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Sonography of Cerebral Infarction in Infancy

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Six infants with cerebral infarcts were examined prospectively with real-time sonography to determine the sonographic characteristics of infarcts and their evolution. Patients' ages ranged from 1 day to 7 months, and serial sonographic and/or CT scans were obtained over a period of 2 weeks to 14 months in the survivors. Among our patients the most characteristic sonographic findings of infarction were absence of gyral definition, absence of vascular pulsations, altered parenchymal echogenicity, and territorial distribution. Mass effect, reflected in ventricular size and shift of midline structures, may also be seen and largely parallels the extent of the infarction. Evolution of infarcts was seen sonographically as gradual return of arterial pulsations and concurrent development of cystic spaces.

Sonography was found to be a valuable tool in the diagnosis of infarction in infancy and in monitoring its evolution, although CT was necessary for adequate initial evaluation in older infants.

Cerebral infarction in infancy is uncommon but by no means unknown. In the past, the diagnosis has usually been made at postmortem examination [1] although there have been several recent studies documenting the CT findings during life (1–7]. Whereas adequate documentation of the sonographic appearance of diffuse cerebral edema and periventricular leukomalacia exists, there is little information about the sonographic diagnosis of both single and multiple territorial infarctions.

At our institution we have encountered six cases of cerebral infarction during the past 1½ years in infants between 1 day and 7 months old. The purpose of this study is to describe the sonographic characteristics of infarction, follow their evolution sonographically, and correlate this information with the clinical and CT findings.

Subjects and Methods

Six infants with cerebral infarction (see Table 1) were examined prospectively with real-time sonography (ATL and Diasonics equipment) using the appropriate frequency transducers. The indications for sonography were either routine screening, exclusion of a hemorrhage prior to institution of anticoagulant therapy, or emergency evaluation of neurologic symptoms. Three neonates were first evaluated with sonography while three older infants had CT scans initially and were followed with sonography and repeat CT studies. The sonograms were obtained by the radiologist and were recorded on videotape for documentation of changes in vascular pulsations. On both sonography and CT, the territorial distribution was estimated from knowledge of the vascular supply of the area of the brain demonstrating the abnormality. The diagnosis was confirmed by CT (five of six patients) and/or serial examinations that were obtained in the survivors over a period of 2 weeks to 14 months. In all cases the images were correlated with the clinical findings. Children with leukomalacia were excluded from the study.

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TABLE 1: Clinical Parameters and Region of Involvement in Patients with Infarctions

Patient No.	Age	Gestational Age	Apgar at 1 min; 5 min	Risk Factors or Associated Problems	CVA Territory	Symptoms	Outcome
1	~7 days	31 weeks	8; 9	Mild RDS	LMCA	Lethargy	Right hemiparesis, 1 year
2	~1 day	38 weeks	8; 9	Bilateral axillary artery emboli	LMCA	None	Diminished right arm function, 4 months
3	Birth	34 weeks	1; 4	Maternal ketoacidosis; asphyxia	Global	Coma	Death
4	5 mos.	—	—	Endocardial cushion defect; S/P cardiac catheterization	RMCA; RPCA	Lethargy	Death 23 days later
5	7 days	—	—	Pneumococcal meningitis	LMCA; RMCA; LPCA; RPCA	Coma; seizures	Death 4 months later
6	6 mos.	—	—	Strangulation	RACA; LACA; RMCA; RPCA; LPCA	Seizures	Cortical blindness; vegetative

Note.—Age = onset of CVA; RDS = respiratory distress syndrome; LMCA = left middle cerebral artery; RMCA = right middle cerebral artery; RPCA = right posterior cerebral artery; LPCA = left posterior cerebral artery; RACA = right anterior cerebral artery; LACA = left anterior cerebral artery.

Results

All six infants with cerebral infarction demonstrated sonographic abnormalities. Five patients manifested at least one of several underlying risk factors (see Table 1), including prematurity (without umbilical catheterization), severe birth asphyxia with acidosis, congenital heart disease with right to left shunting, meningitis, and trauma. One patient (case 2), without other identifiable risk factors, suffered from embolic phenomena elsewhere.

The clinical symptoms at the time of the infarction varied (see Table 1). Two neonates with localized left middle cerebral artery infarction were not detected clinically, as symptoms were mild and nonspecific; therefore, on both these patients, the exact timing of the acute event is not entirely clear (indicated by the symbol ∽ in the table). The infarction in patient 1, a premature infant, was diagnosed on routine screening sonography. Patient 2 had bilateral axillary artery emboli diagnosed angiographically on the first day of life and confirmed surgically; sonography was done prior to institution of heparin therapy. The remaining four patients, all of whom had infarcts involving more than one arterial distribution, presented with generalized symptoms ranging from seizures and severe lethargy to coma.

Although the acute symptoms of localized single vessel infarction may be occult clinically, the prognosis appears to be less optimistic. Patient 1 has mild developmental delay and right hemiparesis at age 1 year. Patient 2, at age 4 months, has diminished function in his right arm. Among the four patients with multiple vessel involvement, three have died. The sole survivor (patient 6) is severely handicapped neurologically.

Both infarcts confined to one arterial territory involved the left middle cerebral artery distribution (Figs. 1 and 2). Among those infants with multiple vessel involvement, one or both middle cerebral arteries were affected in all. The anterior cerebral artery distribution was spared in two of four patients with extensive infarctions (Figs. 3 and 4).

The sonographic findings may be divided into two overlapping stages: stage 1, or the edematous phase (1–2 weeks), and stage 2, or the resolution and atrophy phase (2–8 weeks).

Among our patients, six sonographic characteristics were found to be of diagnostic importance in stage 1: (1) absence of arterial pulsations; (2) absence of gyral definition; (3) altered parenchymal echogenicity; (4) territorial distribution; (5) alteration of ventricular size; and (6) midline shift. Of these findings, only the first four were made consistently. The absence of arterial pulsations was generalized in multiple vessel involvement and could be a reflection of the increased intracranial pressure in these patients. In those with less extensive infarctions, the absence of pulsations was confined to the abnormal area. Normal gyral anatomy was replaced by altered parenchymal echogenicity, which was variable in degree. The intensity of echogenicity does not reflect the presence or absence of hemorrhage: the brightest infarct (patient 2, Fig. 2A) was not hemorrhagic on CT, which showed a diffuse hypoattenuation in the superficial territory of the left middle cerebral artery (Fig. 2C). A right thalamic infarct in patient 5 was seen as abnormally bright echoes in that region (Fig. 4B). Patient 3 exhibited a wide range of echo intensity as her global infarcts evolved. In stage 1, inhomogeneously echogenic parenchyma evolved into markedly increased echoes in the region of the centrum semiovale. Ventricular size was unaffected in both patients with single vessel involvement. However, in the four patients with multiple infarcts there was ventricular compression, and a midline shift was seen in asymmetric involvement (patients 4 and 6, Fig. 4).

During stage 2, resolution of the infarcts was characterized by gradual return of arterial pulsations and variable development of cystic spaces. In patients with single vessel involvement, pulsations gradually returned to the abnormal region over a period of 1–3 weeks, beginning peripherally and extending centrally while becoming more numerous and prominent with time. In patients with multiple vessel infarctions, the return of pulsations began at the base, gradually extending

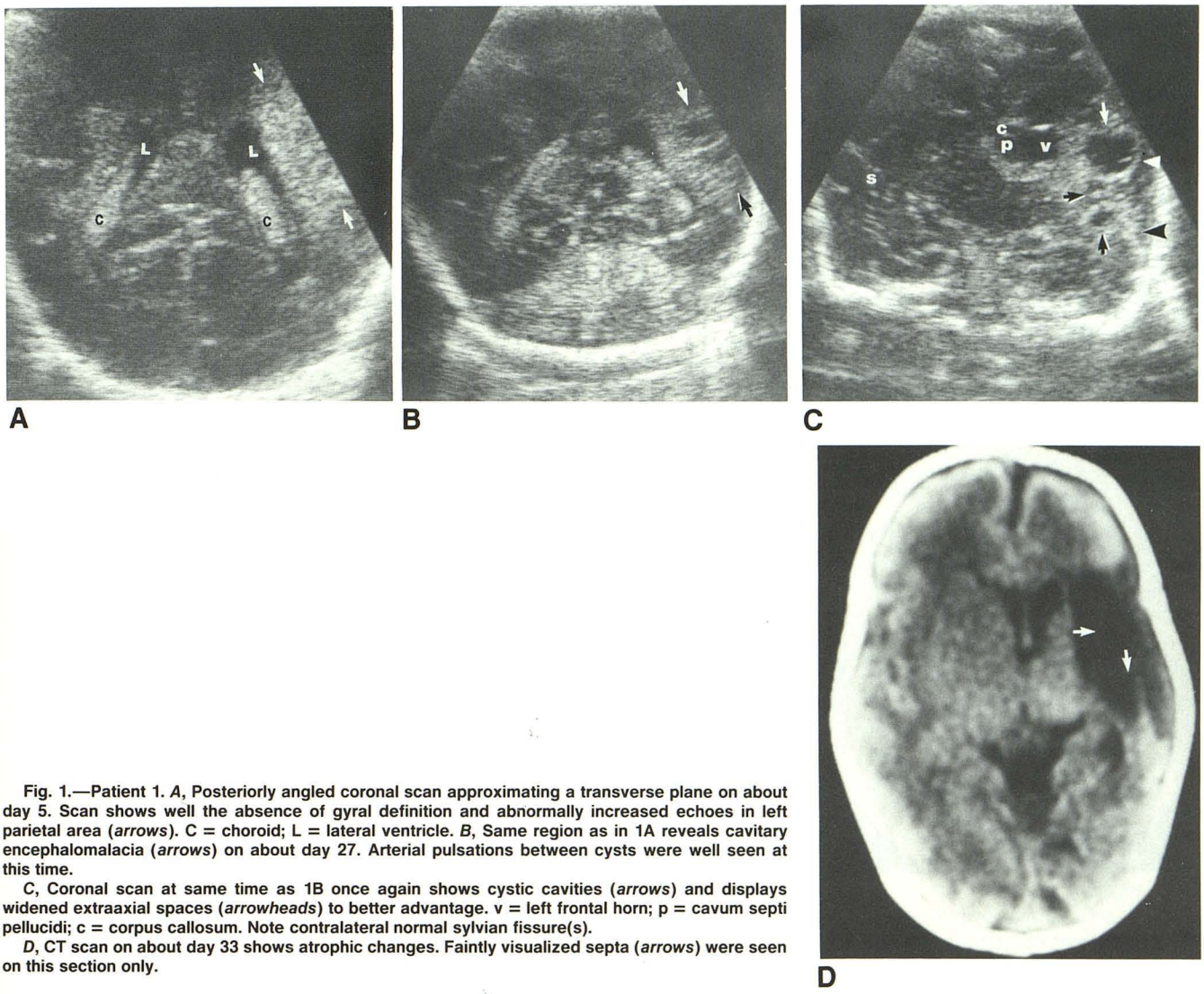


Fig. 1.—Patient 1. *A*, Posteriorly angled coronal scan approximating a transverse plane on about day 5. Scan shows well the absence of gyral definition and abnormally increased echoes in left parietal area (*arrows*). C = choroid; L = lateral ventricle. *B*, Same region as in 1A reveals cavitary encephalomalacia (*arrows*) on about day 27. Arterial pulsations between cysts were well seen at this time.

***C*, Coronal scan at same time as 1B once again shows cystic cavities (*arrows*) and displays widened extraaxial spaces (*arrowheads*) to better advantage. v = left frontal horn; p = cavum septi pellucidi; c = corpus callosum. Note contralateral normal sylvian fissure(s).**

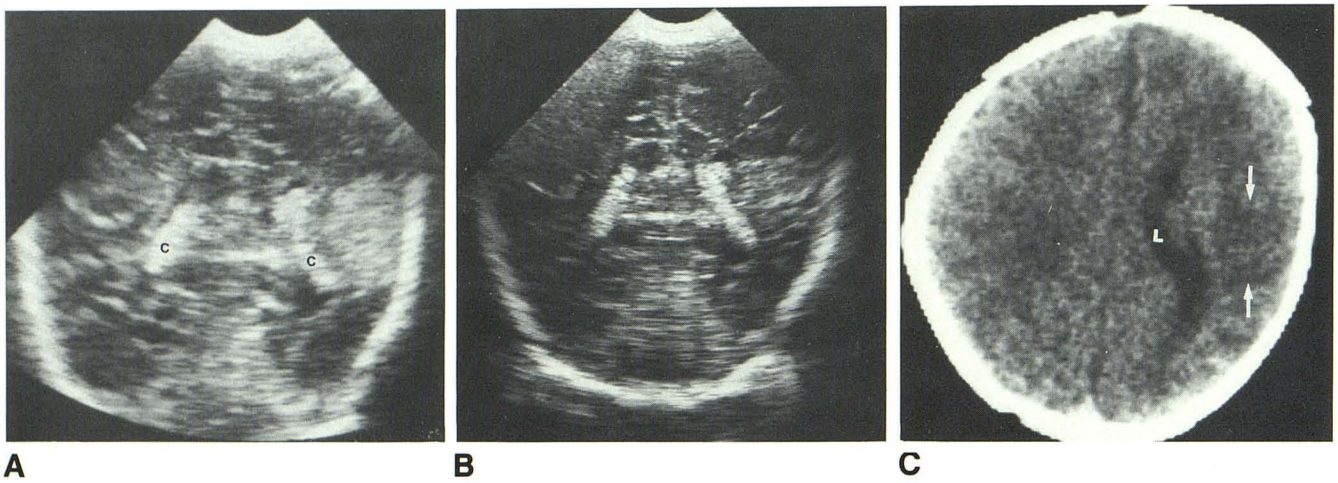
***D*, CT scan on about day 33 shows atrophic changes. Faintly visualized septa (*arrows*) were seen on this section only.**

over the branches of the circle of Willis to the sylvian fissures, reaching the convexities over a period of 3 weeks. This continuum was observed in patient 3, and the first phase of this pattern was seen in patient 4. Cysts developed concurrently with the return of pulsations and were observed in two patients. The time interval for the development of cysts varied between 4 and 7 weeks. In the majority of images depicting the abnormal area, CT did not visualize clearly the septa between cysts, which were obvious sonographically. The echogenicity in the left middle cerebral artery territory of patient 2 slowly diminished over a period of 6 weeks (Fig. 2B). In patient 3 the markedly echogenic centrum semiovale seen at the end of the edematous phase became interspersed with echolucent areas by the 3rd week and multiple cysts were present by the 7th week, surrounded by visible and active pulsations. In patient 5 the return of pulsations was never seen and cystic spaces did not develop. This is probably secondary to persistently raised intracranial pressure due to postmeningitic obstructive hydrocephalus. Patients 4 and 6 were not followed for a sufficiently long period to observe the development of cystic spaces.

Discussion

Cerebral infarction occurs in infancy and, when it does, the clinical symptoms are usually either nonspecific, nonexistent, or difficult to recognize in the ill, sedated infant. There is indication that its occurrence has largely been underestimated in the past. A postmortem series [8] places its frequency at 17% of the term infants and 5.4% of total autopsied neonates.

The reason for the formerly infrequent documentation probably lies in the relative lack of specificity of symptoms and a low clinical index of suspicion. Although in adults and in older children symptoms such as hemiparesis consequent to the loss of function in the involved region are common, in the neonate they are most often lacking [5, 9]. The most common



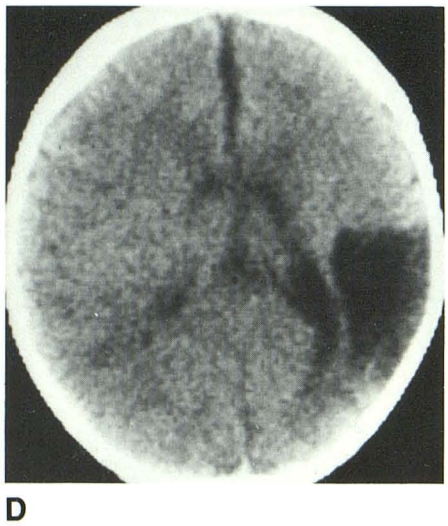


Fig. 2.—Patient 2. *A*, Posteriorly angled coronal scan approaching a transverse plane shows abnormally echogenic area in superficial distribution of left middle cerebral artery on day 2. Vascular pulsations were present only in the periphery of this region. c = choroid plexus.

***B*, Coronal projection similar to 2A shows evolution in echogenicity of infarct on day 42. Multiple pulsations were visible within and around abnormal area.**

***C*, Unenhanced CT scan on day 7 shows hypoattenuation in same distribution (*arrows*). L = lateral ventricle. Asymmetry of scan is due to slightly oblique positioning of patient's head.**

***D*, CT scan on day 45 at level similar to 2C reveals further evolution of infarct with hypoattenuation approximating that of CSF. The area is quite homogeneous, without evidence of cysts.**

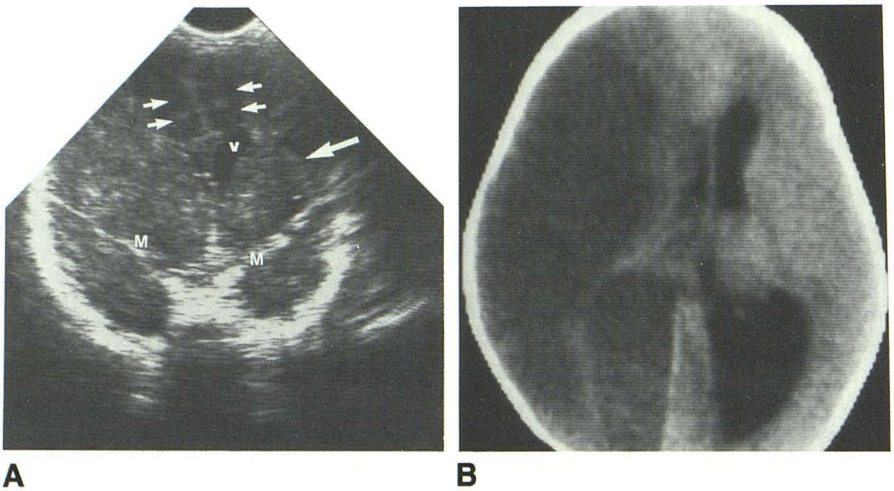


Fig. 3.—Patient 4. *A*, Coronal sonogram on about day 4 shows absence of gyral definition on right, with diffusely increased, disorganized echogenicity and mass effect with midline shift. Note normal gyral anatomy in anterior cerebral artery distribution (*short arrows*) and of left sylvian fissure (*long arrow*). Left frontal horn (v) is enlarged. m = middle cerebral artery.

***B*, Unenhanced CT scan on about day 7 substantiates extensive infarction of the right middle cerebral artery and right posterior cerebral artery territories with secondary enlargement of left lateral ventricle.**

symptoms both in our patients and in prior reports are hypotonia, lethargy, and/or seizures [3, 4]. In a retrospective series of 50 neonates with seizures [1], 14% were found to have stroke as the underlying cause; this figure rose to 31% of 24 nonasphyxiated infants. Yet, prior to 1980, cerebral infarction was not usually included among causes of neonatal seizures [1]. When seizures are the heralding symptoms, the EEG is usually abnormal [3, 4]. Our two patients with single vessel disease had mild and nonspecific symptoms that were superseded by other clinical problems. However, all the in-

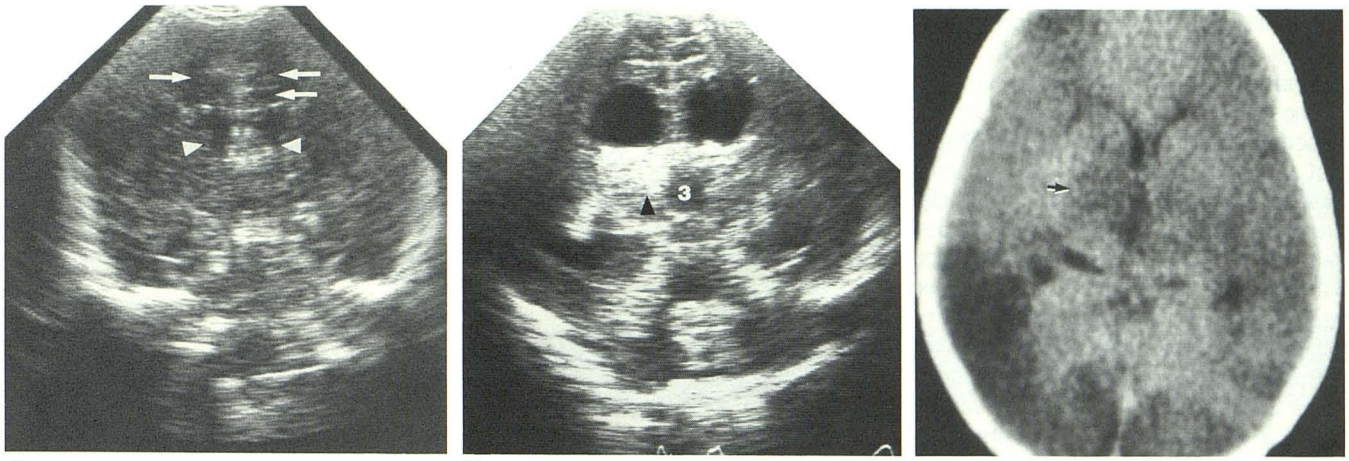


Fig. 4.—Patient 5. *A*, Coronal scan on about day 8. Both lateral ventricles are symmetrical (*arrowheads*). Note amorphously altered echogenicity and inability to identify sylvian fissures bilaterally, with sole preservation of gyral anatomy in anterior cerebral artery distribution (*arrows*). No arterial pulsations could be identified at this time.

***B*, Coronal sonogram on about day 16 angled slightly posteriorly to Fig. 1A. There is ventriculomegaly. Right thalamus is markedly echogenic at this time (*arrowhead*). 3 = third ventricle.**

***C*, Unenhanced CT scan on about day 3. Right thalamic infarct (*arrow*) and sparing of only the anterior cerebral artery distribution are evident.**

fants with extensive infarction in our series had severe CNS symptoms.

There is an extensive list of predisposing factors that includes congenital heart disease, prematurity, asphyxia, polycythemia/hyperviscosity, trauma, meningitis, and embolic phenomena, often with a source unidentified. Although five of our infants fall into one of these known high-risk categories, patients have also been reported in whom none of these risk factors were found [1], and 30–50% of infantile infarcts are currently believed to be idiopathic [9]. Cryptic emboli from an unknown source, possibly placental, have been described [1, 3] and likely played a seminal role in patient 2 and possibly also in patient 1.

The middle cerebral artery distribution was affected 46% of the time among our patients, and the single vesel disease involved the left middle cerebral artery distribution exclusively. A review of 10 prior series [1–5, 8, 10–13] in which 71 vascular territories are clearly identified, yields the following distribution: left sided 53/71 (75%); middle cerebral artery 56/71 (79%); left middle cerebral artery 43/71 (61%). The anterior and posterior cerebral arteries were involved with a relative frequency of 8% and 13%, respectively, with left-sided involvement outnumbering right by approximately 2:1. These figures are in general agreement with stroke distribution in adults as well [14]. The reason for left-sided predominance of territorial infarctions, and involvement of the middle cerebral artery in particular, remains unknown. It has been suggested [1] that regional metabolic differences may render some areas more susceptible to generalized disturbances. It is also possible that the characteristics of the blood flow are such that episodes of hypotension are more likely to be reflected in the territory of the middle cerebral artery. Alternatively, since most of the internal carotid blood flows through the middle cerebral arteries, and since the origin of the left carotid from the aortic arch may afford a more direct route to the brain, it seems appropriate to surmise that embolic events may be more likely to occur on the left side and in the middle cerebral artery distribution. In adults, most middle cerebral artery strokes are believed to be embolic in origin [15]. If the analogy could be carried further, one might hypothesize that many of the idiopathic infantile strokes may in fact be embolic in origin, as it almost certainly was in patient 2.

The prognosis of CNS infarction in infancy is not fully known. Although the potential for recuperation is believed to be greater than in older persons, in fact some permanent functional loss often results. This is especially true in multiple vessel involvement. Our one survivor with multiple vessel infarctions remains in a vegetative state. The literature [1–3, 5] has limited longitudinal studies on the children with territorial infarcts. Single infarcts may be manifested as hemiparesis by 1 year of age, or the child may be neurologically intact at that age.

The characteristic sonographic findings in the edematous phase reflect the pathologic changes occurring at this time. Initially, vasogenic or extracellular edema due to vascular damage, and cytotoxic edema or cellular swelling due to failure of the ATP pump, increase the amount of water in the brain. Grossly, such a brain demonstrates effacement of sulci [16]. This is seen sonographically as loss of the normal gyral and sulcal echoes and absence of vascular pulsations. In addition, the varying degree of disruption of the cells, fragmentation, and cellular debris probably contribute to the number of interfaces generating varying degrees of altered, disorganized echoes. Unlike other investigators [13], we do not believe that the increased echogenicity is related to the interface between normal and abnormal brain; if this were so, the high-level echoes would be limited to the periphery of the lesion, when in fact they are present through its entire extent. Prior reports have stated that increased echogenicity [11–13] and diminished vascular pulsations [11] can be seen sonographically in ischemic injury. Although we substantiate these findings, we have found that the sonographic manifestations

of infarction are not limited to increased echoes; rather, loss of gyral morphology, coupled with diminished or absent pulsations in a territorial distribution is sufficient to suggest the diagnosis. On subsequent scans, evolution of the infarcts is reflected sonographically as return of vascular pulsations and cyst formation. Ventricular size, when normal, was not a reliable indicator of edema as it was only altered in the more extensive pathology. Additionally, a wide variability in ventricular size and even asymmetry can occur in normal infants [17]. The early phase of infarction is seen on CT as generalized hypodensity and local mass effect; an isodense stage may be reached at 2–3 weeks [9].

The return of arterial pulsations heralds the beginning of stage 2. Pathologically, newly formed capillaries begin to appear in the reactive zone as early as 48 hr after the acute event [18], but become numerous after 1 week. These capillaries probably have increased permeability [18]. Concurrent with these events, hypertrophied and proliferating astrocytes will surround the necrotic areas, forming the walls of the gliotic cavities readily seen sonographically. These walls are lined by blood vessels, which are seen pulsating around the cystic cavities. At this time CT will demonstrate areas of atrophy and low attenuation approaching that of CSF. The single patient followed to this stage who did not develop cavities (patient 5) had complicating postmeningitic obstructive hydrocephalus.

Sonography was able to detect an abnormality in all our patients. This technique is most useful in the neonate and in long-term monitoring, and it offers the distinct advantages of portability and lack of need for sedation or IV contrast while the infarct is in evolution [9]. We recommend CT to exclude a hemorrhage in the abnormal area, to confirm the diagnosis when needed, and in all older infants. Sonography should be performed in any neonate with neurologic symptoms or hypotonia/lethargy, especially if he or she belongs to one of the high-risk groups for infarction.

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