Stroke in Children Within a Major Metropolitan Area: The Surprising Importance of Intracerebral Hemorrhage

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Abstract

Our objective was to determine the incidence rate of stroke and stroke subtypes in children. We reviewed the medical records, autopsy records, and brain imaging studies of all children with a possible stroke within the Greater Cincinnati metropolitan area population of nearly 1.3 million during 1988 and 1989. Traumatic brain hemorrhages and germinal matrix hemorrhages were excluded. Of the 295,577 children in Greater Cincinnati, medical records of 178 children were screened. Sixteen cases (13 whites and three blacks) less than age 15 years fit strictly defined criteria for first-ever stroke. The incidence rate for cerebral infarction was 1.2 cases per 100,000 (95% confidence interval, 0.3 to 2.0). The combined incidence rate for intracerebral hemorrhage and subarachnoid hemorrhage was 1.5 cases per 100,000 children (95% confidence interval, 0.4 to 2.3). The incidence rate of all stroke in white children was 2.6 cases per 100,000 (95% confidence interval, 1.2 to 4.1), compared to 3.1 per 100,000 in black children (95% confidence interval, 0 to 6.6). The combined 30-day mortality for intracerebral hemorrhage and subarachnoid hemorrhage was 22% (two of nine) compared to 14% (one of seven) for cerebral infarction. We conclude that in contrast to the picture in adults, hemorrhagic stroke among infants and children is at least as common as ischemic infarction. (*J Child Neurol* 1993;8:250–255).

A study of children in Rochester, Minnesota, during the period 1965 to 1974 has provided the only population-based estimate of how commonly stroke and stroke subtypes occur among children.[1] This study, which included a mean population of only 15,834 children, was completed prior to the availability of brain computed tomographic (CT) scans. The stroke incidence rate of 2.5 cases per 100,000 children was calculated from a total of only four incidence cases of stroke identified during a 10-year period. Subsequently, CT and magnetic resonance image (MRI) scanning of the brain have substantially improved identification of stroke and stroke subtypes among adults, particularly the identification of hemorrhagic stroke.[2,3]

The Greater Cincinnati metropolitan region had a population of 295,577 children under the age of 15 years during 1980, of which 48,663, or 16%, were black, compared to 15% of children for the United States population during 1980.[4] CT or MRI is available at all area hospitals and is part of the standard stroke evaluation within the community. Two epidemiologic studies of hemorrhagic stroke in adults have already been reported for the same study region.[5,6]

The objectives of the present study were to determine (1) how commonly stroke and stroke subtypes occur in a well-defined and large population of children, (2) whether the incidence rate of stroke differs by race or sex, and (3) what the short- and long-term outcomes are following stroke in children.

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Methods

We screened all inpatient, outpatient, and autopsy records of patients at the Cincinnati Children's Hospital Medical Center who had a potential stroke during 1988 or 1989. The Children's Hospital Medical Center serves as the primary facility in the five-county region for the evaluation and care of hospitalized pediatric patients (361 beds, 12,679 admissions per year), as well as those patients who require more than routine outpatient care (277,373 outpatient visits per year). In addition, we screened the inpatient records of all other Greater Cincinnati–Northern Kentucky hospitals that admit children (St Elizabeth Medical Center Hospitals, 33 beds, 1545 admissions per year; Mercy Fairfield Hospital, 30 beds, 180 admissions per year; and St Luke East and West Hospitals, 29 beds, 721 admissions per year) and the coroner's offices of the five study counties for the same time periods.

Medical records to be screened were identified by the following codes from the International Classification of Disease, 9th revision, coding system: 430–438, all cerebrovascular disease diagnoses; 746, arteriovenous malformation; 342, secondary hemiplegia; and 346, migraine (classic, common, hemiplegic, and ophthalmoplegic). Both primary and secondary discharge diagnoses were included. The inpatient and outpatient records of children registered in the sickle cell disease clinic were also reviewed. *Cerebral infarct* was defined as the sudden onset of a neurologic deficit, localized to the brain, which lasted 24 hours or more. Accompanying CT or MRI studies or autopsies showed changes consistent with brain infarction or were normal. *Intracerebral hemorrhage* was defined as a clinical history and examination consistent with an intracerebral hemorrhage (sudden onset of headache, change in level of responsiveness, or focal neurologic deficit) that was accompanied by a focal collection of blood within the brain parenchyma on CT scan, MRI scan, or at autopsy. Traumatic intracerebral hemorrhage and perinatal strokes including germinal matrix hemorrhages were excluded. Hemorrhagic infarcts were classified as infarcts. *Subarachnoid hemorrhage* was defined as nontraumatic subarachnoid hemorrhage on CT scan or at autopsy, or a clinical history and examination consistent with subarachnoid hemorrhage (sudden onset of severe headache or changes in level of responsiveness) with xanthochromia and many red blood cells in the cerebrospinal fluid. *Transient ischemic attack* was defined the same as cerebral infarction except the deficit lasted less than 24 hours. Cases with both intracerebral hemorrhage and subarachnoid hemorrhage were categorized as subarachnoid hemorrhage if the source of bleeding was an aneurysm or if the neuroradiologist's review indicated a subarachnoid origin of bleeding, and as intracerebral hemorrhage if a parenchymal source of bleeding was most likely. Cases with hemorrhage limited to the ventricles were classified as intracerebral hemorrhage.

Inclusion as an incidence case of first-ever stroke required meeting the criteria for a stroke subtype, residence at a zip code within the five-county region, stroke onset during 1988 or 1989, age less than 15 years, and no prior strokes. The age criterion of less than age 15 years was chosen to compare our findings with incidence rates from the Rochester, Minnesota, study, which included only children less than age 15 years. Additionally, we could not rule out the possibility that 17- and 18-year-old stroke patients could have been treated at one of the other 14 area adult hospitals during 1988 or 1989.

The 1980 US census by age, sex, and race for each of the five counties was used for the population denominators during 1988 and 1989. Although age breakdowns of the 1990 US census were not yet available, the overall population of the five-county region increased by only 2.5% between 1980 and 1990, and the black proportion rose from 13.5% to 14.4%. Confidence intervals for the incidence rates were calculated using a Poisson distribution.[7] The 30-day survival for stroke subtypes was calculated by Kaplan Meier life-table analysis.[8] Outcome was graded as follows: normal, no neurologic deficit; mild, neurologic deficit that minimally affected function; moderate, neurologic deficit that affected function or delayed developmental milestones; severe, requiring near-total care; or death.

Results

Of 178 medical records screened, 16 cases (seven white and two black boys and six white and one black girl) were classified as incidence cases, for an overall yearly incidence rate of 2.7 strokes per 100,000 children (95% confidence interval, 1.4 to 4.1). The clinical presentation, radiographic findings, causes and associated conditions, and outcome at the last recorded medical evaluation for these 16 children are listed in Table 1. The incidence rate of all stroke was similar for blacks and whites, as well as for boys and girls (Table 2). The combined incidence rate for intracerebral hemorrhage and subarachnoid hemorrhage of 1.5 cases per 100,000 children (95% confidence interval, 0.4 to 2.3), was slightly greater than the incidence rate for cerebral infarction of 1.2 per 100,000 (95% confidence interval, 0.3 to 2.0).

A cause was identified for all but one of the nine incidence cases of intracerebral hemorrhage or subarachnoid hemorrhage; arteriovenous malformation (three cases), cavernous hemangioma (two), hemorrhage into a hypothalamic glioma (two), and cerebral aneurysm (one). A potential cause or an associated risk factor was identified for all but two of the ischemic strokes (Table 1). Vascular thrombosis associated with infection or dehydration and congenital heart disease were the most common associated conditions.

The combined 30-day mortality for intracerebral and subarachnoid hemorrhage incidence cases was 22% (two of nine) as compared to 14% (one of seven) for cerebral infarction. All three deaths occurred within 2 days of stroke onset. Of the 13 survivors, two were considered neurologically normal, two had a mild neurologic deficit, seven had a moderate deficit, and two had a severe deficit (Table 1).

TABLE 1
Demographic and Radiographic Data, Causes, and Outcome in 16 Incidence Cases of Childhood Stroke

Patient No.	Age, Sex, Race	Type Stroke	Clinical Presentation	Imaging Studies	Causes/ Associated Condition	Follow-up After Stroke	Neurologic Function at Last Recorded Follow-up
1	3 wk, M, W	IVH	Lethargy, high-pitched scream upon movement, bilateral Babinski reflexes	Hemorrhage into R lateral ventricle*	Unknown	22 mo	Slowed motor and mental develop-ment
2	4 yr, M, W	ICH	R hemiparesis, dysarthria	L frontal-parietal hemorrhage*†	Cavernous hemangioma	4 mo	Dysarthria only
3	5 yr, F, W	ICH, SAH	Dysarthria, R hemiparesis while running	L posterior-frontal ICH and SAH†	AVM, L anterior cerebral artery distribution	25 mo	Mild right hemipare-sis
4	8 yr, F, W	ICH	Seizure, R hemiparesis, then unresponsive, GCS-4	Deep L frontal hemorrhage*†	L frontal AVM	11 mo	Dysarthria, mild aphasia, walks with assistance only
5	9 yr, M, W	ICH, SAH	Severe headache, muscle rigidity, unable to speak, arousable	SAH & hemorrhage L lateral ventricle†	AVM, aneurysm	4 mo	Some learning difficulties
6	12 yr, F, W	SAH, IVH	Sudden unresponsiveness, GCS-3	SAH & IVH*	Basilar tip aneurysm	Died 2 days after onset	—
7	14 yr, M, B	ICH	Sudden unresponsiveness, GCS-3, seizure in ER	R frontal lobe and panventricular hemorrhage*	Optic nerve glioma	8 mo	Unable to walk, aphasic, poor visual acuity
8	14 yr, M, W	ICH	Headache, visual blurring, syncope	L parietal-occipital ICH*	Cavernous hemangioma	14 mo	Normal

9	14 yr, M, W	ICH	Sudden unresponsiveness, eyes deviated to left	Hypothalamic tumor with ICH*	Hypothalamic glioma	Died 1 day after admission	—
10	6 wk, M, W	Infarct	Lethargy, seizure	Hemorrhagic infarct*	Sagittal sinus thrombosis, dehydration, 1 wk viral infection	11 mo	Spasticity of left extremities
11	3½ mo, M, B	Infarct	*Haemophilus influenzae* meningitis, decreased responsiveness	Large infarct in middle cerebral artery territory*	Meningitis	19 mo	Does not speak, walk, or crawl
12	2 yr, F, W	Infarct	Mild R hemiparesis	Deep L cerebral infarct*†	Unknown, subsequent migraine attacks	15 mo	Mild aphasia and hemiparesis
13	4 yr, F, W	Infarct	R hemiparesis	Bilateral deep basal ganglia infarcts*†	Cardiac embolism	26 mo	Moderate paresis of arm, clumsy walking
14	5 yr, M, W	Infarct	R hemiparesis, aphasia	R globus pallidus infarct†	Cardiac embolism	9 mo	Awkward gait, mild hemiparesis
15	9 yr, F, B	Infarct	Headache, quadranopia, ataxic gait	? Distal basilar artery thrombus, without stenosis on angiography*	Unknown, recurrent migraine attacks	17 mo	Normal
16	14 yr, F, W	Infarct	Diabetic ketoacidosis, unresponsive	L basal ganglia hemorrhagic infarct*†	Diabetic ketoacidosis protein C deficiency	27 mo	Hemiparesis, aphasia

IVH = intraventricular hemorrhage; ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage; AVM = arteriovenous malformation; GCS = Glasgow Coma Scale.
*Computed tomographic scan.
†Magnetic resonance imaging scan.

TABLE 2
Incidence Rates* for All Strokes in Children

	No. of Cases	Rate	95% CI
Whites	13	2.7	(1.2–4.1)
Blacks	3	3.0	(0–6.6)
Boys	9	3.0	(1.0–5.0)
Girls	7	2.4	(0.6–4.3)

CI = confidence interval.
*Rates per 100,000 population.

There were 13 additional cases of childhood stroke that were evaluated during 1988 and 1989 but did not meet the criteria for an incidence case: eight cases lived outside of the study region, four were age 15 years or older, and one had two prior cerebral infarcts. Of the 13 cases, there were three cases of intracerebral hemorrhage (one cavernous hemangioma, one arteriovenous malformation, and one optic nerve glioma), three cases of subarachnoid hemorrhage (two aneurysms, and one unknown), six cerebral infarcts (two cerebral vein thromboses, one sickle cell disease, one fibromuscular dysplasia, one disseminated intravascular coagulation, and one unknown), and one transient ischemic attack (mycoplasma infection).

Discussion

The yearly incidence rate of 2.7 strokes per 100,000 children in the Greater Cincinnati population during 1988 and 1989 exceeds the reported incidence rate of pediatric brain tumors, the second leading cause of cancer deaths among children.[9] Intracranial hemorrhage occurred as frequently as ischemic stroke, even excluding perinatal strokes such as germinal matrix hemorrhages, which occur in approximately half of premature infants less than 1750 grams in weight.[10] Of the 16 incidence cases in the Greater Cincinnati study, nine were hemorrhagic, as were three of the four incidence cases in the earlier Rochester study. These findings in children contrast markedly with strokes in adults, of which only 15% to 19% are due to hemorrhage.[2,11]

The similar incidence rates of childhood stroke in Rochester, Minnesota, during 1965 to 1974 (2.5 per 100,000 children)[1] and Greater Cincinnati during 1988 and 1989 (2.7 per 100,000) suggest that the frequency of stroke among children has not changed significantly during the past 25 years. However, such a comparison must be made cautiously. The Rochester incidence rates were calculated from a total of only four cases in a small all-white population over 10 years prior to the advent of CT. In addition, the incidence rate of stroke among children in the present study may still be an underestimate. Although all primary and secondary discharge diagnoses of stroke were screened, a few incidence cases associated with neoplasms, infections, or congenital heart disease could have been missed if the stroke was not coded as a secondary diagnosis.

The incidence rate of stroke was similar for blacks and whites, as well as for boys and girls. However, given the small number of cases, detecting statistically significant differences in the risk of stroke between races or sexes would be unlikely even if true differences are present. The US stroke mortality rates among black children less than age 15 years were higher than whites during 1980 to 1987.[12] Further population studies in children are needed to determine whether the higher mortality among blacks is due to an increased stroke incidence rate or to poorer outcome following stroke.

The causes of ischemic stroke were quite diverse. Infections, dehydration, and congenital heart disease were the conditions most frequently associated with cerebral infarction. A community study of childhood stroke in Japan also reported that infection or fever of unknown origin was the most commonly associated condition among children with cerebral infarction.[13] The small number of cases of cerebral infarction in our 2-year study does not include many other reported causes of ischemic stroke in children.[14]

Vascular malformations were the most common cause of intracerebral hemorrhage in the present study. Again, this contrasts with the predominance of ruptured intracranial aneurysms as a cause of subarachnoid hemorrhage[15,16] and chronic hypertensive vasculopathy as a cause of intracerebral hemorrhage[3,6] among adults. The Cooperative Aneurysm Study reported that vascular malformations and aneurysms were equally common causes of subarachnoid hemorrhage below the age of 20 years.[15] Cavernous hemangiomas were a surprisingly frequent cause of intracerebral hemorrhage in our study, but the advent of MRI has enhanced the ability to detect cryptic vascular malformations.[17] Of the nine incidence cases with a hemorrhagic stroke who were hospitalized, five had MRI scans as part of their evaluation.

The overall 30-day survival rate of 81% among incidence cases in this study is similar to the 81% to 83% survival rate reported in community studies of stroke in adults,[2,11] despite the much higher proportion of hemorrhagic stroke among children as compared to adults. The 30-day mortality following intracerebral hemorrhage and subarachnoid hemorrhage among children (22%) was approximately half of that reported for adults (45% to 48%).[2,11] In addition, all of the children who survived the first few days were alive at the last recorded medical follow-up.

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