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Perinatal Stroke in Children With Motor Impairment: A Population-Based Study

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ABSTRACT. *Objective.* Risk factors for perinatal arterial stroke (PAS) are poorly understood. Most previous studies lack an appropriate control group and include only infants with symptoms in the newborn period. We set out to determine prenatal and perinatal risk factors for PAS.

Methods. In a population-based, case-control study nested within the cohort of 231 582 singleton infants who were born at ≥ 36 weeks' gestation in Northern California Kaiser hospitals from 1991 to 1998, we searched electronically for children with motor impairment and reviewed their medical records to identify diagnoses of PAS. Control subjects were randomly selected from the study population. A medical record abstractor reviewed delivery records without knowledge of case status.

Results. The prevalence of PAS with motor impairment was 17/100 000 live births. Of 38 cases, 26 (68%) presented after 3 months of age with hemiparesis or seizures. All 12 newborns with acute stroke symptoms had seizures. A delayed presentation was more common in children with moderate to severe motor impairment than among infants with only mild motor abnormalities (24 of 31 vs 2 of 7). Prepartum risk factors significantly associated with PAS in multivariate analysis were preeclampsia (odds ratio [OR]: 3.6; 95% confidence interval [CI]: 1.1–11.4) and intrauterine growth restriction (OR: 5.3; 95% CI: 1.5–18.6). Newborns with PAS were also at higher risk of delivery complications, such as emergency cesarean section (OR: 6.8; 95% CI: 2.7–16.6), 5-minute Apgar < 7 (OR: 23.6; 95% CI: 4.1–237), and resuscitation at birth (OR: 4.5; 95% CI: 1.6–12.3).

Conclusions. Preeclampsia and intrauterine growth restriction (IUGR) may be independent risk factors for perinatal stroke resulting in motor impairment. Large multicenter studies that include all children with perinatal stroke are needed to determine further the risk factors and outcome of perinatal stroke. *Pediatrics* 2004;114:612–619; *perinatal stroke, epidemiology, neonate, infarction, cerebral palsy.*

ABBREVIATIONS. PAS, perinatal arterial stroke; KPMCP, Kaiser Permanente Medical Care Program; ICD-9-CM, *International Classification of Diseases, Ninth Revision—Clinical Modification*; MRI, magnetic resonance imaging; CT, computed tomography; OR, odds ratio; CI, confidence interval; IUGR, intrauterine growth restriction.

Perinatal arterial stroke (PAS) has received increased attention as an important cause of cerebral palsy and other neurologic disabilities, including epilepsy and cognitive impairment.^{1–8} Arterial stroke is diagnosed primarily in neonates who are born at term^{1,8–10} and is responsible for at least 22% to 70% of congenital hemiplegic cerebral palsy in this population.^{5,11,12}

Perinatal arterial ischemic stroke occurs by definition between 28 weeks' gestation and 7 days of age,³ although studies of PAS often include cerebrovascular events occurring up to 28 days of life. Newborns with arterial infarction either may present acutely during the neonatal period with neurologic symptoms such as seizures^{7,13} or may be clinically asymptomatic until several months of age, when pathologic handedness or seizures are first noted.¹⁴ How the acute and delayed presentation groups differ in timing of injury, underlying pathogenesis, and neurologic outcome is unknown.

The cause of PAS is poorly understood. Investigators have reported a number of obstetric and neonatal complications in the setting of perinatal stroke, including birth asphyxia, preeclampsia, chorioamnionitis, cardiac anomalies, polycythemia, and systemic infection,^{6,7,9,10,15–23} although controlled studies have failed to find a significant difference in the frequency of perinatal complications between infants with PAS and control subjects.²⁴ Recently, genetic thrombophilias have received increasing attention as potential risk factors. Factor V Leiden mutation, hyperhomocysteinemia, and elevated lipoprotein(a) levels all have been described with increased frequency in infants with PAS when compared with healthy control subjects.^{25–27}

Previous studies of PAS are subject to a number of important limitations. Most describe only a small number of children^{6,7,10,15,24,28} or lack an adequate comparison group to assess the significance of potential risk factors.^{1,9,22,29} The majority of reports include only newborns who present acutely with stroke, whereas children with delayed presentation of PAS have been less studied.¹⁴ The clinical diagnosis of "birth asphyxia" has been considered a risk

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factor for PAS⁶ but may in fact refer to clinical signs that are consequences of cerebral infarction and thus may be unrelated to the underlying causal mechanism.

We found previously that PAS accounts for 74% of moderate to severe congenital spastic hemiplegia without a genetic cause and that preeclampsia is more common in pregnancies that result in PAS than in control pregnancies.¹² However, this previous study excluded children who had PAS and demonstrated only minor motor disabilities and did not include data regarding clinical presentation and neuroimaging characteristics of perinatal stroke. Therefore, we set out to evaluate further the risk factors for PAS causing all degrees of motor impairment and to describe the clinical characteristics of PAS in a large population of singleton term and near-term infants who were born in California.

METHODS

This case-control study is nested within the cohort of all singleton infants who were born at ≥ 36 weeks' gestation from 1991 to 1998 in the Kaiser Permanente Medical Care Program (KPMCP). Study procedures were approved by the Institutional Review Boards at KPMCP and at the University of California, San Francisco.

Setting

The KPMCP is a large managed care organization that provides care for >30% of the population in Northern California. The

members of KPMCP are demographically similar to the California population, except that the very poor and the very wealthy are underrepresented.³⁰ Of its 33 facilities, 12 have delivery rooms and 6 have level III neonatal intensive care units. Eighty-three percent of infants in the KPMCP study population for this study were followed for at least 1 year.

Case Ascertainment

We sought to identify children with PAS resulting in motor abnormality. The study population consisted of all 231 582 singleton live births at KPMCP between January 1, 1991, and December 31, 1998. In January 2000, we performed an electronic search within this population for inpatient and outpatient physician diagnoses of motor impairment, as part of a separate study of cerebral palsy.¹² Motor impairment was defined as a physician diagnosis of cerebral palsy (*International Classification of Diseases, Ninth Revision—Clinical Modification* [ICD-9-CM]³¹ 343.0–343.9), paresis (ICD-9-CM 342.1, 342.8, 342.9, 344.0, 344.1, 344.30–344.32, 344.5), or gait abnormality (ICD-9-CM 781.2).

A child neurologist (Y.W.W.) then reviewed outpatient medical records of children who had diagnoses of these motor abnormalities to identify those with an acute or delayed presentation of PAS, as defined by neuroimaging evidence of infarction within the anterior, middle, or posterior cerebral artery distribution(s). The acute presentation group included infants with stroke presenting within the first month after delivery. The delayed presentation group consisted of infants and children who had been considered neurologically normal before 2 months of age and whose PAS was diagnosed after 2 months of age with an old arterial distribution infarct.¹⁴ Of note, all infants who had a diagnosis of PAS became symptomatic either before 2 weeks of life or after 3 months of age.

We excluded infants and children who carried a diagnosis that is inconsistent with the diagnosis of cerebral palsy (Fig 1). The majority of infants who were excluded in this way had a genetic

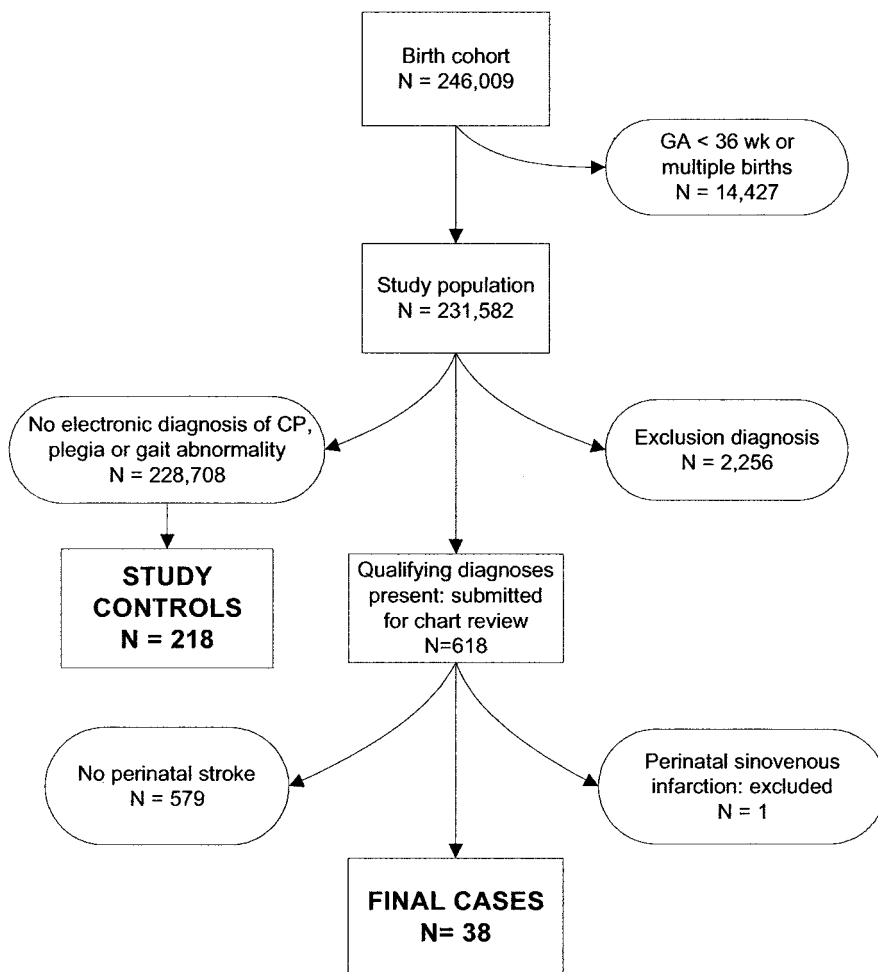


Fig 1. Selection of study subjects.

disorder, neuromuscular disease, or spina bifida (see Appendix for a full list of exclusion diagnoses).³² We excluded infants with a sinovenous thrombosis, watershed distribution infarction, or primary intracerebral hemorrhage and those who presented after 1 month of age with an acute neurologic deficit and neuroimaging evidence of acute ischemia suggesting recent stroke.

Control Selection

We randomly selected 218 infants from the study population to represent control subjects in our previous study of cerebral palsy.¹² Given that the current study of PAS is nested within the same birth cohort, we used the identical control group of randomly selected births.

Data Abstraction

A professional medical record abstractor reviewed obstetric and neonatal charts using a standardized protocol under close supervision of the investigators. IUGR was defined as birth weight <10% for gestational age on the basis of race and gender-specific normative data compiled from California births.³³ Preeclampsia was considered present when a physician diagnosed any of the following: preeclampsia, pregnancy-induced hypertension, eclampsia, or maternal syndrome of hemolysis elevated liver enzymes and low platelets. Chorioamnionitis was considered to be present when a treating physician made a diagnosis of chorioamnionitis or endometritis on the basis of clinical symptoms. "Birth asphyxia" indicated a diagnosis made by a treating physician of either birth asphyxia or hypoxic-ischemic encephalopathy.

We determined the clinical symptoms and age at presentation of stroke by reviewing neonatal and pediatric records. Cerebral palsy was defined as a nonprogressive congenital motor dysfunction with upper motor neuron findings of spasticity, rigidity, or choreoathetosis. Degree of motor impairment was defined as follows: 1) mild = subtle weakness or spasticity but full functional use of the most affected limb, 2) moderate = decreased function of the most affected limb, and 3) severe = lack of any functional use of the most affected limb. The presence of epilepsy, language delay, learning disability, behavioral disorder, and recurrent stroke was determined by electronically scanning all physician diagnoses made at KPMCP during the available years of follow-up.

We reviewed head magnetic resonance imaging (MRI) and computed tomography (CT) reports to determine neuroimaging characteristics and age at diagnosis. The arterial distribution and presence of coexisting hemorrhage, basal ganglia, and internal capsule involvement were determined from radiology reports.

Data Analysis

We calculated univariate odds ratios (ORs) and 95% confidence intervals (CIs) using the exact method. We then calculated multivariate odds ratios by performing a backward stepwise logistic regression,³⁴ with $P < .1$ used as the cutoff for retention in the model. Potential confounders that were found to be significantly associated with PAS on univariate analysis were included in the multivariate model, as well as risk factors that were considered a priori to be potential confounders. Factors that were not considered causative, such as low Apgar scores, emergent cesarean section, neonatal seizures, and a diagnosis of birth asphyxia, were not included in the model. These complications may result from the stroke, in which case adjusting for them would falsely diminish the ORs for perinatal risk factors that could potentially play a causative role. ORs are close approximations of the relative risk, because the outcome of PAS is rare.

RESULTS

Of the 231 582 infants in the study population, the electronic search for physician diagnoses revealed 618 infants and children with a diagnosis of motor impairment. Chart review of these patients then identified 38 children with PAS. The prevalence of PAS causing motor impairment among singleton term and near-term infants therefore was 17 per 100 000 live births (~1/5900).

Clinical Symptoms

Twelve (31%) of 38 infants with PAS and subsequent motor abnormalities were symptomatic during the neonatal period. Seizures were the most common presenting symptom in this group (Table 1) and occurred as early as 12 hours after birth and up to 10 days after delivery. The diagnosis of PAS was made on head MRI (7) or CT (4) within 1 month of age, with the exception of 1 individual who received the diagnosis at 2 months of age.

Of the 26 infants with delayed presentation of PAS, the majority (69%) demonstrated pathologic handedness, whereas the remaining presented with delayed or abnormal walking, postneonatal seizures,

TABLE 1. Clinical Characteristics of 38 Children With PAS and Motor Dysfunction Identified From a Birth Cohort of Singleton Infants ≥ 36 Weeks' Gestation

	Acute Presentation (N = 12)		Delayed Presentation (N = 26)	
	N	%	N	%
Presenting symptom				
Seizure	11	92	4	15
Pathological handedness	0	0	18	69
Delayed/abnormal walking	0	0	3	12
Other*	1	8	1	4
Mean age at presentation	2.4 d	NA	8 mo	NA
Mean age at last visit	8.4 y	NA	7.9 y	NA
Seen by a neurologist	12	100	25	96
Cerebral palsy				
Hemiparesis	10	83	26	100
Paraparesis	0	0	0	0
Quadraparesis	1	8	0	0
Degree of motor disability				
Severe	2	17	2	8
Moderate	5	42	22	88
Mild	5	42	2	8
Postneonatal seizures	11	92	9	36
Language delay or learning disability	6	50	7	28
Behavioral disorder	3	25	2	8

NA indicates not applicable.

*Other presenting symptoms include 1 neonate with hypotonia and jittery movements and a 4-month-old infant with apneic episodes.

or apneic spells (Table 1). The infants who presented with pathologic handedness ranged from 3 to 11 months of age, whereas those who presented with seizures first developed these symptoms at 5 to 14 months of age. Gait abnormalities were the initial signs of neurologic impairment in 3 children aged 12 to 21 months.

The average age at last visit was 8.1 ± 2.7 years and did not differ between the acute and delayed presentation groups (Table 1). All but 1 child with PAS was evaluated by a neurologist. Spastic hemiparesis was diagnosed in 36 (95%) of 38 case children. One child with bilateral infarctions developed spastic quadriplegia, and another infant with neonatal seizures later developed a subtle gait abnormality but did not receive a diagnosis of cerebral palsy given the lack of upper motor neuron signs.

A delayed presentation was more common in children with moderate to severe motor impairment than among infants with only mild motor abnormalities (24 of 31 vs 2 of 7; $P = .02$). In contrast, infants who presented acutely in the neonatal period were more likely to develop epilepsy (11 of 12 vs 9 of 26; $P = .001$). Language delay, learning difficulties, or behavioral disorders were also more common in the acute presentation group, but the differences were not statistically significant (Table 1).

Of the 18 children with PAS and epilepsy, 6 (33%) had refractory seizures that required therapy with either multiple medications or with the ketogenic diet. Two infants developed infantile spasms. Three neonates who experienced seizures in the newborn period were taken off all seizure medications by 2 years of age and were still seizure-free after 5 to 10 years of follow-up. During the available years of follow-up within the KPMCP system, there were no recurrent strokes diagnosed in any of the 38 children with PAS.

Neuroimaging Findings

All infants with a delayed presentation of perinatal stroke received a head MRI, whereas 4 of the 12 infants who presented in the newborn period received only a head CT (Table 2). Unilateral infarctions were more common on the left than on the right (70% vs 30%), and 11% of case children demonstrated bilateral arterial distribution infarcts. The majority (63%) of PASs were in the left middle cerebral artery distribution, and only 2 children had infarctions in the posterior cerebral artery distribution. Although infants with a delayed presentation were more likely to exhibit injury to the basal ganglia and/or internal capsule when compared with newborns with symptoms in the acute newborn period (27% vs 8%; $P = .39$), the numbers were too small to achieve statistical significance. We were unable to identify any radiologic features that were significantly associated with moderate to severe motor sequelae.

Univariate Analysis

Maternal age and race did not differ between the case and control groups (Table 3). IUGR (OR: 5.1; $P = .02$) and a clinical diagnosis of chorioamnionitis (OR: 3.5; $P = .04$) were associated with significantly increased risk of PAS with motor impairment. Pre-eclampsia was associated with a 3-fold increased risk, but this was not quite significant ($P = .06$). Case children were more likely to have undergone an urgent or emergent cesarean section and to have a diagnosis of birth asphyxia. After delivery, infants with PAS were significantly more likely to be given an Apgar score <7 at 5 minutes, to require resuscitation, and to be admitted to the neonatal intensive care unit. No infants with perinatal stroke had a five-minute Apgar score ≤ 3 .

Several delivery and neonatal complications oc-

TABLE 2. Neuroimaging Characteristics of PAS

	Acute Presentation (N = 12)		Delayed Presentation (N = 26)	
	N	%	N	%
Type of neuroimaging				
MRI	8	67	26	100
CT Only	4	33	0	0
Side of stroke				
Left	7	58	17	65
Right	2	17	8	31
Bilateral	3	25	1	4
Size of infarction				
Large	8	67	15	58
Small	2	17	8	31
Unknown	2	17	3	12
Vascular distribution*				
MCA	10	83	24	92
ACA	1	8	0	0
PCA	1	8	1	4
Involvement of deep structures				
Basal ganglia	1	8	6	23
Internal capsule	0	0	2	8
Hemorrhage†	2	17	0	0

MCA indicates middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery.

* One neonate who presented acutely had a stroke in both the MCA and ACA territories.

† Two neonates had punctate hemorrhage within the area of infarction.

TABLE 3. Univariate ORs for PAS With Motor Impairment in Singleton Term Infants

	Cases (N = 38)	Controls (N = 218)	OR	95% CI	P Value
Maternal age ≥ 35	8/38	39/218	1.2	0.5–3.0	0.64
Maternal race					
White	20/38	125/218	Reference	Reference	
Black	2/38	12/218	1.0	0.1–5.2	.96
Hispanic	9/38	33/218	1.7	0.6–4.4	.23
Asian	3/38	32/218	0.6	0.1–2.1	.41
Other	2/38	5/218	2.5	0.2–16.5	.28
Unknown	2/38	11/218	1.1	0.1–5.8	.87
Prepartum complications					
History of infertility	0/38	8/215	—	0–2.7	.61
IUGR	5/38	6/207	5.1	1.1–21.0	.02
Gestational diabetes	1/38	10/215	0.6	0.01–4.1	1.00
Preeclampsia	5/38	10/215	3.1	0.8–10.7	.06
Intrapartum complications					
Clinical chorioamnionitis	5/38	9/215	3.5	0.9–12.3	.04
Rupture of membranes ≥ 24 h	4/37	13/202	1.8	0.4–6.2	.34
Breech	1/38	5/215	1.1	0.0–10.5	.63
Cesarean section (urgent or emergent)	14/38	17/215	6.8	2.7–16.6	<.0001
Forceps	2/38	2/215	5.9	0.4–83.1	.11
Vacuum	3/38	17/215	1.0	0.2–3.7	.65
Meconium (mild or trace)	2/38	31/215	0.3	0.0–1.4	.19
Meconium (moderate to severe)	7/38	20/215	2.2	0.7–6.0	.09
Tight nuchal cord	2/38	6/215	1.9	0.2–11.3	.34
Infant characteristics					
Male gender	18/38	115/211	0.8	0.4–1.6	.42
Gestational age, mean wk	39.5	39.6	NA	NA	.87
Birth weight, mean g	3217	3477	NA	NA	<.01
5-Min Apgar <7	7/38	2/211	23.6	4.1–237	<.001
Cord pH <7.0	4/17	0/28	—	2.0	.01
Diagnosis of birth asphyxia	3/38	0/211	—	4.7	<.01
Resuscitation at birth	9/38	14/218	4.5	1.6–12.3	<.001
Neonatal intensive care unit admission	16/38	17/210	8.3	3.4–20.0	<.001

curred more frequently in infants with an acute presentation than in those with a delayed presentation, including emergent cesarean section (62% vs 25%; $P = .04$), 5-minute Apgar <7 (38% vs 8%; $P = .07$), and neonatal resuscitation (54% vs 8%; $P = .004$). The frequency of maternal risk factors did not differ significantly between the 2 presentation groups.

Only 7 placental histologic examinations were performed in the 38 infants with PAS. One revealed an umbilical vein thrombosis, and 4 others had evidence of acute chorioamnionitis or funisitis. Six control placentas were submitted for pathologic examination, 1 of which also revealed acute chorioamnionitis. No placental infarctions were noted on gross examination in the delivery room.

Multivariate Analysis

The following variables were included in the logistic regression model: maternal age, maternal race, gender, clinical chorioamnionitis, IUGR, preeclampsia, and tight nuchal cord. The risk factors that remained independently associated with PAS with motor impairment in the multivariate model were preeclampsia and IUGR (Table 4).

DISCUSSION

This is the first population-based study of perinatal stroke in children with later motor disability. We found that among term and near-term infants, maternal preeclampsia and IUGR both independently increase the risk of PAS resulting in long-term motor impairment. In addition, children with motor im-

TABLE 4. Multivariate ORs for PAS With Motor Impairment in Singleton Term Infants*

	OR	95% CI	P Value
IUGR	5.6	1.6–19.6	.01
Preeclampsia	3.4	1.1–10.5	.04

* Variables dropped from the stepwise logistic regression include maternal age >35, ethnicity, clinical chorioamnionitis, gender, and tight nuchal cord.

pairment as a result of PAS are more likely to present outside the neonatal period than during the immediate newborn period, and the degree of motor disability is more severe among those with a delayed presentation.

Prevalence

The prevalence of PAS is unclear. Previous population^{35,36} and hospital-based^{13,22,24} estimates range from 18 to 93 per 100 000 live births. These figures underestimate the true prevalence of PAS, given that they do not include infants and children who present outside the newborn period. In addition, because the diagnosis relies on neuroimaging, it is not possible to ascertain infants who have PAS and remain asymptomatic or do not receive neuroimaging.

We found that PAS leading to subsequent motor impairment was diagnosed in 17 per 100 000 term and near-term births. Our prevalence figure diverges from previous estimates in that infants without long-term motor impairment are not included in our estimate. However, our study provides for the first time

a population-based estimate of PAS causing motor impairment that includes infants at all ages at presentation.

Risk Factors

The cause of perinatal arterial infarction remains unclear in the majority of cases.^{7,10,37–39} None of the case children in our cohort received a diagnosis of recognized risk factors, including cardiac abnormalities, polycythemia, and neonatal infection.^{16,22,23,40}

Preeclampsia was associated with a 3.6-fold increased risk of PAS. Previous investigators have suggested an association between preeclampsia and a variety of adverse pregnancy outcomes, including IUGR, neonatal encephalopathy, neonatal sinovenous thrombosis, and fetal death.^{41–45} However, this is the first report of preeclampsia acting as an independent risk factor for PAS.

The mechanism by which preeclampsia might increase the risk of cerebral infarction in the fetus is unclear. Preeclampsia is thought to result from a vascular defect in the placental bed, resulting in reduced uteroplacental blood flow.^{45–47} Maternal prothrombotic disorders have been proposed as causal factors in the pathogenesis of preeclampsia,^{48–50} and preeclampsia has been associated with thrombotic lesions in the placenta⁵¹ as well as with a maternal history of thromboembolism.⁵² It is possible that preeclampsia and PAS both are consequences of a vasculopathy and clot formation within the placenta. Alternatively, they both may stem from a common underlying prothrombotic condition, without underlying placental pathology. Although the role of prothrombotic disorders in the cause of PAS is beyond the scope of this study, we plan to determine the presence of genetic prothrombotic disorders in our patient population, to investigate this issue further.

The finding that IUGR conferred a 5-fold increased risk of PAS was unexpected and has not been previously reported to our knowledge. IUGR is a multifactorial disorder that is associated with preeclampsia,⁵³ placental insufficiency,⁵⁴ thrombotic lesions in the placenta,⁵⁵ and increased maternal thrombin formation.⁵⁶ IUGR in term infants is also associated with a number of perinatal complications, including fetal death and increased perinatal mortality. Whether maternal and fetal prothrombotic disorders and possibly placental thrombosis are responsible for the association between IUGR and PAS deserves additional study.

Investigators have implicated hypoxia-ischemia⁶ and birth trauma^{15,57} as potential causes of PAS, yet others have failed to identify a significant difference between case patients and control subjects with respect to fetal heart rate abnormalities, mode of delivery, and 5-minute Apgar scores.²⁴ In our study, 17% of infants with PAS had a low 5-minute Apgar score, and 3 (8%) received a diagnosis of “birth asphyxia.” However, each of the 3 pregnancies that were complicated by birth asphyxia in our study had coexisting complications suggesting that long-standing abnormalities had been present: 1) a markedly fibrotic placenta, 2) IUGR and placental evidence of funisitis, and 3) preeclampsia. Therefore, the term

“birth asphyxia” may be misleading, especially in the setting of PAS.

Outcome

A recent review of 579 infants with PAS described in the literature found that 40% were neurologically normal at follow-up.³ In contrast, the single study dedicated to children with a delayed presentation of PAS reported that all 22 study subjects had persistent hemiparesis on long-term follow-up.¹⁴ We found that among infants with PAS and motor impairment, a delayed presentation was associated with a more severe degree of motor impairment. Although it is somewhat counterintuitive that the more severely affected infants tend to be asymptomatic in the newborn period, it is a hemiparesis that often triggers a diagnosis of PAS in infants with a delayed presentation, thus explaining the high incidence of persistent motor deficits in this group. Why symptoms in the newborn period occur in some and not in others is not known but may depend on the timing and location of the infarction.

Others have found that the presence of internal capsule involvement portends a worse motor outcome after PAS.⁵⁸ Because our study included only infants with long-term motor sequelae and PAS thus was incompletely identified, we were unable to test this hypothesis. Similarly, although epilepsy was more common among infants who were symptomatic in the newborn period, infants with PAS resulting in epilepsy but no motor impairment would not be identified in our study. Therefore, we are unable to comment on the risk of epilepsy in those with acute versus delayed presentation of PAS.

Several factors may have contributed to underascertainment of PAS with motor impairment. Seventeen percent of our cohort was lost to follow-up by 1 year of age. Children with subtle or nonspecific motor difficulties, such as mild incoordination or motor delay, would not have been identified by our search for motor abnormalities and may in some instances have had a PAS. Children with significant motor impairment due to PAS who did not receive a head imaging study would also remain undiagnosed. Other limitations of our study include that we did not review radiology films directly, relying instead on clinical radiology reports. Therefore, we cannot comment accurately on infarct size or other imaging characteristics, such as subtle white matter injury, that may have been present in conjunction with the focal infarction. We did not examine our study subjects and did not test for prothrombotic abnormalities.

These limitations are offset by several strengths of our study, including the population-based setting, the selection of an appropriate control group, a duration of follow-up that exceeds that reported in most previous studies, and the ability to compare infants with PAS who presented acutely with those who had a delayed presentation. Future multicenter studies with complete ascertainment of PAS including children with both normal and abnormal motor outcome, as well as systematic testing for prothrombotic disorders; comprehensive perinatal, placental,

radiologic and outcome data; and appropriate control populations are needed to elucidate further the pathogenetic mechanisms responsible for PAS.

APPENDIX: EXCLUSION DIAGNOSES

ICD-9 code	Condition
237.7x	Neurofibromatosis
275.1	Wilson's disease
277.2	Lesch-Nyhan syndrome
277.5	Mucopolysaccharidosis
331.8	Reye syndrome
333.6	Idiopathic torsion dystonia
334.x	Spinocerebellar disease, including ataxia telangiectasia
335.x	Anterior horn cell disease
336.x	Other diseases of spinal cord
340	Multiple sclerosis
349.82	Toxic encephalopathy
358.x	Myoneural disorders (myasthenia gravis)
359.x	Muscular dystrophies and other myopathies
741.xx	Spina bifida
742.5x	Spinal cord anomalies
754.59	Arthrogryposis
755.55	Apert syndrome
756.16	Klippel-Feil disease
757.33	Bloch-Sulzberger disease (incontinentia pigmenti), xeroderma pigmentosum
758.x	Chromosomal anomalies
759.5	Tuberous sclerosis
759.81	Prader-Willi syndrome
759.89	Cornelia de Lange syndrome, Lawrence Moon Biedl syndrome, Rubenstein-Taybi syndrome, Carpenter's syndrome, cerebrohepatorenal syndrome, Cockayne's syndrome, Menkes kinky hair disease

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WOMEN ASPIRE TO BE CHIEF AS MUCH AS MEN DO

“Ambition knows no gender. But success does. That’s clear from a new study showing that a majority of senior executives, both male and female, at the country’s 1,000 biggest companies want to become their employer’s chief executive. The survey by Catalyst, a New York research group, indicates women with children at home yearn to occupy the corner office as much as those without children, according to the poll of 948 officials at the vice president level and above. . . . The study dispels the popular notion of why few women hold high-level business posts—because they supposedly don’t aim high enough. The finding that 55% of women and 57% of men aspire to be CEO ‘challenges the assertion that there aren’t more women at the top because they don’t want to be there,’ the report said.”

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Noted by JFL, MD