Arterial ischaemic stroke in childhood

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Abstract

Stroke in childhood is poorly recognised amongst the public and healthcare professionals. Stroke in any age group should be considered a medical emergency and yet in children the diagnosis is often delayed with subsequent doubt regarding optimal management or treatment. Adult management protocols have been applied to children with limited evidence and uncertain success. This review looks at childhood arterial ischaemic stroke in the non-neonatal age group i.e. 1 month-16 years and summarises current guidelines and literature. The investigation and management of suspected and confirmed arterial ischaemic stroke, and stroke due to venous sinus thrombosis is discussed. Although thrombolysis is well-established in adult ischaemic stroke care, more studies are required to definitively guide the safe use of this medical therapy in the acute phase in children.

Keywords brain infarction; child; ischaemia; stroke

Definitions

The World Health Organisation in 1978 defined Stroke as 'a clinical syndrome typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting more than 24 hours or leading to death, with no apparent causes other than of vascular origin'. This definition could be updated to reflect the crucial diagnostic role of neuroimaging in current stroke practice. The clinical syndrome must now, in addition to evolving neurological deficit, correlate with characteristic findings on brain imaging.

Arterial ischaemic stroke (AIS) is 'a clinical stroke syndrome due to cerebral infarction in an arterial distribution'. Paediatric AIS is any neurological presentation, including seizures, associated with radiological evidence of ischaemia or infarction in a correlating arterial vascular distribution. A diagnosis of Transient Ischaemic Attack (TIA) infers the same process but that the neurological deficit resolves within 24 hours. Rapid brain imaging is mandatory for accurate diagnosis, subsequent referral and, in particular, to exclude conditions requiring urgent neurosurgical intervention.

Perinatal ischaemic stroke affects neonates i.e. occurring between 20 weeks gestation and 28 days postnatal life. Perinatal stroke occurs primarily in term infants and accounts for a significant proportion of stroke; approximately 25%–30% of all AIS in children. 'Perinatal stroke' is considered a separate entity from 'childhood stroke' and is not included in this discussion. Childhood strokes are ischaemic (55%) or haemorrhagic (45%). The focus of this paper will be childhood arterial ischaemic stroke in the non-neonatal age group i.e. 1 month-16 years and to review the recent literature and evidence for its diagnosis and management.

Epidemiology

The incidence of childhood AIS has been variably reported. Estimations of incidence have varied between 0.63 and 7.9 per 100,000. In the UK, Mallick et al. recently published a large prospective epidemiological childhood AIS study. They reported almost 100 confirmed cases in 12 months (2008–9) in the South of England (a population of 5.99 million children) giving an incidence of childhood AIS of 1.6 per 100,000 person years (excluding neonates). Annually, the US reports at least 2400 cases per year. The incidence is similar to that of childhood brain tumours.

The International Paediatric Stroke Study (IPSS) Group has analysed more than 600 children with confirmed childhood stroke (between 2003 and 2007 at 30 centres worldwide) and has reported various epidemiological findings from its Registry of childhood stroke. This group has found a male predominance in all types of AIS with 60% of cases affecting males, regardless of age or history of trauma. Studies from the USA suggest black children have a higher risk of stroke, above that expected for their higher incidence of sickle cell disease. The South of England study also found a higher relative risk in Asian and Black children compared to white British children. Childhood stroke has an estimated mortality of 0.6/100,000. Up to 10% of children with a stroke will die and 50–85% of children will have persistent functional or neurological deficits including seizures, learning or developmental problems.

Aetiology

There are many risk factors for stroke in children. Sickle cell disease (SCD) is strongly associated with AIS with 11% of children having a clinically apparent stroke before the age of twenty. The specific management of SCD or stroke prevention in this group requires specialist consideration and is not discussed further in this paper.

Congenital heart disease is an equally important risk factor for stroke. The Canadian Pediatric Ischemic Stroke Registry (CPISR) found heart disease in 19% of 288 children with arterial thrombosis, and the IPPS found 30% of their 667 cases had either congenital or acquired heart disease. Most children are known to have cardiac diagnosis prior to their stroke, but the lesion may be discovered only afterwards. Complex cardiac anomalies involving both valve and myocardial defects are most commonly implicated, but any cardiac lesion can lead to a stroke. Cyanotic cardiac lesions with polycythaemia are of particular concern due to the increased potential for thrombotic and embolic phenomena. An asymptomatic patent foramen ovale (PFO) is reported consistently in 20% of healthy individuals however the incidence of PFO in cryptogenic stroke patients is higher (reported in up to 40%). The decision whether or not to close a PFO when found in a young patient with no other risk factors for stroke remains

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controversial and is currently not recommended in current national guidelines.

Risk factors for stroke are divided into eight main categories as proposed by the IPPS and subsequently also used in the South of England study. These risk factors are listed in Table 1.

The prevalence of various risk factors varies by age group. IPPS data published in 2011 by Mackay et al. demonstrated that in all childhood age groups, at least one risk factor for stroke is present in at least 83% of affected children. In the under 5 years, arteriopathy was identified in nearly half of their cohort, and cardiac disorders one third. Arteriopathy consistently has the highest incidence in their findings, present in at least 49% of all age groups. They reported the younger the child, the more likely general systemic infections will be complicated by stroke. Minor infections are also associated; a Californian case-control study (cohort of 2.5 million children) demonstrated that an outpatient medical encounter for a minor acute infection increased a child's risk of AIS 4-fold. No specific 'type' of acute infection predominated and included respiratory tract infections, otitis media and gastroenteritis. Head and neck trauma was also identified by this study as an important independent risk factor. In this study, 12% had a history of head/neck trauma in the preceding 12 weeks (compared to 2% of controls) and was strongly associated with AIS. Indicators of more severe trauma (with loss of consciousness or hospital admission) increased the risk further. This type of injury is in addition to that seen with the well-recognised risk of AIS with artery dissection after trauma. There are a proportion of children presenting with AIS, in whom no cause (30%) or risk factor (9–28%) is identified.

International Paediatric Stroke Surveillance scheme risk factor categorisation for childhood arterial ischaemic stroke

Risk factor	Examples of diagnoses
Arteriopathy	Arterial dissection, sickle cell arteriopathy, post-varicella arteriopathy, moyamoya, vasculitis, unspecified arteriopathy
Cardiac disorders	Congenital heart disease (cyanotic or acyanotic), acquired heart disease, isolated PFO, post cardiac surgery (within 72 hours), previous cardiac surgery or catheterisation, arrhythmia, extracorporeal membrane oxygenation
Chronic systemic disorders and treatments	Sickle cell disease, genetic disorders e.g. Trisomy 21, iron deficiency anaemia, connective tissue disorder, haematological malignancy, L-aspariginase (chemotherapy), solid extracranial tumours, oral contraceptive pill
Prothrombotic states	Methylenetetrahydrofolate reductase deficiency, hyperlipoproteinaemia (a), factor V Leiden or other genetic or acquired thrombophilia, protein C deficiency, protein S deficiency, antithrombin III deficiency, hyperhomocysteinaemia, prothrombin 20210A mutation
Acute systemic conditions	Shock, dehydration, acidosis, hypoxia, fever for >48 hours, sepsis (confirmed in blood/urine/CSF)
Chronic head and neck disorders	Migraine, intracranial malignancy, cerebral aneurysm, ventricular shunt, PHACES syndrome
Acute head and neck disorders	Head/neck trauma, meningitis, head/neck surgery, pharyngitis, tonsillitis, sinusitis, mastoiditis
Risk factors for atherosclerosis	Hypertension, hyperlipidaemia, Type 1 diabetes mellitus (adults)

Table 1

As with adults, infarcts in children are most commonly located in the anterior circulation. This is thought largely to be the result of high prevalence of arteriopathy in the anterior circulation. Arterial dissection is a recognised cause of stroke in both anterior and posterior circulation and can be associated with head/neck trauma.

Cerebral venous sinus thrombosis is an important cause of childhood stroke. Thrombosis within the cerebral venous system results in outflow obstruction, venous congestion, oedema and ultimately venous infarction. Predisposing conditions include common childhood illnesses such as fever, infection, dehydration, and anaemia, as well as acute and chronic medical conditions such as prothrombotic states, congenital heart disease, nephrotic syndrome, systemic lupus erythematosus, and malignancy.

Moyamoya is a progressive arteriopathy of unknown origin affecting branches of the internal carotid artery (ICA). Also named 'Spontaneous occlusion of the circle of Willis' this arteriopathy causes luminal narrowing and ischaemia presenting as TIA's or AIS. Moyamoya affects an estimated 1:1,000,000 children in the US but is implicated in 6–10% of all childhood strokes. The pathognomonic 'moyamoya' appearance in the arteriogram (meaning 'puff of smoke' in Japanese) confirms the diagnosis. Moyamoya should be considered in any child who presents with symptoms of cerebral ischaemia particularly if the symptoms are precipitated by physical exertion, hyperventilation, or crying. There are no known methods of arresting the underlying arteriopathy. Treatment seeks to restore cerebral blood flow by surgical revascularization utilising unaffected carotid vessels. Surgical revascularization may provide long-term reduction in stroke risk (a reported 4% risk of recurrence with and 40% without surgery).

Clinical presentation

Stroke should be suspected in all cases of acute onset focal neurological deficit.

Children tend to present with any combination of focal neurological signs, hemiparesis or speech disturbance. Altered consciousness, headache and seizures (particularly in infants with AIS) are also common. Generally the impairment is very acute, e.g. noted on waking from sleep, or with a collapse.

Sometimes other causes of acute focal neurological deficit may not be easy to distinguish from the history or even