

'Idiopathic' Neonatal Cerebral Infarction

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• **Neonatal cerebral infarction is infrequently reported in the living newborn and is usually associated with perinatal risk factors, trauma, and asphyxia. This report describes two cases of full-term newborns with no predisposing problems who had unequivocal left cerebral infarctions associated with seizures in the first 24 hours of life. Radiological studies suggested an embolic cause in one case.**

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Cerebral infarction is infrequently reported in the living newborn. Nonetheless, a series of newborns from an intensive care unit who had undergone autopsies indicated that 17% of full-term infants had suffered this insult.¹ Thromboemboli from placental and umbilical vessels or the ductus arteriosus and sepsis with disseminated intravascular coagulation have been emphasized in pathophysiological formulations.^{1,2} To our knowledge, these phenomena have not been demonstrated during life in newborn infants. Recent investigators have described an association with seizures^{1,3} and a variety of predisposing clinical conditions, such as traumatic delivery,^{3,4} birth asphyxia,^{3,5} prematurity,^{1,3} meningitis,^{6,7} polycythemia,⁸ and vascular catheterization.^{9,10}

We have cared for two full-term newborn infants with cerebral infarctions and seizures, but without apparent predisposing conditions. We have designated these cases as "idiopathic" to emphasize the absence of known causes. Although the proximate cause of the infarct in one case was an appar-

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ent intracranial embolus, the source of the embolus is not known. We describe these infants to call attention to the unexpected occurrence of stroke in the unstressed full-term newborn.

REPORT OF CASES

CASE 1.—A 4,200-g full-term female infant was born to a 29-year-old primigravida mother. The prenatal course was complicated by maternal mixed-cell thyroid carcinoma; the thyroid was surgically removed at 14 weeks' gestation. The mother subsequently received thyroid replacement therapy for the duration of the pregnancy and had no further difficulties. Labor began spontaneously, proceeded without complication, and led to vaginal delivery without instrumentation six hours later. Apgar scores were 9 and 9 at one and five minutes, respectively, and the infant was transferred to the well-baby nursery.

She appeared to be well until 8 hours of age, when she had an apneic episode followed by repeated episodes of horizontal deviation of the eyes to the right and clonic jerking of the right arm. She was then transferred to the infant intensive care unit. On initial examination, she was a normal-appearing infant who was alert, crying, and moving all extremities spontaneously. Her head circumference was 36 cm, and the anterior fontanel was flat. Intermittent sucking and facial jerking, as well as clonic jerking of the right arm, were observed several times during the examination. There were no abnormalities of extraocular movements, fundi, or facial, palatal, or tongue movement. Her muscle tone, deep-tendon reflexes, and spontaneous movements of the limbs were symmetrical. Suck, Moro, and grasp reflexes were present.

On admission, laboratory evaluation included a normal CBC count and concentrations of serum electrolytes, glucose, calcium, magnesium, and arterial blood gases. A lumbar puncture disclosed slightly xanthochromic spinal fluid with 1,200 RBCs and two mononuclear WBCs per cubic millimeter. The protein concentration

in the CSF was 104 mg/dL, and the concentration of glucose was 53 mg/dL. An EEG obtained at 36 hours of age demonstrated paroxysmal abnormalities in the left hemisphere (Fig 1, top).

Frequent clonic seizures involving the right arm and face, and subtle seizures, including eye jerking and repetitive sucking movements, continued. The infant was additionally treated with 20 mg/kg of phenytoin (Dilantin) and ultimately 0.3 mL/kg of rectal paraldehyde before the seizures became infrequent. Seizures did not recur after 72 hours of age.

A computed tomographic (CT) scan performed without contrast on the third day of life showed an area of mixed increased and decreased density in the left cerebral hemisphere (Fig 2, top left). Administration of contrast medium confirmed a left middle cerebral artery (MCA) distribution abnormality (Fig 2, top right). This was interpreted as a left MCA infarction with hemorrhage. A technetium Tc 99m brain scan performed on the next day showed a wedge-shaped area of increased uptake in the distribution of the left MCA (Fig 2, bottom left). Because of the unusual nature of these findings, a cerebral arteriogram was performed on the tenth day of life; it showed a narrowed segment of the proximal left MCA consistent with a resolving embolic occlusion (Fig 3).

During hospitalization, the child had persistent mild lethargy with diffuse hypotonia and reduced tone of the right arm compared to the left. At 12 months of age, she had a spastic right hemiparesis but normal overall development as judged by the Bayley Scales of Infant Development. A CT scan performed at that time showed atrophy and porencephaly in the left hemisphere (Fig 2, bottom right).

CASE 2.—A 4,252-g full-term male infant was born to a 25-year-old primigravida mother. Prenatal course was uncomplicated, except for a maternal urinary tract infection requiring parenteral treatment with ampicillin sodium for ten days, six weeks before delivery. Labor began spontaneously, proceeded without complication, and led to a vaginal delivery without

any instrumentation within 12 hours. Apgar scores were 9 and 9 at one and five minutes, respectively; the child appeared to be well and was transferred to the well-baby nursery. Within eight hours, the infant was noted to be irritable with a reduced suck. Cultures of the blood, urine, and CSF were done, and the infant was given ampicillin sodium, 200 mg/kg/day, and gentamicin sulfate, 5 mg/kg/day. At 24 hours of age, he had several brief episodes of clonic jerking of the right upper and lower extremity and was transferred to the infant intensive care unit of this hospital for further treatment.

On initial physical examination, repeated episodes of staring, chewing, and clonic jerking of the right arm and leg were noted. There was mild hypertonia of all extremities. Extraocular movements, fundoscopic examination, and facial, palatal, and tongue movements were normal. Deep-tendon reflexes were brisk, greater in the lower extremities than in the upper extremities.

Admission laboratory studies included a normal CBC count and serum concentrations of electrolytes, glucose, calcium, and magnesium, and normal arterial blood gas levels. Lumbar puncture produced slightly xanthochromic CSF, with 54,000 RBCs and 39 WBCs (70% polymorphonuclear) per cubic millimeter, a protein concentration of 112 mg/dL, and a glucose level of 56 mg/dL. An EEG on the second day of life showed multifocal paroxysmal abnormalities, maximal in the central portion of the left cerebral hemisphere (Fig 1, bottom).

A CT scan without contrast medium on the second day of life suggested an area of hypodensity in the left MCA distribution (Fig 4, top left), and a CT scan with contrast medium on the seventh day of life was consistent with an extensive cerebral infarction in this distribution (Fig 4, top right). Technetium Tc 99m brain scan the following day showed increased uptake in the left MCA distribution (Fig 4, bottom).

The seizures decreased after a single 20-mg/kg dose of phenobarbital. The child had only occasional mild jerking of the right arm until 96 hours of age, when all seizure activity ended. Subsequent examination disclosed diffuse hypotonia with poor head control, but symmetrical spontaneous and reactive movements, normal deep-tendon reflexes, and no apparent focal abnormalities. The infant was discharged on the tenth day of life.

Follow-up at 6 months of age demonstrated a severe right spastic hemiparesis with a right visual field defect and reduced appreciation of tactile stimulation of the right upper and lower extremities as well as the trunk. Overall development was within

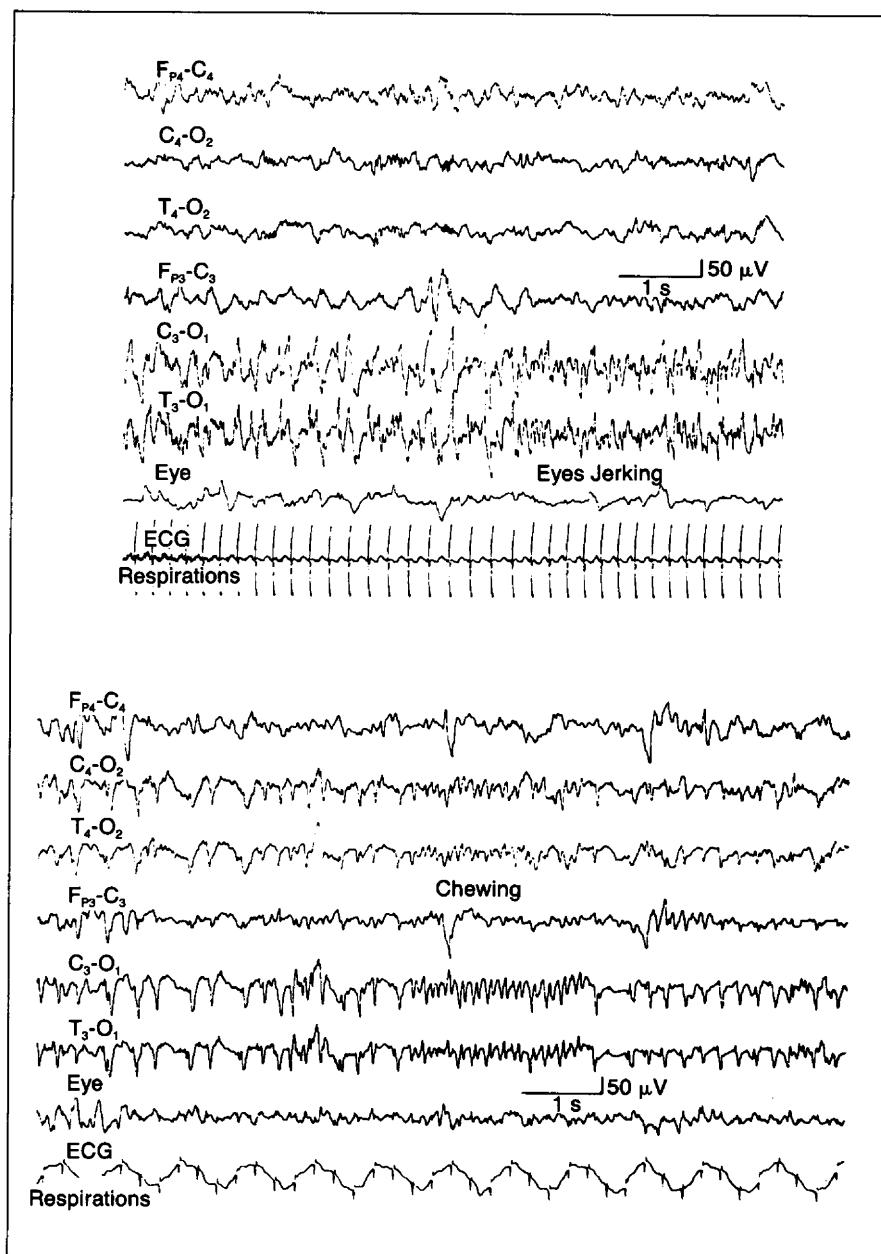


Fig 1.—Top, Case 1. Electroencephalogram shows recurrent spike activity in left temporoparieto-occipital regions coincident with rhythmical eye jerking to right. Bottom, Case 2. Electroencephalogram shows spike, slow-wave, and spindle activity in left temporoparieto-occipital area with contralateral spreading and coincident with involuntary chewing.

the normal range on the Bayley Scales of Infant Development.

COMMENT

Little is known about the pathogenesis and clinical evolution of cerebral infarctions in newborns. None of the previously described risk factors for neonatal stroke was present in our infants. Both infants probably suffered an insult of unknown cause

around the time of birth, given the initial asymptomatic period and the onset of seizures from eight to 24 hours after birth. The evolution of cerebral changes with maximal radiological abnormalities seven to ten days after birth is also consistent with this view.¹¹ It is also likely that, at least in patient 1, the infarction was due to an embolus. The angiographic findings ten days after birth support the diagnosis

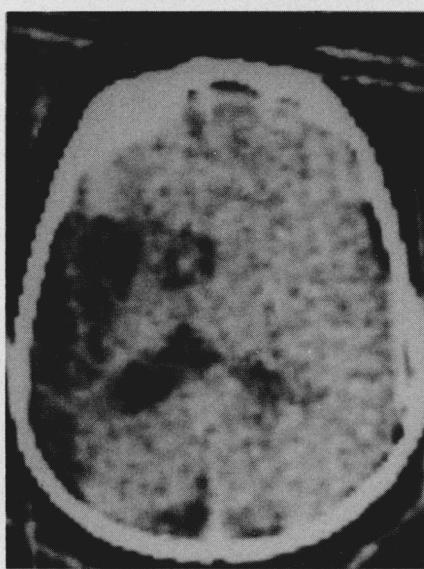
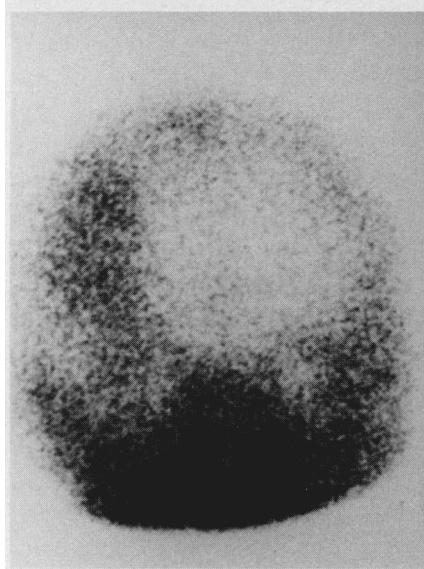
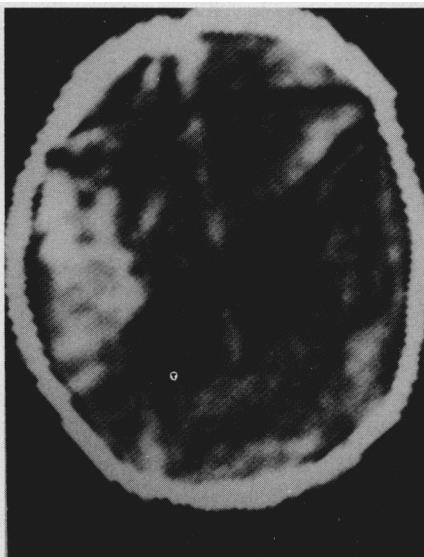
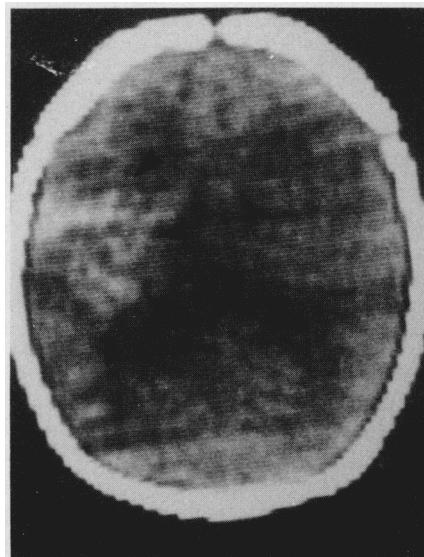


Fig 2.—Case 1. Top left, Computed tomographic (CT) scan without contrast medium shows left middle cerebral artery (MCA) distribution hemorrhagic infarction (arrowheads). Top right, After injection of contrast medium, CT scan shows left MCA distribution infarction. Bottom left, Posteroanterior view of nucleotide scan shows left MCA distribution abnormality. Bottom right, At 12 months of age, CT scan shows left hemisphere volume loss and porencephaly.

of a resolving embolic occlusion with narrowing of the proximal left MCA. Congenital stenosis cannot be entirely excluded, but is less likely, given the focality and location of the lesion and the normal appearance of all other vessels. The distribution and hemorrhagic nature of the infarct are also consistent with the usual postmortem findings in newborns with arterial occlusion.^{1,2}

To our knowledge, this is the first demonstration of intracranial embolic infarction during neonatal life. The

source of such an embolus is speculative, and the cause of the infarction in the second patient is unknown. Both infarcts were single and involved the MCA distribution, the most common location in other studies.¹⁻³ Unfortunately, the placenta and umbilical vessels were not examined in detail in either case, but no gross placental abnormalities were noted at the time of delivery.

The other report of surviving newborns with strokes differs in the presence of major perinatal risk factors,



Fig 3.—Case 1. Top, Lateral view of left carotid angiogram shows stenosis of left middle cerebral artery (MCA) (large arrow) at its bifurcation with pericallosal artery (broken line). Main branches of MCA (smaller arrows) are of normal caliber. Center, Anteroposterior view of left carotid angiogram shows same area of stenosis (arrow) in proximal left MCA. Bottom, Lateral view of normal right carotid angiogram. Area of proximal right MCA corresponding to stenotic region on left is indicated for comparison. No pericallosal vessels originate from right side.

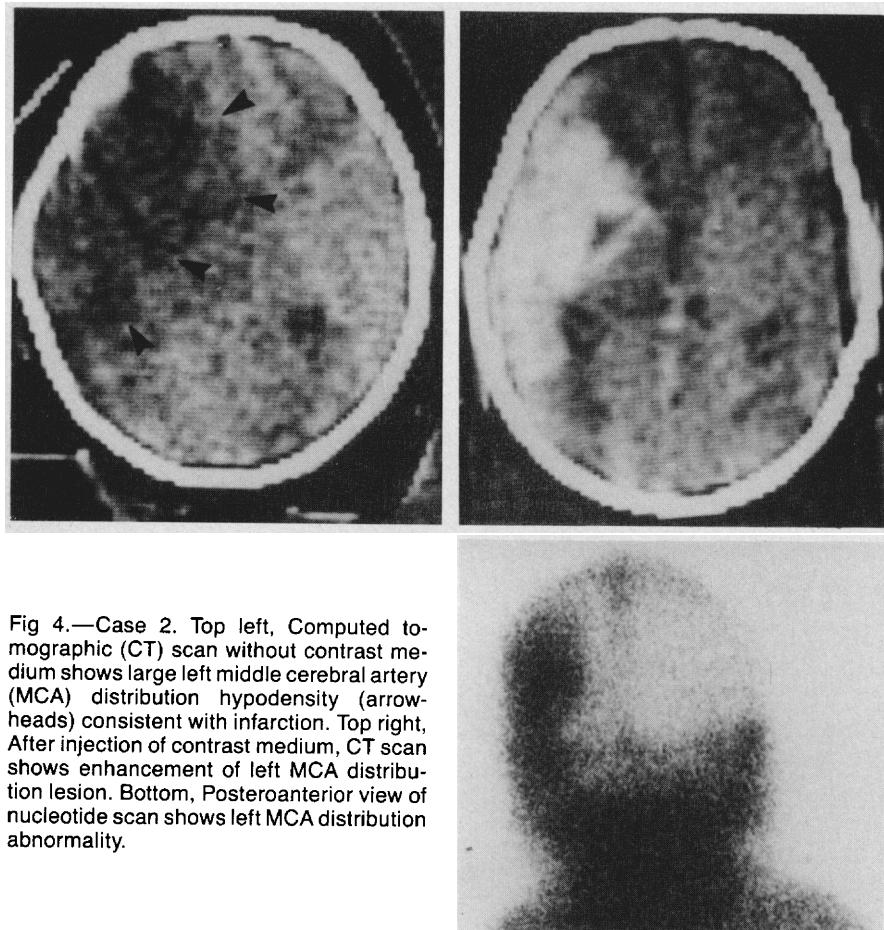


Fig 4.—Case 2. Top left, Computed tomographic (CT) scan without contrast medium shows large left middle cerebral artery (MCA) distribution hypodensity (arrowheads) consistent with infarction. Top right, After injection of contrast medium, CT scan shows enhancement of left MCA distribution lesion. Bottom, Posteroanterior view of nucleotide scan shows left MCA distribution abnormality.

including mechanical trauma and hypoxic-ischemic insults.³ The single exception in that series was a 30-week premature infant with severe respiratory distress who had a focal left occipital hemorrhage between days 3 and 6 of life. Two appended cases to that report may be similar to our patients, but complete data are not available. Although both of our patients had complications of their gestations, we are not aware of any reported association between maternal thyroid carcinoma or urinary tract infection and neonatal cerebrovascular disease. Since coagulation studies were not performed, maternal or infant hypercoagulability cannot be excluded as possible pathogenetic factors.

Noteworthy clinical features in our patients include the prominence of seizures and the abnormal CSF. Although seizures similar to those in our patients have been described in newborns with stroke,^{1,3} cerebral infarction without overt trauma or asphyxia

is not mentioned among the usual causes of neonatal seizures.⁵ The seizures in our infants were subtle and focal-clonic in type, and reminiscent of those seen after hypoxic-ischemic insults. The CSF in both cases was hemorrhagic, which was not believed to be due to traumatic lumbar punctures. These findings may indicate associated primary subarachnoid hemorrhage, or extravasation of blood from the site of cerebral infarction itself. Bloody CSF may prove to be a useful bedside clue for the presence of neonatal cerebral infarction, if confirmed by further study.

These infants with seizures and bloody CSF in the first 24 hours of life raised the questions of isolated subarachnoid hemorrhage, intracerebral hematoma, or inapparent hypoxic-ischemic insult.¹² Without CT and nucleotide scans, both infarctions would probably have been overlooked in the neonatal period. Although a recent report has shown that cranial ultra-

sound may also identify focal ischemic lesions in newborns, these studies were not performed in our patients.¹³ An angiogram was performed on our first patient because of concern that a vascular anomaly was possibly causing the hemorrhagic lesion. With increased recognition of cerebral infarctions in newborns, however, such invasive studies should not be necessary in most cases.

The presentation of these two infants within 12 months to our nursery suggests that neonatal cerebral infarction may occur more frequently than previously suggested. Examination of all infants with seizures, using CT or nuclear brain scans between the fourth and tenth days of life, may lead to increased recognition of this disorder and more information about its pathogenesis and prophylaxis.

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