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A Newborn with Intermittent Posturing

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CASE PRESENTATION

History

A 2-day-old male infant presented with intermittent posturing while in the nursery. He was born weighing 3340 g at 39 $^{3}/_{7}$ weeks' gestation to a 40-year-old gravida 3 para 0011 mother. All serologies, including hepatitis B, HIV, rapid plasmin reagin, and VDRL testing, were negative. Group B streptococcus culture also was negative.

The pregnancy history revealed that the mother started prenatal care at 6 weeks and took only prenatal vitamins during the pregnancy. She did not use recreational drugs, alcohol, or tobacco during the pregnancy. She developed hypertension in the third trimester that did not require therapy.

The labor was complicated by prolonged fetal descent and fetal heart rate decelerations. Spontaneous rupture of membranes occurred 7 hours before delivery. No prophylactic antibiotics were given. The infant's head was in the transverse lie position for an unknown period of time, which led to a decision to deliver via cesarian section.

In the delivery room after birth, the infant needed minimal resuscitation. He was warmed, dried, and given blow-by oxygen for 30 seconds for poor color. Apgar score was 8 at 1 minute and 9 at 5 minutes. He had some right-sided molding of his head but an otherwise normal physical examination and was transferred to the regular term nursery.

The infant was noted to be a slow feeder. He was not vigorous at sucking at breast or bottle, but he improved by day 2 of life. He was reported to have occasional jitteriness. On day 2 of life, the nursery staff and parents observed that the infant was experiencing intermittent episodes of overextended posturing to the left side.

Key Point

Repetitive posturing, which is the intermittent, repetitive unusual body position assumed by an infant, is an abnormal finding and warrants further investigation.

Physical Examination

Upon initial assessment, the infant was sleeping in the bassinet and was lying in the standard newborn position with his arms and legs flexed. Vital signs included rectal temperature of 99.4°F (37.4°C), respiratory rate of 44 breaths/min, and heart rate of 134 bpm. Oxygen saturation was 99% on room air. During the examination, the infant awoke, was vigorous, and moved all extremities equally. As he was observed further, he overextended his left arm and neck to the left side. Subsequently, his head would rotate to the left side. This posturing episode would last approximately 3 to 4 minutes, followed by spontaneous resolution. When lifted during this posturing, the patient returned to a normal position. During a 20-minute period of evaluation, he had 3 separate episodes of overextension to the left side. There also was some left arm jitteriness that extinguished with touch.

The head was normocephalic with a flat anterior fontanelle. The right-sided molding that was documented in the delivery room had resolved. No posterior fontanelle was palpable. The ears were normally set and the palate was intact. No dysmorphic facial features were observed. The neck was supple, with good range of motion. The infant exhibited some increased tone in the left sternocleidomastoid muscle during the posturing episodes, but the hypertonicity resolved with resolution of the posturing. No cervical masses were palpable. The clavicles were intact. The chest was symmetrical, and the lungs were clear bilaterally. The heart

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rate was regular with no murmur. Femoral pulses were palpable. The abdomen was soft with no masses or hepatosplenomegaly. The genitourinary examination showed normal male genitalia and descended testes bilaterally. The anus was patent. No deformities were noted in the spine or back. The patient used all 4 extremities symmetrically. There were no skin lesions. He was jaundiced to mid-abdomen.

The neurologic examination was normal, except for the intermittent left-sided posturing. His strength and tone in all 4 extremities were appropriate and symmetrical. There was only a mild increase in tone in the left upper extremity during the posturing. He had the appropriate rooting, sucking, Moro, grasp, tonic neck, and doll's eye reflexes.

LABORATORY STUDIES

Results of laboratory tests obtained on day 2 of life are summarized in **Table 1**. Electrolytes were all within normal limits. A complete blood count showed acceptable levels of hemoglobin and platelets. There were no indicators of infection.

Retrospectively, the placenta was considered to have had no pathology. No thrombosis was detected.

Table 1. Laboratory Values for the Case Patient

Parameter	Result
Blood chemistries	
Sodium	135 mEq/L
Potassium	5.8 mEq/L
Chloride	98 mEq/L
Bicarbonate	25 mEq/L
BUN	5 mg/dL
Creatinine	0.8 mg/dL
Glucose	82 mg/dL
Calcium	9.7 mg/dL
Total bilirubin	12 mg/dL
Direct bilirubin	0.6 mg/dL
Complete blood count	
Leukocytes	
Total	13.7 x 10^3/mm^3
Neutrophils	32%
Lymphocytes	43%
Hemoglobin	19 g/dL
Platelets	377 x 10^3/mm^3

BUN = blood urea nitrogen.

DIFFERENTIAL DIAGNOSIS

Intermittent posturing in the neonate is a nonspecific neurologic sign. At this point in the patient's presentation, seizure should be considered as a possible etiology because of its subtle presentation in an infant. Additional etiologies to consider are benign myoclonic activity, motor automatisms, uterine malposition, brachial plexus injury, and gastroesophageal reflux.

Neonatal seizures have many potential causes, including hypoxic-ischemic injury, neonatal cerebral infarction, intracranial hemorrhage, and metabolic abnormalities, such as hypoglycemia, hypocalcemia, hypomagnesemia, hyponatremia, and pyridoxine dependence. The most common cause of neonatal seizure is hypoxic-ischemic encephalopathy; neonatal stroke is the second most common cause.[1] Other causes of seizures in the neonatal period are infection (meningitis, sepsis, TORCH syndrome [toxoplasmosis, other agents, rubella, cytomegalovirus, herpes simplex virus]), neonatal drug withdrawal, inborn errors of metabolism, anesthetic agents given to the mother during delivery, drug toxicity, developmental abnormalities of the brain (lissencephaly, proencephaly), trauma, hydrocephalus, polycythemia, kernicterus, benign familial seizures, and fifth-day fits.[2]

In this patient, metabolic disturbances, infection, drug withdrawal, anesthetic agents, drug toxicities, polycythemia, kernicterus, and familial seizures were ruled out by history, physical examination, and laboratory evaluation. As the patient's symptomatology was truly intermittent, brachial plexus injury was unlikely. Additionally, the patient's hyperextension and increased tone did not fit with a brachial plexus injury. Hypoxic-ischemic encephalopathy, cerebral infarction, intracranial hemorrhage, developmental brain abnormalities, and hydrocephalus were still possible etiologies. Benign myoclonic activity and motor automatisms also were still under consideration. Finally, the overextension to the left side involving the left neck and arm could be related to the uterine malposition since the patient spent a significant portion of labor in the transverse lie position.

Key Point

Seizures present differently in neonates than in children and adults. It is sometimes difficult to assess whether a neonate is indeed seizing. Seizures can present with eye movements, jaw or tongue movements, bicycling movements, or intermittent posturing movements. Therefore, it is important to always include neonatal seizures in the differential diagnosis of vague posturing.

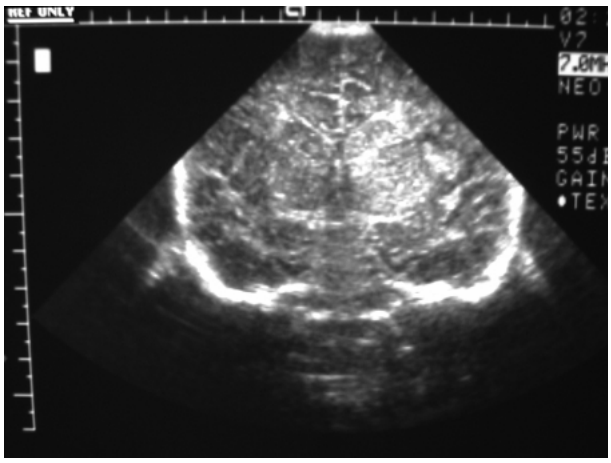

Figure 1. Ultrasonogram of the infant's head demonstrating increased echogenicity in the left basal ganglia and thalamus.

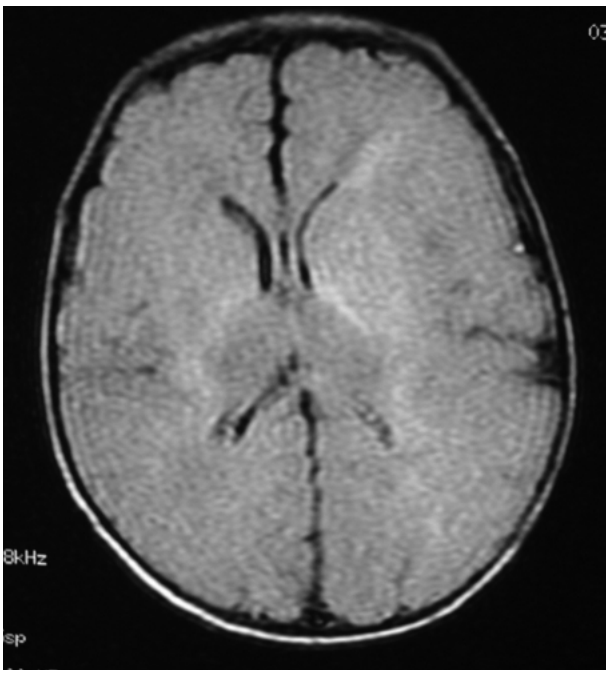

Figure 2. Magnetic resonance image of the infant's head demonstrating the area of infarct in the left frontal lobe with involvement of the basal ganglia, perisylvian region, and insular cortex.

RADIOGRAPHIC EVALUATION

Upon the recommendation of the neurology service, a head ultrasound was performed to assess for any trauma or anatomic abnormalities (**Figure 1**). The head ultrasonogram showed diffuse asymmetry and increased echodensity on the left side of the brain in the basal ganglia and the thalamus. Magnetic resonance imaging (MRI) showed an infarct in the major portion of the left frontal lobe, with complete involvement of the insular cortex, perisylvian region, and basal ganglia (**Figure 2**). The left parietal and temporal lobes were affected, whereas the occipital lobe was spared. A subtle midline shift was noted. The conclusion was that the infant had a complete infarct of the left middle cerebral artery distribution. An echocardiogram was normal. Magnetic resonance angiography of the head and neck showed no flow in the left middle cerebral artery, which was consistent with the infarct seen on the MRI. An electroencephalogram (EEG) on day 6 of life showed increased spikes over the area of the infarct, which was a poor prognostic indicator (as was the size of the infarct).

HOSPITAL COURSE AND POSTDISCHARGE MANAGEMENT

By day 4 of life, the infant had stopped posturing. The neurologic examination on day 5 of life showed some increased tone in the right extremities. The infant was still feeding well and moving all his extremities. On the day 6 of life, he appeared to have a brief myoclonic seizure during the EEG examination and was started on phenobarbital. He was discharged on day 7 of life with the diagnosis of neonatal stroke, despite a subtle nonspecific clinical presentation. His seizures were treated with an anticonvulsant. He was referred to a pediatrician with expertise in developmental pediatrics.

NEONATAL STROKE

Epidemiology

Stroke occurring in the neonatal or perinatal period is defined as a cerebrovascular ischemic event that can occur anywhere between 28 weeks' gestation and the 28th day of life. It is the tenth most common cause of death in the neonatal period and is recognized in 1 in 4000 births annually.[3] The incidence of neonatal stroke has not changed over time.

Stroke is increasingly being recognized as a source of morbidity and mortality for neonates. Some studies have shown that stroke is the second most common cause of seizures in the neonatal period.[1] Nonetheless, neonatal stroke it is still an underdiagnosed condition. It is important, therefore, for physicians to recognize that neonatal stroke does occur. Early identification of neonatal stroke may allow for earlier intervention and better prognosis for affected children.[4]

Etiology

Neonates are more susceptible to stroke for several reasons. The maternal hypercoagulable state, perinatal

asphyxia, and mechanical stresses of delivery are potential etiologies during the birth process. Transient right-to-left cardiac shunts, a relatively high hematocrit, a low level of anticoagulant factors, and potential dehydration in the first few days of life are perinatal risks for a neonatal stroke.[5]

The 3 types of strokes are hemorrhagic, sinovenous thrombosis, and arterial ischemic stroke. Because this patient presented with an arterial ischemic stroke, the discussion will focus on this type. The incidence of arterial strokes is 93 out of 100,000 births. Arterial ischemic strokes usually present with lethargy or seizures, causing 12% to 14% of neonatal seizures.[5] These strokes usually involve large vessels, most commonly the middle cerebral artery. The carotid circulation is affected 5 times more frequently than the basilar circulation.[5]

Arterial ischemic strokes in neonates usually are caused by a thromboembolism from intracranial or extracranial vessels, heart, or placenta. Review studies have found cardiac disorders to be the origin of 10% of arterial strokes. Some studies have found perinatal complications to be involved in 50% of neonates with stroke. Various studies have described acute illness and prothrombotic disorders as the etiology in 25% to 68% of neonatal arterial ischemic strokes.[3] Prothrombotic disorders include deficiencies of anti-clotting factors, such as antithrombin 3, protein C and S, and plasminogen; and gene mutations, such as prothrombin 20210A and factor 5 Leiden. Autoimmune factors, such as lupus anticoagulant or anticardiolipin antibody, dysregulate phospholipids involved in the thrombolytic process. The maternal hypercoagulable state leads to thrombosis because of decreased levels of protein S and activated protein C. Thrombin generation and fibrinogen are increased in the maternal hypercoagulable state.[5] Other etiologies of ischemic stroke include infection, vascular anomalies (vasculitis and dissection), indwelling catheters, and trauma. Some cases remain idiopathic.

Evaluation

Neonatal stroke does not present with specific signs. The presence of stroke is initially insidious, and many atypical cases are not properly diagnosed in the neonatal period.[6] Sophisticated imaging techniques have been able to detect stroke more frequently.[7] Imaging, however, usually is performed when the patient presents later in life with the neurologic sequelae from stroke. It is at this point that a stroke that occurred during the neonatal period is detected.[6]

Imaging studies are the most effective method of detecting strokes. Studies have found that computed tomography (CT) of the head is the best initial study and is preferred over ultrasound. Although a head ultrasound is an easier study to perform in neonates, ultrasound does not show peripheral strokes as well as a CT scan.[3] An MRI scan with diffusion-weighted imaging (DWI) (**Figure 3**) and magnetic resonance angiography are used to define the extent of stroke. One study examined DWI in association with MRI. This study found that DWI is useful in acute ischemic brain injury and seizure etiology as it detects the cytotoxic injury induced edema; therefore, it detects infarcts sooner than MRI alone or CT.[8] Other recommended studies include echocardiogram and EEG. It is important to evaluate for any aberrant electrical activity because it is a poor prognostic indicator.

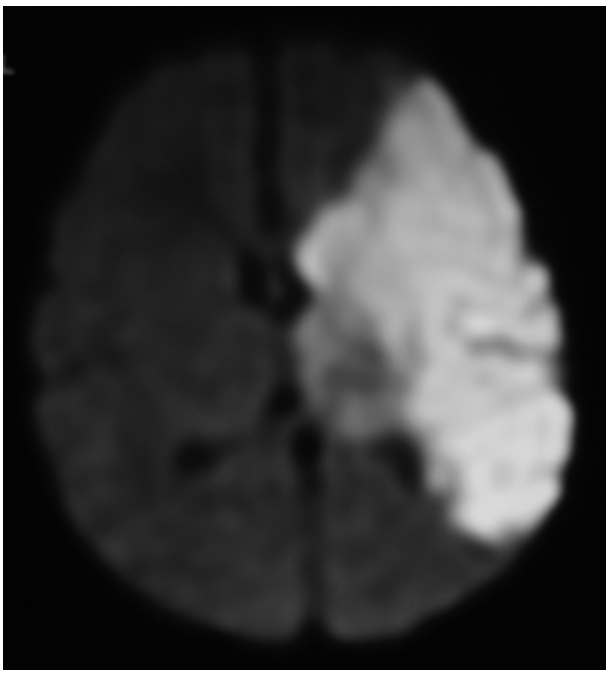

Figure 3. Magnetic resonance image (MRI) of the infant's head with diffusion-weighted imaging. This image intensifies and defines the affected area better than MRI alone.

Hematologic studies should include complete blood count, prothrombin time, partial thromboplastin time, protein C level, protein S level, antithrombin and plasminogen levels, anticardiolipin antibodies, hexagonal phospholipid antibody levels, and homocysteine level. Chromosomes need to be studied for factor 5 Leiden and prothrombin gene mutation. The timing of drawing blood for these studies is controversial. There is a significant amount of blood required from a neonate. Furthermore, neonates tend to have different levels of clotting factors than adults, which can make interpretation difficult. It is recommended

that most of this hematologic work-up be conducted after 6 months of age. One study, however, recommends that antibody levels be drawn early in the neonatal period to determine maternal anticardiolipin and hexagonal phospholipid antibodies.[9]

Key Point

Regardless of the size of the infarcted area, the clinical presentation of stroke is often insidious. However, sequelae from the stroke may be significant. It is, therefore, imperative that physicians are aware of this diagnosis and consider it in infants with appropriate symptoms. Better imaging techniques have permitted the proper diagnosis and delineation of stroke. CT is a better initial study than ultrasound for detecting stroke, but the diagnostic "gold standard" is MRI with DWI.

Management of Stroke

The best treatment plan for neonatal stroke is still unknown as there are no significant clinical trials upon which to base management strategies. Results of stroke trials in adults cannot be extrapolated to newborns because neonatal risks for developing strokes are different from those for adults. Furthermore, the neonatal neurologic, cerebrovascular, and coagulation systems differ markedly from those of adults. Finally, disability from a stroke cannot be predicted from the neonatal physical examination, unlike the ability to predict outcome from examination in adults.[5]

The use of anticoagulants and thrombolytics in the neonatal period is controversial. Anticoagulation is not recommended in newborns with large infarcts or significant central nervous system hemorrhage.[5] Unfractionated heparin has been used in adults with stroke. However, there are no studies in neonates. Heparin catalyzes antithrombin and anti–factor Xa activity, which activates the thrombolytic process. Using heparin requires frequent monitoring and blood drawing. Complications in older children and adults include major bleeding, heparin-induced thrombocytopenia, and osteoporosis.[5]

Warfarin is another anticoagulant used in adults. Most studies using warfarin in children have included infants older than 3 months.[5] Warfarin is a vitamin K antagonist and functions as an anticoagulant by decreasing functional concentration of vitamin K–dependent factors. Because vitamin K–dependent factors already are reduced in the neonatal period, it is difficult to ascertain the correct dosing of warfarin in neonates. Furthermore, the effects of warfarin are diet dependent. Formula is supplemented with vitamin K; therefore, formula fed babies are more resistant to warfarin. Breast milk has low levels of vitamin K, and thus breast-fed newborns are more sensitive to warfarin.[5] The advantage of warfarin is that it is an oral anticoagulant as opposed to an injected one. Complications of prolonged use include negative effects of warfarin on bone density in children and bleeding. It should be avoided in the neonatal period.[5]

Studies of low-molecular-weight heparin (LMWH) in newborns are more extensive than those of heparin. However, these studies have included infants up to 3 months of age and are not exclusively limited to newborns.[5] The optimal dose of LMWH in newborns again is difficult to determine. The advantages of LMWH are minimal monitoring, subcutaneous injections, and less osteopenia as compared to heparin. Bleeding is a complication of LMWH.[5]

There is minimal information on the clinical use of thrombolytics in neonates. The 3 types of thrombolytics are streptokinase, urokinase, and tissue plasminogen activator. Thrombolytic agents convert plasminogen to plasmin, which acts to dissolve the thrombus. Decreased levels of fibrinogen in the neonatal period make thrombolytics less effective. Most studies in neonates have specifically involved urokinase, but the current agent of choice in adults is tissue plasminogen activator.

The use of thrombolytics in children may carry a high risk of bleeding. One study found that 20% of pediatric patients on thrombolytics had bleeding and required transfusions. Because of the potential risk of bleeding and the lack of information, thrombolytic therapy is reserved for life-, organ-, and limb-threatening situations.[5] The Canadian Pediatric Ischemic Stroke Registry maintains a "stroke hotline" (1-800-NO-CLOTS) that provides valuable advice regarding decisions on treatment.

Keypoint

The use of anticoagulants and thrombolytics in the treatment of neonatal stroke is controversial. Thrombolytics are indicated in attempts to save life, limb, or organ. The use of anticoagulants depends on the age of the infant.

Management of Seizure

Seizures need to be treated immediately as they accelerate anoxia-induced neuronal death. Furthermore, the electrical activity of the brain post-infarct becomes an important prognostic indicator. Neonates with seizures should receive anticonvulsants; phenobarbital is the anticonvulsant of choice. Close follow-up by a pediatrician for neurologic sequelae and developmental and

learning disabilities should be established. Supportive care with early intervention by speech, physical, and occupational therapy is necessary.

Key Point

Seizures during and after stroke may be subtle and need to be recognized and treated immediately. Untreated seizure activity can accelerate damage from the stroke.

Prognosis

The outcomes reported for neonatal strokes vary among studies because different outcomes are studied, duration of follow-up varies, and the populations studied vary.[7] An overall review of the studies has found that the mortality rate from neonatal stroke is less than 10%. One third of newborns develop normally without neurologic sequelae[10]; this may be the result of a significant growth of healthy tissue into the margins of the infarcted tissue.

Hemiplegia, language deficits (prose and comprehension), visual impairments, seizures, and learning disorders are long-term sequelae of stroke.[7] EEG and neuroimaging studies provide measurements of long-term outcomes. The extent of the lesion on MRI can help determine which infants are likely to develop hemiplegia. Involvement of the hemisphere, internal capsule, and basal ganglia is always associated with an abnormal outcome, whereas involvement of only one or two of these areas may result in a normal outcome.

Neonates with abnormal EEG activity within the first week after the stroke occurs usually develop hemiplegia. The infant with abnormal background EEG activity after the first week is more likely to develop hemiplegia than is the infant with seizure activity in the presence of normal background EEG activity.[11]

The recurrence rate of neonatal stroke is less than that of childhood stroke. In the Canadian Pediatric Ischemic Stroke Registry, the recurrence rate in children with neonatal stroke is 3% to 5%.[7] The outcome was normal in 33% of these children.[7]

CONCLUSION

Neonatal strokes are an important cause of morbidity in children. Despite their subtle presentation, it is important for physicians to consider and recognize the diagnosis. Appropriate evaluation and intervention is necessary for improving the long-term outcome. Use of anticoagulants and thrombolytics is controversial in the treatment of stroke. However, it is essential that seizures be treated with anticonvulsants. Early involvement with speech, physical, occupational, and special educational services will help improve quality of life for these patients. **HP**

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