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Original Article

Childhood Stroke: Results of 130 Children From a Reference Center in Central Anatolia, Turkey

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ABSTRACT

BACKGROUND: Although stroke among children is rare, it can cause significant morbidity and mortality. We aim to share our experience of children with arterial ischemic stroke. **METHODS:** The initial symptoms, demographical features, risk factors, neurological examination, neuroradiological findings, and clinical follow-up data of 130 Turkish children seen between 2002 and 2013 were retrospectively analyzed. **RESULTS:** Sixty-eight patients were male. Thirty of the children were aged from 1 to 12 months (seven of them died in this period). Focal neurological signs were the most common presentation, and hemiplegia or hemiparesis were the most common focal signs. Underlying risk factors were detected in 103 patients. Infections and congenital heart disease were the most common risk factors. Seven of the nine children with recurrent arterial ischemic strokes had one or more underlying diseases (moyamoya disease in two children along with factor V Leiden mutation, tuberculous meningitis, congenital heart disease, homocystinuria, and hemiconvulsion-hemiplegia-epilepsy syndrome). The arterial ischemic stroke was located in the middle cerebral circulation in 68 (36 left and 32 right) and in the posterior cerebral artery in 41. Eighteen children died. The neurological outcome was assessed in 98 children. Of these children, 66 children have neurological deficits and 52 children have seizures. Stroke in the first year of life is more often fatal. Recurrent stroke is associated with poor prognosis. **CONCLUSION:** Tuberculous meningitis is still a risk factor for arterial ischemic stroke in Turkey. Arterial ischemic stroke in the first year of life and recurrent arterial ischemic stroke represent poor prognostic features.

Keywords: arterial ischemic stroke, children, prognosis, clinical features, neuroradiological findings

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Introduction

Childhood stoke is a major topic of interest for pediatric neurologists, hematologists, and other clinicians. The term “stroke” is defined by the World Health Organization as a clinical syndrome typified by rapidly developing signs of focal or global disturbance of cerebral functions, lasting >24 hours or leading to death, with no apparent causes other than of vascular origin.[1] Pediatric stroke is an

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important cause of long-term disability, including seizures in 15%, long-term significant neurological deficits in 60-70%, and death in 6-10%.[2-10] Risk factors for stroke in childhood are different from those traditionally observed in adults. Pediatric stroke has heterogenous risk factors, but in approximately one third to one half of children no specific cause can be determined.[2-10] The incidence of childhood stroke from population-based studies is estimated at 2.1-13.0 per 100,000 children per year.[2,3,11-19]

We present our experience of children with arterial ischemic stroke (AIS). This study summarizes the etiology, risk factors, initial complaints, clinical features, laboratory, radiological findings, and clinical follow-up data of the children with ischemic stroke.

Patients and Methods

Erciyes University Children's Hospital is a tertiary hospital in the city of Kayseri, in Central Anatolia, Turkey. This hospital is the sole pediatric referral center, serving a population of approximately 10 million, including the surrounding cities in the Cappadocia region.

Acute AIS was defined as an acute focal neurological deficit with evidence of cerebral infarction in an arterial distribution on brain imaging, regardless of duration of the clinical signs. The diagnosis of AIS was confirmed in all patients by cranial imaging studies. One hundred thirty consecutive children with AIS, followed in Erciyes University Children's Hospital, were retrospectively enrolled in to the study from January 2002 to January 2013. Ethical permission for a review of all records was granted by the Ethics Committee of Erciyes University.

Children aged <1 month and >16 years, who had hemorrhagic stroke, transient ischemic attack, hypoxic-ischemic encephalopathy, neonatal stroke, and congenital hemiplegia, were excluded from the study.

A full history was determined for all patients, with special emphasis on the onset of stroke, its clinical presentation, any history of previous similar attacks, or a history of a chronic systemic illness. In addition, the family histories were also evaluated for evidence suggestive of strokes in all enrolled subjects. Patients were examined carefully to evaluate their neurological condition and to detect any evidence of systemic illness. Age, sex, neurological manifestations, other clinical features, and radiological findings on admission and during follow-up were recorded. Baseline investigations comprised testing for complete differential blood count, blood glucose, electrolytes, triglycerides, total cholesterol, C-reactive protein, chest radiography, electrocardiography, and echocardiography at admission. Additional investigations included hematologic, lipometabolic, coagulation, and metabolic screening, including liver function test, blood urea nitrogen, creatinine, serum electrolytes, serum iron level, serum iron binding capacity, serum ferritin level, complete blood count, sedimentation rate, protein C, protein S, fibrinogen level, antithrombin III level, factor VIII, factor IX, activated protein C resistance, prothrombin time, activated thromboplastin time, lupus anticoagulant, anticardiolipin factors, homocysteine levels, cerebrospinal fluid analyses, and microbiologic examination by microscopy, culture, polymerase chain reaction, D-dimer, and serum virus antibody tests. Genetic investigations were conducted for factor V Leiden G1691 A, factor II G20210A, and methyltetrahydrofolate reductase (MTHFR) C 677 T. All patients were investigated by brain computed tomography (CT) or magnetic resonance imaging (MRI) with or without conventional angiography, magnetic resonance angiography, or CT angiography, and carotid Doppler ultrasonography for identification of etiology. All imaging studies were evaluated by the same pediatric neuroradiologists (H.D. and A.C.).

Results

One hundred thirty consecutive children with AIS between January 2002 and January 2013 were retrospectively analyzed. Sixty-eight patients (52%) were male. The male-to-female ratio was 1:1. The age of first episode varied between 1 month and 16 years. The median age at the first stroke was 58 months. When the patients' data were assessed, the following ages of admission were determined: 30 of the children who were admitted were aged from 1 to 12 months (seven children died in this period); 28 of the children who were admitted were aged from 13 to 36 months (four children died in this period); 26 of the children were aged from 36 to 60 months (two children died in this period); 27 of the children were aged from 6 to 10 years (three children died in this period); and 19 children who were admitted were aged >11 years (two children died in this period). One child with moyamoya disease had a sibling with the same disease.

Focal neurological signs (87%) were the most common presentation and hemiplegia and/or hemiparesis was the most common focal sign. Focal or generalized convulsions were the second most common presentation (58%) (Table 1).

Underlying clinical conditions or circumstantial risk factors were detected in 103 patients (79%); 27 patients (21%) did not have known risk factors (Table 2). The risk factors are listed in Table 2. Four patients (3%) had more than one risk factor. The risk factors were cardiac disease plus MTHFR mutation, cardiac disease plus elevated homocysteine level, cardiac disease plus factor V Leiden mutation plus, and factor V Leiden mutation plus prothrombin 20210A mutations. Nine children (7%) had recurrent episodes of stroke. The distribution of interval between the recurrent episodes of AIS was 1-36 months, with a median time of 6 months.

Associated conditions were identified in seven children with recurrent AIS. These children had moyamoya disease (two children), factor V Leiden mutation, tuberculous meningitis, congenital heart disease, homocystinuria, and hemiconvulsion-hemiplegia-epilepsy syndrome. We were unable to identify a risk factor in two of the patients with recurrent AIS. The five most common risk factors were infectious diseases (18%), cardiac diseases (13%), MTHFR polymorphisms (10%), trauma (8%), and moyamoya disease (5%) (Table 2). Three children with AIS who underwent surgery for spinal dysraphism in infancy subsequently developed

TABLE 1.
Presenting Complaint Among 130 Children With Ischemic Stroke

Symptom and/or Sign	n
Fever	16
Seizure	76
Diffuse neurological signs	
Altered state of consciousness	19
Headache	8
Nausea and/or vomiting	14
Focal neurological signs	
Hemiparesis and/or hemiplegia	63
Cranial nerve palsy	18
Speech impairment	9
Visual impairment	2
Extremity weakness, other	14
Gaze palsy	7