, Kawasaki disease and the dermatomyositis / polymyositis complex are rare associations with childhood stroke due to associated arteriopathies[11].

Stroke-like episodes in a nonvascular distribution are seen in mitochondrial encephalomyopathy with lactic acidaemia and stroke-like episodes (MELAS). This disorder is due to a mutation of mitochondrial DNA and may require muscle biopsy to confirm.

In one third of thrombotic carotid artery occlusion, a preceding infection is noted, often in the pharynx or cervical area. Pharyngitis, cervical adenitis, tonsillitis, sinusitis and retropharyngeal abscess have all been reported to be precursors of internal carotid artery thrombosis. The mechanism is likely to be local inflammation of the arterial wall.

Cat-scratch fever, mycoplasma, and viral encephalitis have also been associated with vasculopathies causing stroke in children and varicella vasculopathy is described more often in children than others [12].

Trauma to the neck may predispose to carotid thrombosis. This can be a blunt injury to the neck, intraoral trauma, i.e. falling with a pencil in the mouth, or trauma to the cervical spine. Carotid dissection should always be considered as a cause of stroke. It may be spontaneous or follow a neck injury. In a dissection, a tear in the arterial wall leads to an expanding haematoma which obstructs blood flow. The patient may complain of neck pain or referred pain to the eye or forehead.

Various drugs, illicit and legally prescribed, have been linked to strokes. Cocaine, phencyclidine (PCP), and amphetamines predispose to vascular injury via hypertension, vasospasm and vasculitis. Steroids may cause endothelial hyperplasia and increase platelet adhesiveness.

In young girls the intake of oral contraceptive pills may also contribute by way of creating a hypercoagulable state predisposing to a state of cerebral venous sinus thrombosis.

Moyamoya disease is another rare cause of late childhood stroke which is characterized by an angiographic picture of occlusion of internal carotid arteries and the development of a fine web-like collection of abnormal anastomotic vessels (puff of smoke) [13].

Migraine-related stroke has been reported. Diagnosis of migraine-related stroke is suggested by a family history of migraine, prior migraines in the patient, and exclusion of other aetiologies by a thorough diagnostic evaluation [14].

Approximately a quarter to one third of children with strokes, have no recognizable cause. It may be that the clinical knowledge, the expertise in interpreting investigation results and the unavailability of high tech investigations on childhood stroke is not adequate.

In addition to the ischaemic strokes the causes for hemorrhagic strokes include arteriovenous malformations and aneurysms. Bleeding diathesis (thrombocytopenia, leukaemia, sickle cell disease and coagulopathies) and rarely intracranial tumours could also be incriminated.

Differential Diagnosis

Focal cerebral ischaemia
Intracranial haemorrhage
Cerebral abscess
Encephalitis (herpes simplex virus)
Brain tumor
Multiple sclerosis
Epilepsy: post-ictal Todd's paralysis or a focal inhibitory seizure
Complicated migraine

Once the diagnosis of a stroke is determined the cause for the stroke needs to be evaluated. This may be a challenging task for the clinician.

It is always important to obtain a very good history regarding the onset, progression and the disabilities, immediate or recent events preceding the stroke, a detailed birth and a developmental history, past medical history of similar illnesses or any cardiac disease and migraine, family history of premature atherosclerosis, heart disease and of unexplained thrombotic episodes and migraine.

A social history should include the sexual history, drug abuse and engagement in body contact sports like rugby and karate.

A detailed general examination with regard to dysmorphism, neurocutaneous stigmata and evidence of connective tissue disorders like butterfly rash, palpable purpura etc.

It is necessary to auscultate the neck and skull for any bruits.

A good cardiovascular system examination and a very detailed neurological examination is a must to detect clues to the diagnosis.

Once the history and the examination are completed, an array of investigations waiting in order to aid in detecting the cause. There are mandatory preliminary investigations that need to be carried out and if the preliminary investigations fail to detect a cause, it is necessary to go onto the second and third line investigations. However, still there could be about a third where the cause is unknown.

Investigations

1st Line

CT scan of brain
MRI of brain /MR angiogram /MRV
Complete blood count
ESR
BUN, creatinine
Urinalysis
Random glucose
Liver function tests
PT/APTT
SE, Ca, Mg,
Chest x-ray
ANA
Echocardiogram (transthoracic) with saline contrast
12-lead ECG

2nd Line

Holter monitor
Transcranial and / or carotid dopplers
Cerebral angiogram (transfemoral)
EEG
Antithrombin III
Protein C (activity and antigen)
Factor V (laiden) mutation
Antiphospholipid antibody
Anticardiolipin antibody
Lupus-anticoagulant
fibrinogen levels - qualitative/quantitative
Factor viii levels

3rd Line

Urine for organic acids
Hemoglobin electrophoresis
Complement profile
VDRL
Lactate / pyruvate
Ammonia
CSF: cell count, protein, glucose, lactate
PCR TB
Blood culture
Lipid profile
HIV
Mycoplasma titers
Echocardiogram (transesophageal)
Muscle Biopsy
DNA testing for MELAS
Leptomeningeal biopsy
Serum homocystine after methionine load
Genetic studies

Management

The acute treatment of cerebral ischemia is largely supportive and requires an intensive care setting. Attention to oxygenation, fluid and electrolyte status, seizures, and infections are critical. Treatment should be directed to the underlying cause if it is identifiable.

Cerebral oedema is maximal over the first 72 hours. Initially, oedema is cytotoxic, although a vasogenic component occurs after two to three days. Edema is usually effectively managed with hyperventilation and fluid restriction. In general, the use of steroids and osmotic agents are not indicated. However, in case of progressive deterioration, mannitol and cranial flap removal may be life saving [16].

The use of anticoagulation in pediatric ischemic stroke is controversial, although it is often used in the presence of a definable and recurrent source of emboli or evolving thrombotic stroke [15]. Anticoagulation is contraindicated in hemorrhagic infarct and uncontrolled hypertension. Long-term anticoagulation with warfarin is indicated in deficiency of protein C,S, antithrombin III and in the presence of anti-phospholipid antibodies. Rehabilitation through aggressive physical, occupational, and speech therapy is essential for all patients. Behavioral problems and learning disabilities may become apparent upon returning to school. Children may need neurocognitive testing and special educational classes [17].

Prognosis

The prognosis for childhood strokes is variable. With aggressive rehabilitation most would be near normal in activities of daily living when compared with adults.

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