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Paediatric stroke: case series

兒科中風：病例系列

Five cases of paediatric stroke are reported. Two patients presented with idiopathic stroke, another following vertebral artery dissection, one secondary to Moyamoya disease, and one patient with the syndrome of mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes. The presentation, investigation, and management of paediatric stroke are discussed.

本文報告了五個小兒科中風的病例。兩名患者為自發中風，一名是脊椎動脈撕裂而引致的，一名是 Moyamoya disease ，而另一名是患有線粒體腦病、乳酸毒症和類中風發作綜合症。作者對兒科中風的臨床徵狀、診斷和治療方法進行了討論。

Introduction

Paediatric stroke is probably more common than once suspected, although far fewer children are affected by stroke than adults. It has been reported in all racial and ethnic groups. The annual incidence is estimated at 2.5 cases per 100 000 children. Half of the reported cases are ischaemic in origin, and the other half are haemorrhagic.[1] This case series is of patients with paediatric ischaemic stroke identified in the past 3.5 years (from January 1996 to June 2000) in a regional hospital.

Case reports

Case 1

A 13-year-old girl with no medical history of note was admitted because of acute right-sided weakness. Initially, she was admitted to the orthopaedic ward with the provisional diagnosis of brachial neuritis. Further questioning revealed that the weakness started in the right hand and forearm. This was followed by weakness of the right arm and right lower limb 2 days later. Physical examination revealed right hemiparesis, with proximal power grade 3/5 and distal power grade 0/5. Computed tomography (CT) brain imaging showed an infarct in the posterior limb of the left internal capsule. She complained of right facial numbness and weakness 1 day after admission. Repeated CT brain imaging did not reveal any changes in infarct size, and there was no evidence of haemorrhage. In view of the clinical deterioration, she was given low molecular weight heparin for 5 days. Aspirin 300 mg daily was also started. There was no further neurological deterioration. Other investigations, including magnetic resonance angiogram of the brain, were completed and no predisposing cause was found for the stroke. Significant recovery was seen following intensive rehabilitation. Nonetheless, the patient continued to walk with a mild hemiplegic gait and there was a residual loss of dexterity in her right hand.

Case 2

A 7-year-old mentally retarded boy was admitted because of fever and a generalised convulsion lasting 20 minutes. His recent health history was unremarkable apart from a urinary tract infection. Initial diagnosis was febrile convulsion with the possible focus of infection in the urinary tract. Subsequently, left limb preference was noted. Physical examination revealed power of grade 0/5 and an up-going plantar reflex on the right side. Computed tomography brain imaging showed a massive left cerebral infarct with moderate mass effect. The child then developed features of increased intracranial pressure with impaired level of

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consciousness and hyperventilation, which responded to supportive therapy. After the acute event, the boy received intensive physiotherapy and showed good recovery of function. Investigation did not yield any predisposing cause for the stroke.

Case 3

An 8-year-old previously healthy girl presented with sudden collapse and generalised convulsion. Subsequently, she became comatose. Physical examination showed upper motor neuron signs in all four limbs. Computed tomography brain imaging revealed a bilateral occipital infarct. Conventional catheter angiography showed dissection of the left vertebral artery, with extensive thrombus in the basilar artery. Heparin and warfarin were given. Magnetic resonance angiography (MRA) of the brain after heparinisation showed partial recannalisation of the basilar artery, but the left vertebral artery thrombus persisted. After the acute insult, quadriplegia and cognitive impairment were evident. She was started on aspirin (75 mg on alternate days). Repeated MRA at the age of 9 years showed the left occipital infarct and complete occlusion of the left vertebral artery.

Case 4

A 6-year-old boy with normal previous health and development presented with episodic frontal headache for 1 month in duration and gradual left-sided weakness and clumsiness for 1 week. Physical examination revealed left hemiparesis and left-sided facial droop. Computed tomography brain imaging revealed multiple right frontal and parietal infarcts. Magnetic resonance angiography revealed bilateral internal carotid artery stenosis with meningeal collaterals (Fig 1).

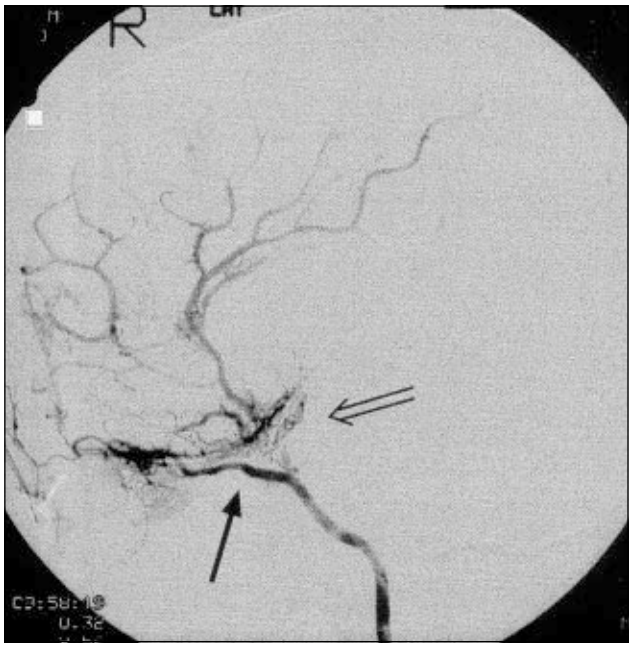

Fig 1. Angiogram of the right internal carotid artery
This shows narrowing of the terminal part of the internal carotid artery (solid arrow) and a network of collateral vessels (hollow arrow) at the skull base compensating for the reduced internal carotid artery flow. These are characteristic findings of Moyamoya disease

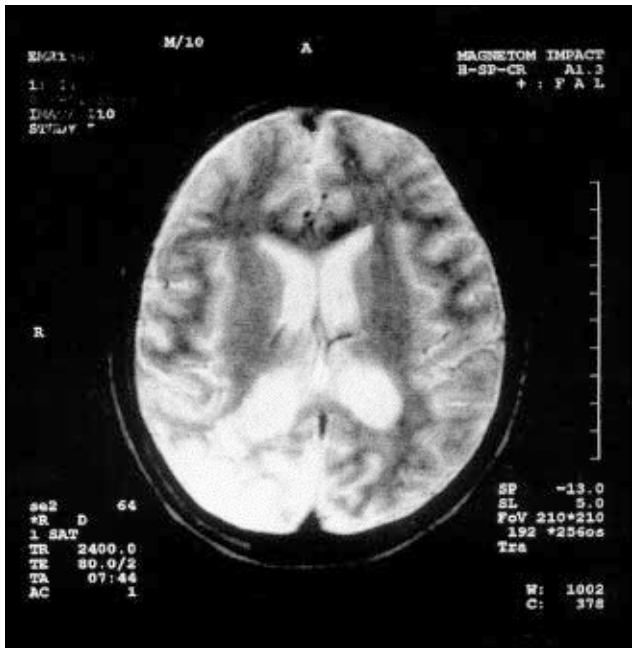

Fig 2. T2-weighted magnetic resonance imaging of the brain showing increased signal intensity in both occipital lobes and the right parieto-temporal region
In mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, multiple infarcts typically involve the parieto-occipital regions and do not conform to cerebral vascular territories

The diagnosis made was Moyamoya disease. After the acute episode, the patient was treated with aspirin 80 mg three times daily. He recovered well and returned to school. Subsequently, right encephalo-duro-arterio-synangiosis—whereby a strip of galea and its blood supply were sutured to the dura mater—was performed. The patient were monitored for 3.5 years. No recurrence of stroke or neurological deterioration occurred during this period.

Case 5

This case has been described in more detail in a previous publication.[2] In brief, at age 12 years the boy was admitted to Caritas Medical Centre for residential care. He was cognitively impaired, quadriplegic, deaf, and blind. He had suffered from migraine-like headache and vomiting episodes in early childhood. At the age of 7 years, developmental regression and intractable epilepsy was noted. Computed tomography of the brain at age 10 years showed multiple cerebral infarcts, involving the right parieto-occipital and left tempo-occipital regions. Magnetic resonance imaging at age 11 years showed increased signal intensity of T2-weighted images in both occipital lobes and the right parieto-temporal region (Fig 2). At the age of 14 years in addition to the neurological deficits, he also had a history of supraventricular tachycardia and paralytic ileus.

Investigations for the cause of developmental regression and quadriplegia were completed at the age of 14 years. Results showed an elevated serum lactate level of 4.9 mmol/L (normal range, 0.5-2.2 mmol/L). His cerebrospinal fluid lactate level of 6.0 mmol/L was also high (normal range, 0.8-2.2 mmol/L). Genetic study on various tissues showed

a heteroplasmic A to G mutation in the mitochondrial DNA at nucleotide position 3243. A clinical diagnosis of mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) was made. After screening the family, the younger brother of this patient was found to have the same mutation in the mitochondrial DNA although he did not have the clinical disease. The brother was given coenzyme Q.

Discussion

The pathophysiology of ischaemic stroke includes thrombosis and embolism. While atherosclerosis and cardiac diseases such as mitral stenosis are the major predisposing causes of thromboembolism in adults, these are rare in children. The Table summarises predisposing causes of paediatric ischaemic stroke. This long list reflects the diversity of causes that may lead to ischaemic stroke in children.[1,3-7] The presence of a predisposing cause is identified in 70% of cases,[4,6,8] with congenital heart disease being the most common cause.[3,4,8]

The clinical presentation of ischaemic stroke depends on the anatomical distribution of the vascular supply affected, and the associated brain damage. The most common presenting symptom in childhood ischaemic stroke is hemiplegia. This symptom occurred in 91% of cases in a series reported by Dusser et al.[9] In children, symptoms and signs can be difficult to detect. Hemiparesis may present as a limp, or asymmetry in the use of the hands. Hemianopia may manifest as lack of awareness of people approaching from the side. One feature of childhood stroke, which is rarely seen in adults, is seizure. Seizures may develop shortly after hemiparesis. In this case series, the patient reported in case 1 presented with right-sided weakness and was initially misdiagnosed as suffering from brachial neuritis. Similarly, the initial diagnosis for the patient in case 2 was febrile convulsion. Careful examination might have revealed left limb preference earlier. The patient in case 5 was admitted for residential care because of developmental regression and multiple cerebral infarcts. The diagnosis of multiple strokes due to MELAS was reached only when further investigations were carried out.

After confirmation of stroke by imaging, comprehensive investigation to determine the most likely predisposing cause is necessary.[1,3-7,10] The investigations utilised are summarised in the Box. In children, echocardiography and angiography are important diagnostic tools. Magnetic resonance angiography was completed for most patients in this case series, and confirmed the diagnosis of Moyamoya disease in one child. Conventional catheter angiography was performed for the patient in case 3 and demonstrated vertebral artery dissection. Subsequently, her disease progress was monitored by MRA.

Acute management of paediatric stroke generally follows the guidelines for management of ill children. The

Table. Predisposing causes for paediatric ischaemic stroke

Embolism	
Cardiogenic embolism from congenital heart disease, eg ventricular septal defect, atrial septal defect, patent ductus arteriosus, coarctation of the aorta, tetralogy of fallot	
Septic embolism, eg from bacterial endocarditis	
Complication of arterial dissection	
Thrombosis	
Vascular dysplasia	Moyamoya disease
	Fibromuscular dysplasia
	Sturge-Weber syndrome
Vascular trauma	Neck injury/intra-oral trauma
	Arterial dissection
Vasculitis	Related to local head/neck infections, eg tonsillitis, meningitis
	Related to systemic infection, eg postvaricella, AIDS, coxsackie A9 virus
	Autoimmune disorders, eg systemic lupus erythematosus, polyarteritis nodosa, Takayasu arteritis
	Isolated angiitis of the central nervous system
Vasospasm	Associated with drug abuse, eg cocaine abuse
Haematological	Polycythaemia, eg from cyanotic heart disease, from dehydration
	Sickle cell disease
	Thrombocytosis
	Presence of antiphospholipid antibodies,* eg lupus anticoagulant, anticardiolipin antibodies
	Abnormal anticoagulation, eg protein C deficiency, protein S deficiency, antithrombin III deficiency, factor V Leiden mutation,† plasminogen deficiency
	Hypercoagulable state, eg lymphoreticular cancers, disseminated intravascular coagulation
Metabolic disorders	Homocystinuria
	Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes
	Carbohydrate-deficient glycoprotein disorder
	Organic acidaemia
	Hyperlipidaemia
Atherosclerosis	

* Antiphospholipid antibodies were first associated with thrombotic or embolic cerebrovascular events in patients with systemic lupus erythematosus but have since been identified in stroke patients who do not have other evidence of an underlying immune-mediated illness. These antibodies are now considered an independent risk factor for cerebral thrombosis

† Protein C, together with cofactor protein S, inhibits the activated form of coagulation factors VIII and V. Antithrombin III inhibits activated factor X and thrombin. Thus, deficiency of either antithrombin III, protein C, or protein S are risk factors for thrombosis. A further disorder due to mutation of factor V is known to be related to thrombosis. Its presence is indicated by increased activated protein C resistance

Evaluation of stroke aetiology in children

Imaging
Computed tomography brain scan
Magnetic resonance imaging brain scan
Magnetic resonance angiography brain scan
Cardiac echocardiography
Carotid ultrasound
Conventional catheter angiography (if indicated)

Blood
Complete blood count
Renal function tests
Liver function tests
Glucose
Erythrocyte sedimentation rate
Prothrombin time, activated partial thromboplastin time
Immunoglobulin level
C3
Rheumatoid factor
Antinuclear factor
Anti-ds DNA
Lupus anticoagulant
Anticardiolipin antibody
Protein C*
Protein S*
Antithrombin III*
Activated protein C resistance*
Lipid profile
Haemoglobin pattern (if indicated)
Sepsis investigation (if indicated)
Viral titre (if indicated)
Relevant metabolic studies (if indicated)
Toxicology screening (if indicated)

* Levels of protein C, protein S, antithrombin III, or activated protein C resistance may be abnormal after an acute stroke episode. Repeated testing several months later together with testing of the parents may be required

use of anticoagulation is controversial. There is a lack of research on the use of anticoagulants in children. Despite this, use of heparin or low molecular weight heparin may be considered in children with cardiac embolism, arterial dissection, coagulation disorders, and recurrent stroke.[8,10] Anticoagulant treatment may be indicated in a child with progressive deterioration, or during initial evaluation of a new cerebral infarction.[8] Low-dose aspirin (3-5 mg/kg) is recommended if anticoagulation is not given.[1,8] In this case series, the patient in case 1 had a left internal capsule infarct and was initially treated with low-dose molecular weight heparin for 5 days. This was followed by treatment with aspirin 300 mg daily. The patient in case 2 had a massive left cerebral infarct concurrently with focal haemorrhage and hence, neither heparin or aspirin were given. The patient in case 3 with left vertebral artery dissection received heparin and warfarin as acute treatment.

In adults, treatment with aspirin for prevention of secondary cerebral vascular events has been shown to be effective.[11] Although paediatric data are lacking, it is reasonable to start treatment with low-dose aspirin in children who have a history of ischaemic stroke.[1,10] Three of the patients received aspirin prophylaxis (cases 1, 3, and 4).

Identification of the predisposing causes for cerebrovascular disorders in children is very important, as some respond to treatment, thus reducing the risk of subsequent strokes. The patient in case 4 was found to suffer from Moyamoya disease. Moyamoya disease is characterised by progressive narrowing of the intracranial internal carotid arteries. Left untreated, the disease may result in repeated neurological insults.[12] After the acute stroke episode, the patient in case 4 was given aspirin prophylaxis and later he received encephalo-duro-arterio-synangiosis, a surgical procedure for enhancing cerebral perfusion.

The patient in case 5 suffered from MELAS. Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes is a mitochondrial disorder resulting from mutation of maternal mitochondrial DNA. Systems other than the central nervous system may also be involved in this disorder.[13] Administration of substances such as coenzyme Q10, vitamins K1 and K3, vitamin C, and thiamine help to augment the residual mitochondrial function and prevent progression of the disease. The patient in case 5 did not receive these coenzymes and vitamins. His clinically healthy younger brother was found to have the same mutation in mitochondrial DNA and was given coenzyme Q. The brother has maintained good health and normal development to date.

Specific measures for the following conditions as outlined can reduce the incidence of stroke in children:
(1) periodic blood transfusion for patients with sickle cell disease[1,3,4,6];
(2) long-term anticoagulation for selected patients with congenital or acquired heart disease[6,7];
(3) long-term anticoagulation for selected patients with hypercoagulable disorders[1,4,6];
(4) a trial of pyridoxine or a special diet for patients with homocystinuria[9]; and
(5) immunosuppressant and anticoagulant treatment for patients with antiphospholipid syndrome.[3,6]

Rehabilitation can begin immediately after the acute phase. Children with stroke have unique rehabilitation considerations. For instance, special disability scores are used in children.[14] In addition to assessing the patient's physical disability, the overall functional, cognitive, and behavioural impairment should also be assessed and a rehabilitation programme with definite goals set. These goals may need to be modified as the child ages. Input from a paediatric neurologist, physiotherapist, occupational therapist, speech therapist, teacher, psychologist, social worker, family, and others may be required to establish an appropriate rehabilitation programme.[15,16] The prognosis after stroke in children is relatively positive compared with that of adults, probably due to brain plasticity. Positive outcomes were, indeed, observed for the patients reported in cases 1, 2, and 4.

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