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Evaluation of Pediatric Stroke Patients

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Abstract

Objective: Childhood stroke is common than expected due to increased availability of imaging studies. We aim to evaluate clinical and radiologic findings of stroke.

Method: In this study 23 children (15 boys, 8 girls) aged 3 months to 17 years were included. Clinical findings and etiologic causes of the patients with radiologic confirmed stroke and treatment options are considered.

Result: Clinical signs of our patients include hemiparesis, seizure, speech disturbance, headache, facial nerve palsy, confusion, cerebellar signs, syncope, visual field defect, headache. Most frequent presenting symptoms are hemiparesis and seizure.

Conclusion: In our study most frequent risk factors are prothrombic states, infection, vasculopathy, cardiac disease, trauma, vascular malformation respectively.

Keywords: Stroke; Child; Central nervous system

Introductıon

Childhood stroke is a significant cause of morbidity that leads to residual neurologic impairement [1]. İncidence is between 2-13/100000 children per year [2]. Etiology and risk factors are numerous and different from adults [3-6]. No single risk factor predominates stroke in childhood [5]. Childhood stroke is more common than expected because of increased availability of imaging studies. Although the incidence is increasing, the diagnosis of stroke is usually delayed due to variable presenting signs and symptoms and misdiagnosis. Therefore no distinct guideline exists for the treatment as for adults. In this study we investigated clinical findings and etiologic causes of the patients with radiologically confirmed stroke.

Material and Methods

In this study 23 children (15 boys, 8 girls) aged 3 months to 17 years admitted with acute neurological symptoms of stroke to the child neurology deparment at Eskışehir University, Faculty of Medicine. They were retrospectively evaluated. The diagnosis of stroke was made by both clinical and neuroimaging findings. All patients had baseline investigations including complete blood count, sedimentation rate, liver function, serum electrolytes, total lipid, cholesterol profiles, electrocardiography, echocardiography, thrombophilia testing containing protein C, protein S, antithrombin III, activated protein C resistance, factor V leiden mutation, MTHFR polymorphism, homocysteine, lipoprotein a, Lupus anticoagulant, partial thromboplastin time, prothrombin time, Factor 8. Echocardiography (ECHO), electroencephalography (EEG) (when necessary), magnetic resonance imaging (MRI) with diffusion weighting series or computerized tomography (CT) studies were performed. Magnetic resonance angiography (MRA) and magnetic resonance venography (MRV), conventional arterial angiography (when necessary) were performed for some patients. The diagnostic criteria of arterial ischemic stroke was described as sudden onset transient or permanent focal neurologic deficit lasting more than 24 hours with definite infarction area in a vascular distribution on CT or MRI [7]. Patients with neonatal stroke, traumatic brain hemorrhage, intracranial hemorrhage without ischemic infarction were excluded.

Results

Six patients (5 male and 1 female) were younger than two years of age. 17 patients (7 female and 10 male) were older than 2 years of age.

In our study risk factors are prothrombic states (14 patients), infection (10 patients), vasculopathy (9 patients), cardiac disease (4 patients), trauma (3 patients), vascular malformation (2 patients). Clinical signs included hemiparesis, seizure, speech disturbance, headache, facial nerve palsy, confusion, cerebellar signs, syncope, visual field defect, headache.Most frequent presenting signs were hemiparesis (11/23) and, seizure (10/23). Five patients with seizure were younger than two years of age. One patient with hemipareis had died because of sudden cardiac arrest due to restrictive cardiomyopathy (Table 1). Cranial MRI revealed middle cerebral artery infarctıon in 10 patients; basal ganglia infarction in 2 patients; thalamic infarction in 5 patients, one of them also had multiple cranial infarctions; cerebellar infarction in 3 patients also one had multiple cranial infarctions; sinovenous thrombosis in 3 patients, vascular malformation in 1 patient, multiple infarctions with thalamic involvement in 1 patient, Moya Moya disease in 1 patient, basillary artery occlusion in 1 patient. MRA or conventional angiography obtained from 10 of 16 patients with arterial ischemic stroke in whom 8 of them revealed vasculitis and one of them revealed Moyamoya disease, one of them was normal (Table 2 and Figure 1).

Discussion

The clinical presentation of stroke varies according to the age, cause and involved arterial territory [7,8]. Most children with stroke present with hemiparesis. Children may have gaze palsy, visual field defects, head turning to the lesion, seizures with or without focal neurologic deficit, deterioration in the level of consciousness, aphasia, ataxia, dizziness, tremor, nystagmus and, vomitting; stroke in posterior circulation can present as ataxia, vertigo and vomiting [9-11]. In ınfancy, typıcal presentation includes seizure, lethargy, apnea often without focal neurologic deficits where as focal weakness is the most common presenting sign of stroke beyond infancy [8,9]. Headache, vomiting,

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§Clinical features:	Patients ≤ 2years of age number(%)	Patients >2 years of age number(%)
Hemiparesis	7	10
Seizure	5	5
Headache	-	4
Speech disturbance	-	3
Facial nerve palsy	2	3
Ataxia		4
Confusion	3	3
Visual field defect	-	1
Syncope		2
‡Risk factors:		
Prothrombotic states	6	10
Vasculopathy	3	10
Infectıon	5	6
Trauma	1	2
Cardiac disease	2	2
Treatment:		
Unfractionated heparin	2	5
LMWH	1	3
Aspirin	-	4
Warfarin	1	6
Outcome with hemiparesis	6	5
§:more than one sign in a patient; ‡: more than one risk factor in a patient.		

Table 1: Clinical features of children with stroke.

Vascular territory		Patients ≤2years of age	Patients >2 years of age	Clinical features
MCA	Cortical involvement	5	3	Confusion, headache, vomiting, hemiparesis, convulsion, central facial nerve palsy
	Putamen+globus pallidus	1	2ϕ	Hemiparesis
ACA	Caudate nucleus		1§	Hemiparesis, central facial nerve palsy
PCA	Thalamus	1	1•	Hemiparesis, convulsion
Basillary artery			1	Confusion, syncope
Cerebral artery hypoplasia			1	Confusion, hemiparesis, speech disturbance, ataxia, central facial nerve palsy
Cerebellar a.	PICA Superior cerebellar		1 1	Headache, vertigo Vertigo, speech disturbance, ataxia, vomiting
Multiple cranial infarction	Left MCA+right cerebellar artery		1	Speech disturbance, confusion, vomiting, ataxia
	Left PCA(with thalamus)+right cerebellar artery		1	Ataxia, visual field defect, hemiparesis
Moya Moya			2	Confusion, hemiparesis, syncope
SVT	Superior sagital sinus		1	Convulsion, hemiparesis
	Cavernous sinus		1	Headache, vomiting, proptosis, painful eye movements
	Lateral Sinus			headache

§: with globus pallidus and putamen
ϕ: with caudate nucleus involvement
•: with MCA involvement

Table 2: Vascular territory and clinical findings.

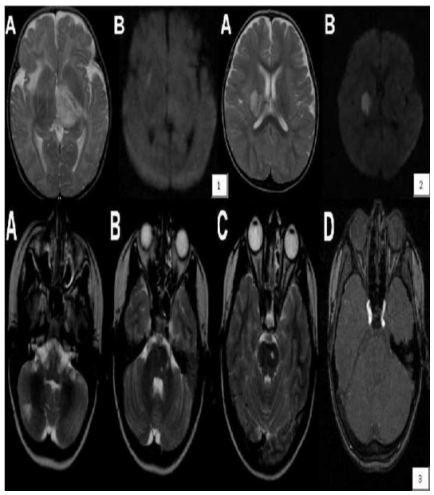

Figure 1: MRI of some patients. 1A) T2 hyperintensity in left thalamus, right external capsule; 1B) High T2 signal intensity in right external capsule, left thalamus on DWI; 2A) T2 hyperintense area in right putamen, genu-posterior limb of internal capsule, thalamus; 2B) İnfarct area at the same level on DWI; 3A) Multiple hyperintense areas in the right cerebellar hemisphere; 3B) Left Pons, middle cerebellar pedincle, mesencepahlon
3C) Chronic ischemic changes; 3D) low flow signal in the basillary artery suggesting severe stenosis on MRA.

decreased level of consciousness, seizures, language and speech difficulties may be seen with hemorrhagic stroke [11]. Headache, seizure, lethargy, or focal or generalized neurologic deficit may occur with cerebral sinovenous thrombosis [7]. Todd's palsy, hemiplegic migraine, meningoencephalitis, tumors, acute disseminated leukoencephalopathies, cerebellitis, alternating hemiplegia, metabolic disorders, epilepsy, psychogenic disorders, traumatic extradural and subdural hematomas, migraine should be considered in differential diagnosis [9,10]. Risk factors are variable [3-6]. Congenital or acquired heart diseases, hemotologic, metabolic disorders, infections are the most frequently seen risk factors for stroke in children. It may be related with prothrombic, inflammatory, immune-mediated, or metabolic causes [12-16], mechanical trauma and distortion of blood vessels with local thrombus formation [4], non atherosclerotic arteriopathies (especially focal transient arteriopathies) are the most common risk factor for childhood stroke [17]. Head and neck infections may cause cerebral sinovenous thrombosis [18]. In our study 3 patients had sinovenous thrombosis due to bronchitis, pansinusitis, mastoiditis with prothrombotic risk factors. Two of our SVT patients had headache and seizure.

Congenital heart disease is frequently seen risk factor in childhood stroke. Its incidence is between 15-30% [19]. Major congenital cardiac malformations may predispose children to embolic state; also hypoxia, hypotension, polycythemia may increase stroke with underlying cardiac disease [19]. Patent foramen ovale is seen four times higher than general population at pediatric stroke [20]. Patent formane ovale prevelance has been increased in children and young adults who do not have other risk factors [19]. In our study three patients had patent foramen ovale, restrictive cardiomyopathy, ASD and mitral insufficiency due to rheumatic heart fever. Congenital or acquired prothrombotic abnormalities are present in 30-50% of childhood arterial ischemic stroke and 33% to 96% of sinovenous thrombosis at children [4]. Factor V leiden mutation, protein C defficiency, lipoprotein a, lupus

anticoagulant (LA), MTHFR C677T polymorphism may cause stroke formation [4,21]. MTHFR C677T and 1298C alleles could also play a role by tissue changes in the arterial wall structure, with consecutive blood extravasation resulting in hemorrhagic stroke [21-23]. Acquired prothrombotic states include systemic lupus erythematosus, malignancy, nephrotic syndrome, exogenous prothrombotic medications, sepsis, viral infections for example varicella [4,18]. In the present study 12 of 19 patients had prothrombotic abnormalities. Mutations of MTHFR A1298C, C677T were found with other risk factors.

Transient cerebral arterıopathies (TCA) are the most common type of arteriopathy in pediatric stroke. Transient cerebral arteriopathy is acute vasculitis of large and medium vessels caused by infections, mostly viral origin and/or inflammation and 44% of TCA are associated with varicella zoster infection seen within 12 months prior to acute ischemic stroke causing post-varicella arteriopathy [7,23]. In our study three patıents with transient arteriopathy have history of varicella infectıon 2 to 5 months before the symptoms. Progressive arteriopathies such as vasculitis and Moyamoya disease are rare which is characterized by progressive cerebrovascular occlusion with spontaneous development of collateral vessel formatıon called Moyamoya vessels [23]. It is rarely seen in childhood. Moyamoya disease mostly manifests as cerebral ischemia [24]. It is charecterized by bilateral stenosis or occlusion at the terminal portion of the internal carotid artery (ICA), at the proximal portion of the anterior (ACA) and middle cerebral arteries (MCA) and abnormal net-like vessels at the base of the brain [24]. Moya moya may be seen secondariliy in children with sickle cell disease, neurofibromatosis, Down syndrome. Children mostly present with acute cerebral infarction but also transient ischemic attacks, alternating hemiplegia, chorea and other movement disorders may be seen. Language dysfunction, chronic headache may develop [25].

One patient with Moyamoya disease was presented as syncope that reflects transient ischemic attack. We could not find any etiologic factor underlying the disease. The second patient with Moyamoya had Down syndrome. She had admitted with acute neurologic deficit and she had high factor 8 level.

Stroke should be considered in children with new onset seizure combined with focal neurologic deficit [26]. Brain MRI should be obtained to demonstrate parenchymal infarcts reflecting arterial territories [7]. A normal CT within 48 hours of symptom onset does not rule out the diagnosis of arterail ischemic stroke [7]. Brain MRI (magnetic resonance imaging) is the investigation of choice, CT(computerized tomography) may exclude hemmorhage ıf MRI is not available. After acute period conventional angiography must be obtained to exclude arteriovenous malformation, aneurysm in cerebral hemmorrhage, when magnetic resonance angiography (MRA) is normal to rule out small vessel disease [9,10]. Brain MRI with diffusion weighted images is very useful in diagnosing ischemia at earlier stages of arterial ischemic stroke. If MRI finding is consistent with venous infarction magnetic resonance venography (MRV) should be performed because cerebral venous sinus thrombosis may be asociated with hemmorhagic stroke [9,27]. There is no standart treatment protocol for childhood stroke. Treatment with anticoagulants and antiplatelet agents are controversial and there are few data about treatment protocol for children [28,29]. Anticoagulation therapy may be used in children with proven arterial dissection, cerebral sinus venous thrombosis and cardiac disease [29].

One patient diagnosed SVT treated with aspirin, second one with unfractıonated heparin then continued with warfarin. Eleven patients with arterial ischemic stroke had been treated with antiagregating and anticoagulating agents. Prognosis of pediatric stroke remains controversial. Pediatric stroke study group reported a mortality rate of 3.4% to 20% [9]. Survivors of acute stroke may have long term physical disabilities and cognitive impairment [9]. Most common neurologic sequela is hemiparesis [9]. In our study 9 of 19 patients admitted with hemiparesis, one patient died, two of them improved with mild monoparesis of the hand; 6 patients had hemiparesis as the sequela, one patient had visual field defect. There is no clear laboratory testing for the assesment of pediatric stroke. In differential diagnosis of any child presenting with new onset focal deficits, altered speech and consciousness, stroke should be evaluated. Childhood presenting symptoms of the stroke, prognosis and, treatment may be different. Patient based treatment plan must be formed for the management.

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