Cystic periventricular leukomalacia: sonographic and CT findings.

D Schellinger, E G Grant and J D Richardson

AJNR Am J Neuroradiol 1984, 5 (4) 439-445
http://www.ajnr.org/content/5/4/439

Cystic Periventricular Leukomalacia: Sonographic and CT Findings

Dieter Schellinger[1]
Edward G. Grant
James D. Richardson

Periventricular leukoencephalopathy (PVL) is a pathologic process that has attracted little attention in neurodiagnosis. It is the second most common acquired central nervous system abnormality in neonates, outranked only by germinal matrix hemorrhage. Autopsy series suggest a 7%–22% incidence, but clinical recognition is poor. The diagnosis usually signals a less favorable neurodevelopmental outcome. Twenty-one cases with PVL and later cavitation (cystic PVL) were reviewed. Sonography was compared with computed tomography (CT) where applicable. In this series 4.8% of all neonates referred from an intensive care nursery developed cystic PVL. Hemorrhagic and nonhemorrhagic forms were observed. Sonography depicted both forms as strong periventricular echoes. Small cysts developed in the subacute phase. CT was unreliable in diagnosing the nonhemorrhagic form of PVL and had a tendency to miss the development of white-matter cysts. Sonography proved to be an excellent method for establishing the initial diagnosis and recognizing late sequelae. Late CT changes consisted of periventricular cysts, irregularity of the ventricular wall, ventricular enlargement, and cerebral atrophy.

Periventricular leukoencephalopathy (PVL) is the second most common cerebral abnormality in neonates [1]. Its late sequelae can be more serious than those of germinal matrix hemorrhage and include what is commonly termed "cerebral palsy" [2–4]. Autopsy series suggest a 7%–22% incidence [1, 2, 5, 6]. Computed tomography (CT) has proven to be insensitive in diagnosing neonatal PVL [7–10].

The diagnostic role of sonography in this disease entity is just emerging and limited to a few reports with a small number of cases [11–13]. Twenty-one cases of PVL are the basis of this report. All patients shared three characteristics: immaturity, PVL, and development of periventricular cysts.

Cystic PVL is not considered a separate pathologic entity but rather a subgroup of PVL that shares the presence of periventricular cysts as a common pathologic end point. Our experience emphasizes the diagnostic usefulness of sonography and the limited value of CT.

Materials and Methods

During a 3 year period, 440 neonates were examined by sonography for cerebral disease, predominantly for changes associated with neonatal cerebral anoxia/ischemia. The infants were referred from the intensive care nursery. In- and outborn infants were not analyzed separately. All patients were premature and had signs of perinatal distress of varying duration and severity. Sonographic diagnosis of cystic PVL was made in 21 neonates. This represents an overall incidence of 4.8%. In 18 patients the evolution of periventricular cysts could be observed on successive sonograms. Late sequelae could be evaluated in 11 patients. This analysis was usually conducted with CT only. Four patients who were followed long enough to judge neurodevelopmental outcome showed mental retardation, motor instability, developmental delay, spastic diplegia, or a combination of these. Only one patient died. An autopsy was not performed.

Thirteen patients had no evidence of preceding or concomitant subependymal or intraven-

Received September 1, 1983; accepted after revision December 28, 1983.

Presented at the the annual meeting of the American Society of Neuroradiology, San Francisco, June 1983.

[1] All authors: Department of Radiology, Georgetown University Medical Center, 3800 Reservoir Rd., N.W., Washington, DC 20007. Address reprint requests to D. Schellinger.

AJNR 5:439–445, July/August 1984
0195–6108/84/0504–0439 $2.00

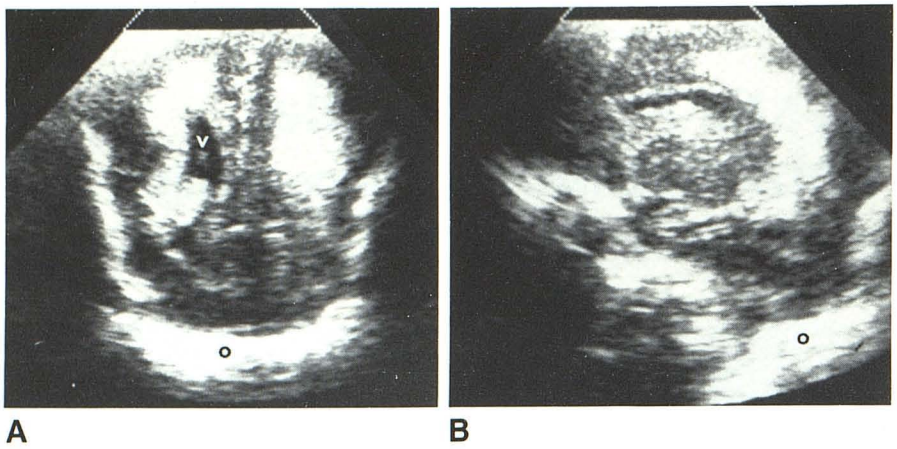

Fig. 1.—Premature neonate with hemorrhagic PVL proven by CT. **A**, Axial sonogram showing periventricular echogenicity. **B**, Angled sagittal view with dense echoes surrounding posterior ventricular body and trigone. v = ventricle, o = occipital bone.

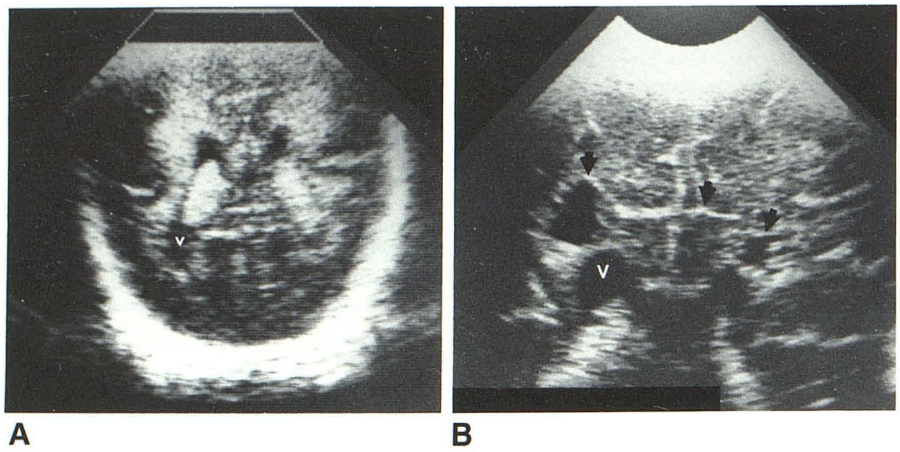

Fig. 2.—PVL. Early CT not performed. Hemorrhagic and nonhemorrhagic variant not distinguished. **A**, Early sonogram at 2 weeks of age shows periventricular echogenic halo. **B**, Follow-up sonogram 3 weeks later shows bilateral cysts in corona radiata (*arrows*). v = ventricle.

tricular hemorrhage, while five patients did show such an association. In all cases the sub- or intraventricular hematoma was rather subtle. In three cases very early sonograms were not obtained, and a statement about presence or absence of subependymal and/or intraventricular hemorrhage cannot be made.

Sonography was performed initially with an Advanced Technology Laboratories Mark III real-time sector scanner, using a 5 MHz transducer. More recently, a 7.5 MHz transducer was used. Coronal and parasagittal sonograms were obtained through the anterior fontanelle. Usually, sonography was performed within 72 hr of birth or, in the case of outside referrals, within 48 hr of admission. During the infant's stay in the intensive care nursery, follow-up sonograms were obtained on all neonates with abnormal sonograms at intervals of 1 day to 1 week, depending on pathology. The patients in this group had an average of five serial sonograms. A few patients had up to 15 sonograms. Serial sonograms were obtained until the cerebral changes had stabilized.

One hundred thirty patients also had CT scans that were obtained on a Philips 310 and Pfizer 200 FS scanner. CT scans were obtained only in those patients who had indeterminate sonograms or whose clinical conditions were not explainable on the basis of the sonographic findings. CT examinations were also performed as a means of late follow-up, frequently months after dismissal from the intensive care nursery.

Results

Sonographic Observations in Cystic PVL

In each of the 21 cases the earliest sonographic abnormally consisted of a broad band of bilateral, strong, periventricular echoes merging imperceptibly with surrounding white matter. This commonly occurred within the first 10 days of life. We previously referred to this as a periventricular halo [14]. It is best seen on the high axial sections but is seen also on the sections showing the lateral ventricles and on the angled parasagittal slices (figs. 1 and 2A). It is most pronounced around the posterior half of the lateral ventricles and posterior to the trigone. The region surrounding the lateral angle of the frontal horns was also frequently involved. In a few cases the echo halo was asymmetric, being stronger in one of the two hemispheres.

High-level echoes may denote hemorrhagic or nonhemorrhagic PVL. Among seven patients in whom early CT/sonography comparison permitted a more precise tissue characterization, the increased periventricular echogenicity proved to represent edema in four and white matter hemorrhage in three. Therefore, sonography did not reliably differentiate

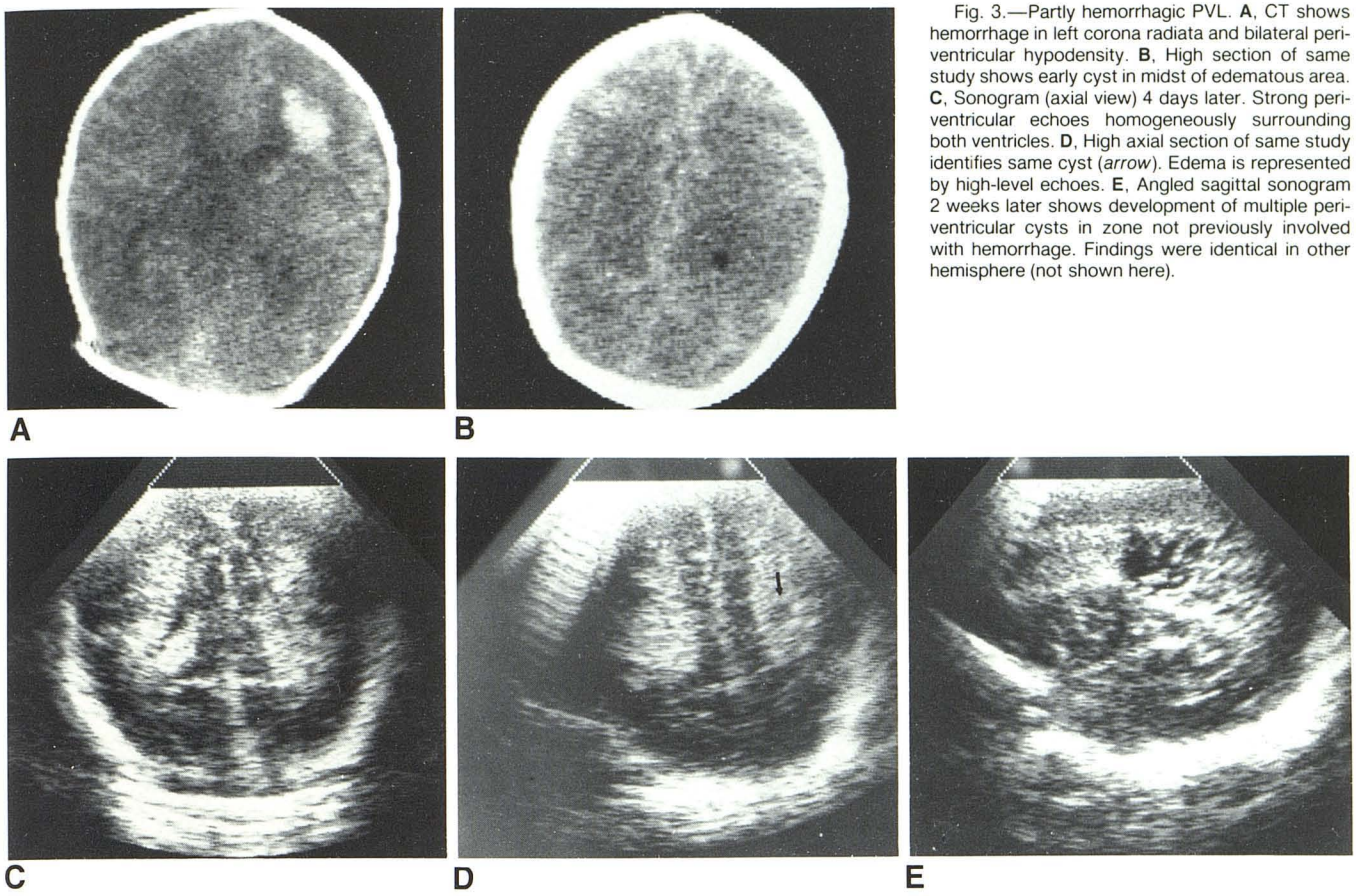

Fig. 3.—Partly hemorrhagic PVL. **A**, CT shows hemorrhage in left corona radiata and bilateral periventricular hypodensity. **B**, High section of same study shows early cyst in midst of edematous area. **C**, Sonogram (axial view) 4 days later. Strong periventricular echoes homogeneously surrounding both ventricles. **D**, High axial section of same study identifies same cyst (*arrow*). Edema is represented by high-level echoes. **E**, Angled sagittal sonogram 2 weeks later shows development of multiple periventricular cysts in zone not previously involved with hemorrhage. Findings were identical in other hemisphere (not shown here).

hemorrhagic from nonhemorrhagic forms of PVL as the degree of echogenicity was similar in both.

The periventricular cysts usually commenced as small lucencies 1–3 mm in diameter (fig. 3E). They developed 10–20 days after the stage represented by periventricular echoes and occurred as solitary lesions or in multiples. They were distributed randomly throughout a certain anatomic area of white matter or were parallel to the superior or superolateral border of the ventricles. The trigonal region was most often involved, followed by corona radiata. The cysts tended to progress in size. They became confluent and reached sizes of 1 cm or more or remained small. They sometimes merged imperceptibly with the adjoining ependyma. The larger cysts often showed septations within, testifying to their multifocal origin (fig. 4). They differed from the porencephalic cyst evolving from intracerebral hematoma in that they were smaller, occurred in multiples, and had a predictable relation to the lateral ventricles. Also, posthematoma porencephalic cysts usually were not septated.

The cysts always occurred within the zone of increased echogenicity, but they were often unilateral. As a rule the high-level echoes disappeared within 2 weeks, leaving behind the cavitations and slowly expanding lateral ventricles.

The presence of periventricular cysts in the nonhemorrhagic form of PVL supports the notion that they develop independent of preceding hemorrhage in same territory. In one case of combined hemorrhagic/nonhemorrhagic PVL the cysts developed in the nonhemorrhagic part of PVL, distant from the hemorrhagic component (fig. 3).

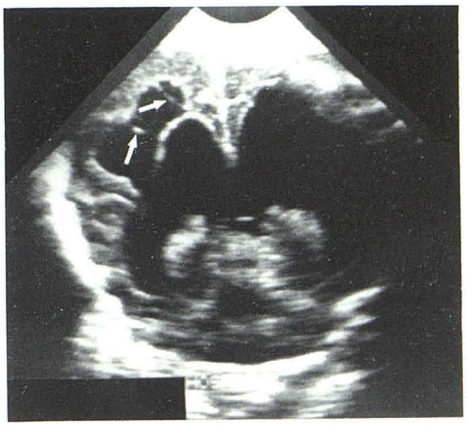

Fig. 4.—Axial sonogram. Confluent, large periventricular cyst with septa (*arrows*).

CT Observations in Cystic PVL

The CT equivalent of the echohalo was periventricular hypodensity of varying degrees (figs. 3 and 5) or periventric-

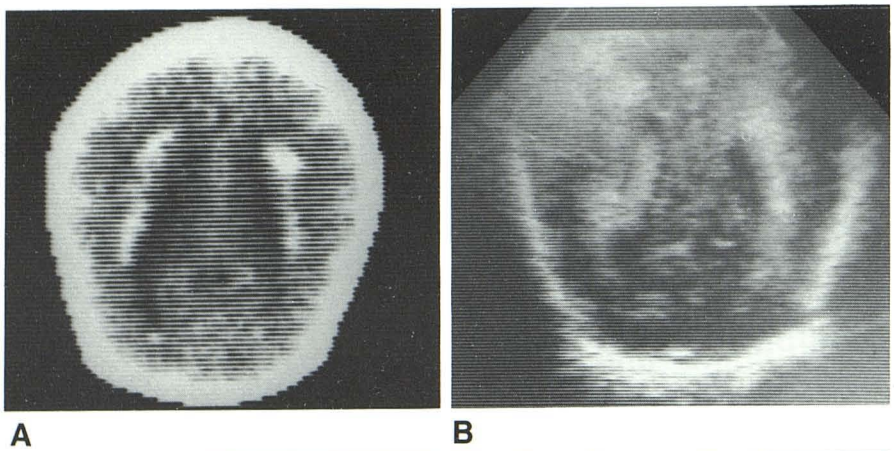

Fig. 5.—Hemorrhagic and nonhemorrhagic PVL. **A** and **B**, Hemorrhagic PVL with increased attenuation on CT and echogenic centrum semiovale on sonogram. **C** and **D**, Nonhemorrhagic PVL produces periventricular low density on CT and similar high-level echoes on sonogram.

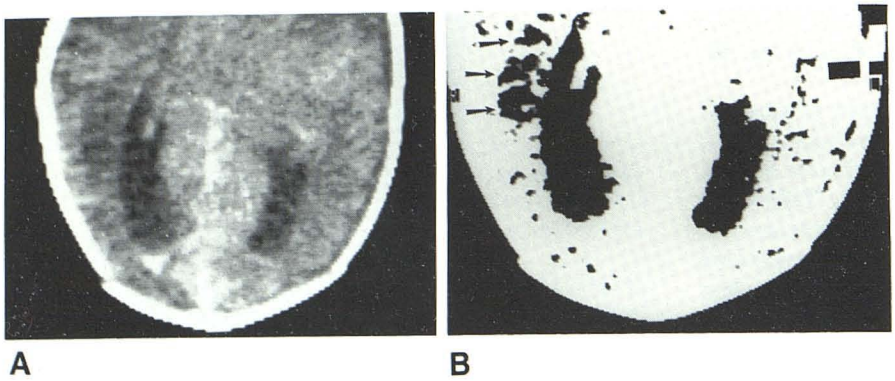

Fig. 6.—3-week-old premature neonate. **A**, Periventricular hypodensity on CT. **B**, Manipulation of window level and window width identifies multiple small cysts (*arrows*) along lateral border of right lateral ventricle.

ular white-matter hemorrhage. A common finding on early CT scans was the presence of diffuse periventricular low attenuation, involving virtually all white matter. In delineating the extent of the process, the correlation between high echo texture and decreased CT attenuation was not very close.

Occasionally periventricular cysts could be seen clearly on early CT scans (Fig. 3B), but more often they were difficult to discern. Sometimes they could be recognized only retrospectively after appropriate window manipulations (fig. 6). When located close or adjacent to lateral ventricles they were misinterpreted on CT as focal ventricular irregularities or as indistinct borders, while sonograms clearly identified them as cysts (figs. 7 and 8).

In all 11 patients who were followed up to 12 months, late CT scans invariably showed diffuse atrophy with marked prominence of the interhemispheric fissure. Ventricular dilatation of varying degrees was another constant finding, especially trigonal expansion. The periventricular cysts were seen as clearly demarcated, focal low densities in periventricular white matter, either solitary or multiple (figs. 9 and 10).

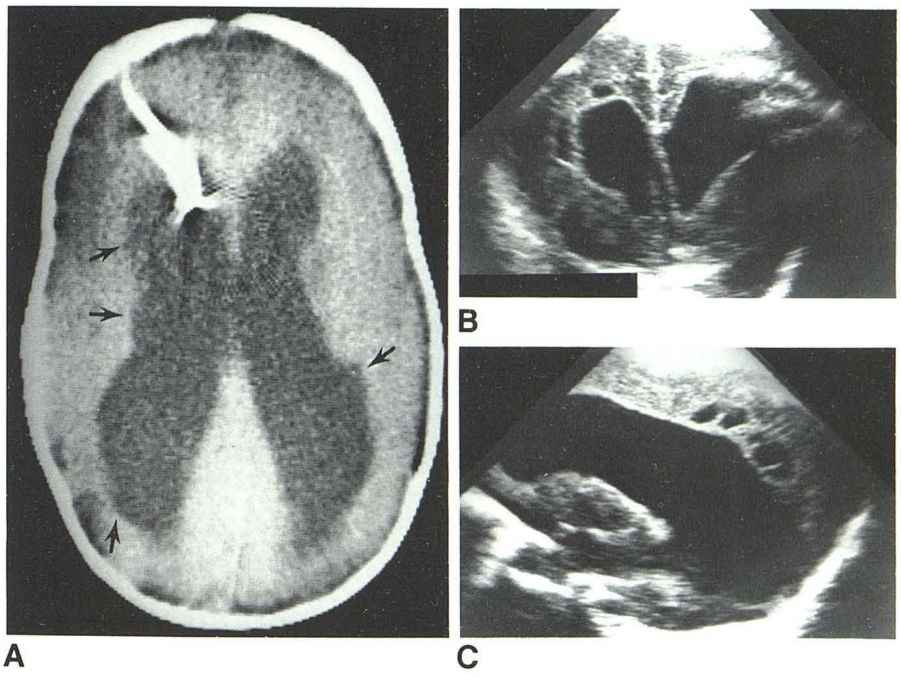

Fig. 7.—Contour irregularity of lateral ventricles caused by periventricular cysts in 3-month-old infant with shunted hydrocephalus. **A**, CT shows irregular, bumpy contour of ventricles (*arrows*). Coronal (**B**) and angled sagittal (**C**) sonograms show intact ependyma. Irregular contour of ventricles is caused by well demarcated periventricular cysts.

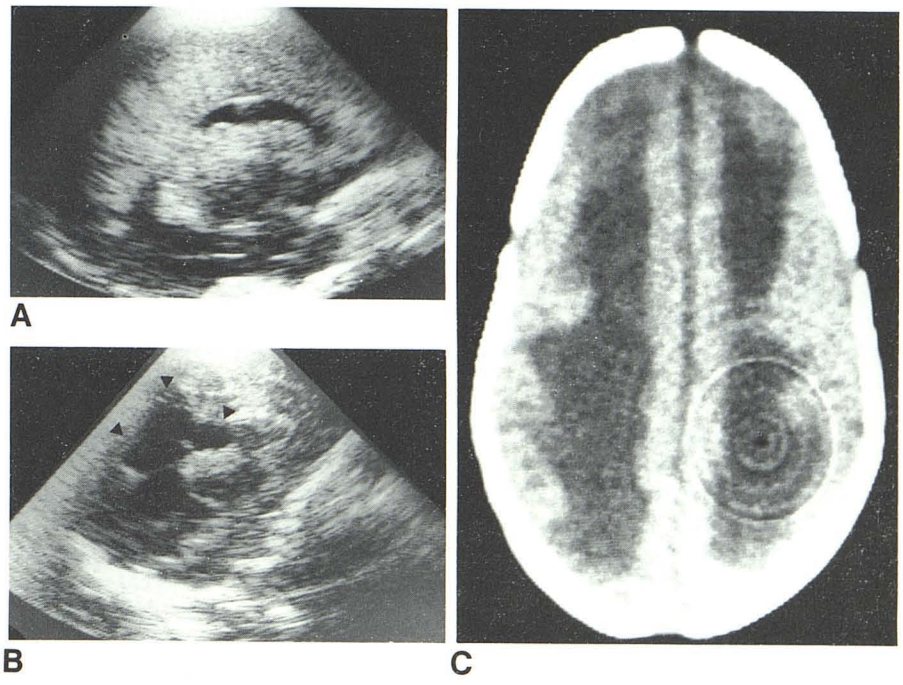

Fig. 8.—Contour irregularity of lateral ventricles caused by periventricular cysts in neonate. **A**, Angled sagittal sonogram. Echogenic zone surrounding posterior part of lateral ventricles. **C**, 2 weeks later. Large cysts have developed in same area. **C**, 4 weeks later. CT shows irregular contour of ventricles, caused by juxtaposed periventricular cysts.

Discussion

While there is now great familiarity with germinal matrix and intraventricular hemorrhage in neonates [14], periventricular leukomalacia remains a relatively enigmatic diagnostic entity. Autopsy series suggest an incidence as high as 22% [1], but the overall incidence in the neonatal population is not established firmly. Since PVL can lead to rather devastating long-term sequelae with spastic diplegia, dementia, choreoathetosis, ataxia, and visual and speech dysfunctions [6], it is important to identify sonographic or CT features that suggest its presence in early life.

Like the usual forms of cerebroventricular hemorrhage, PVL

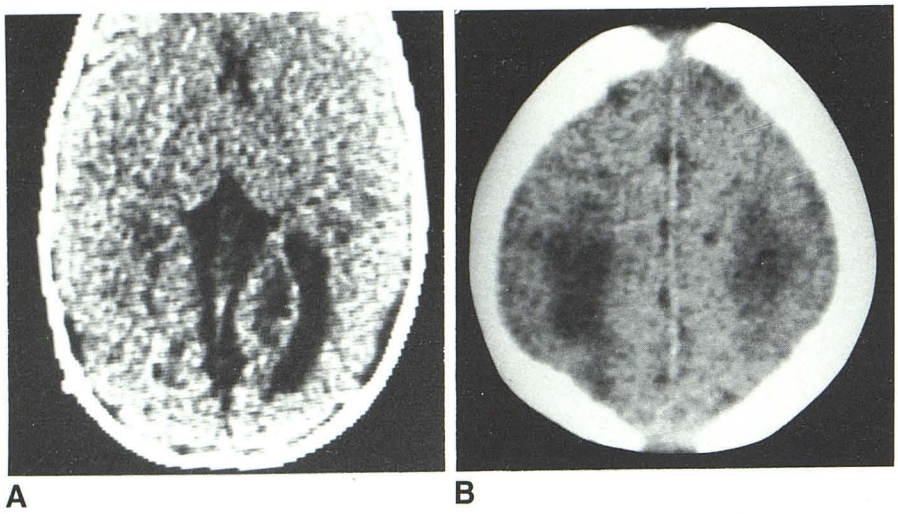

Fig. 9.—Late follow-up CT scans in two different patients show large cysts in occipital areas (**A**) and multiple small cysts in both cerebral hemispheres (**B**).

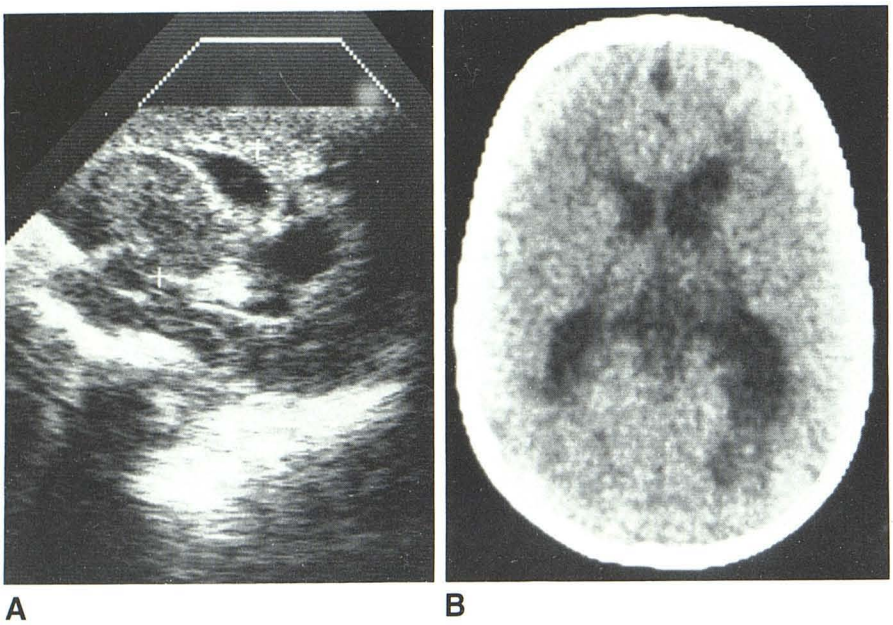

Fig. 10.—10-month-old infant with periventricular cysts. **A**, Angled sagittal sonogram shows large cyst close to trigone. **B**, Axial CT scan shows poorly defined low density in corresponding area.

is a marker of deranged cerebral blood flow [5]. PVL is found in the deep border zone between anterior, middle, and posterior cerebral arteries between the ventriculopetal and ventriculofugal arteries [16]. PVL consists of foci of coagulation necrosis [1] with associated edema [15] and tissue softening. Tissue breakdown may leave periventricular cavitations [3, 16] that then become the most prominent change [2]. All patients in our series showed such cavitations. PVL is not to be confused with nonhemorrhagic or hemorrhagic focal infarction. The latter is localized or multifocal, occurs more in the periphery of brain in the watershed zones between major cerebral arteries, and is more common in term infants [17].

Armstrong and Norman [5] reported a 25% incidence of focal or diffuse hemorrhage within the affected white matter. Associated subarachnoid, subependymal, or intraventricular hemorrhage has been reported [5, 16], and may be as high as 59% [6]. It occurred in 28% of our cases. Hill et al. [12] documented hemorrhagic PVL in a premature infant using sonography. It was characterized by echogenic zones surrounding the lateral ventricles. Postmortem evaluation showed subacute periventricular infarction complicated by secondary hemorrhage. Cystic degeneration of white matter was not observed in their case. We [14] previously reported two cases with findings identical to those identified by Hill et al. Cavitation occurred in both. In the pediatric literature Levene et al. [13] reported nine patients with hemorrhagic PVL. Five of these developed cysts. Levene et al. defined hemorrhagic PVL as an area of increased echogenicity in the periventricular region. However, it is unclear how the hemorrhagic nature of PVL was established. In their material the incidence of PVL (with or without cysts) was 7.5%.

Babcock and Ball [18], reporting on the sonographic diagnosis of postasphyxial encephalopathy in full-term infants, observed diffusely increased cerebral echogenicity that was shown to represent cerebral edema. Three patients in their series developed cysts within the zones of increased echo-

genicity. Sonographically documented cysts, occurring subsequent to various forms of focal infections, have also been described. These were found randomly distributed throughout the hemispheres [19] or localized to the subependymal germinal matrix [20].

Our data support observations in the neuropathology literature, which indicate that leukomalacia may present in either hemorrhagic or nonhemorrhagic forms. Sonography is unable to distinguish between the two. CT can depict the hemorrhagic variant but is rather unreliable in diagnosing the nonhemorrhagic form [7–10].

Sonography recognizes easily the development of cystic white matter breakdown. CT's inferiority in showing small periventricular cysts has been observed by others also [11, 13, 18]. We suspect that it is related to volume averaging. Also, axial slices may mistake pathologies adjacent to the ventricles for small ventricular irregularities. However, late sequelae of cystic PVL are easier to show on CT scans as the pathologic changes become larger and more clearly demarcated. Despite this, periventricular cysts may still escape recognition.

We have focused on a group of PVL that can be diagnosed reliably by virtue of developing cysts. However, this group should represent but a fraction of all PVL cases, usually the ones damaged most severely. The neuropathologic literature indicates that PVL frequently does not lead to gross tissue cavitation. These cases may become identifiable by virtue of a positive echo halo.

The reliability of the echo halo sign as the single diagnostic indicator for PVL has not been tested sufficiently. However, the cases reported by Hill et al. [12] and Levene et al. [13] as well as the findings by Babcock and Ball [18] suggest that increased echogenicity does indeed denote tissue abormality. Therefore, a strong echo halo should alarm the diagnostician to probable white-matter edema and/or hemorrhage. In the more severe cases—those selected for this report—the emergency of periventricular cysts affirms the diagnosis of PVL.

We surmise that cystic PVL is more prevalent than previously assumed and that the incidence in our series understates the factual frequency. In our series the incidence of cystic PVL increased markedly in the most recent cases. Undoubtedly, this is the result of our greater awareness of this entity and improvement in sonographic technology.

REFERENCES

1. Leech RW, Alford EC. Morphologic variations in periventricular leukomalacia. *Am J Pathol* **1974**;74:591–600
2. Banker BQ, Larroche J-C. Periventricular leukomalacia of infancy. *Arch Neurol* **1962**;7:386–410
3. Abramowicz A. The pathogenesis of experimental periventricular cerebral necrosis and its possible relation to the periventricular leucomalacia of birth trauma. *J Neurol Neurosurg Psychiatry* **1964**;27:85–95
4. Volpe JJ. Perinatal hypoxic-ischemic brain inuury. *Pediatr Clin North Am* **1976**;23:383–397
5. Armstrong D, Norman MG. Periventricular leucomalacia in neonates. Complications and sequelae. *Arch Dis Child* **1974**; 49:367–375
6. Shuman RM, Selednik LJ. Periventricular leukomalacia. A one year autopsy study. *Neurology* (NY) **1980**;37:231–235
7. Flodmark O, Becker LE, Harwood-Nash DC, Fitzhardinge PM, Fitz CR, Chuang SH. Correlation between computed tomography and autopsy in premature and full-term neonates that have suffered perinatal asphyxia. *Radiology* **1980**;137:93–103
8. Albright L, Fellows R. Sequential CT scanning after neonatal intracerebral hemorrhage. *AJNR* **1981**;2:133–137, *AJR* **1981**; 136:949–953
9. Estrada M, El Gammal T, Dyken PR. Periventricular low attenuation. A normal finding in computerized tomographic scans of neonates? *Arch Neurol* **1980**;37:754–756
10. Schrumpf JD, Sehring S, Killpack S, Brady JP, Hirata T, Mednick JP. Correlation of early neurologic outcome and CT findings in neonatal brain hypoxia and injury. *J Comput Assist Tomogr* **1980**;4:445–450
11. Taboada D, Olague A, Mulas F, Andres V. Radiologic diagnosis of periventricular and subcortical leukomalacia. *Neuroradiology* **1980**;20:33–41
12. Hill A, Melson GL, Clark HB, Volpe JJ. Hemorrhagic periventricular leukomalacia: diagnosis by real time ultrasound and correlation with autopsy findings. *Pediatrics* **1982**;69:282–284
13. Levene MI, Wigglesworth JS, Dubowitz V. Hemorrhagic periventricular leukomalacia in the neonate: a real time ultrasound study. *Pediatrics* **1983**;71:794–797
14. Grant EG, Schellinger D, Richardson JD, Coffey ML, Smirniotopoulos JG. Echogenic periventricular halo: normal sonographic finding or neonatal cerebral hemorrhage. *AJNR* **1983**;4:43–46, *AJR* **1983**;140:793–796
15. Fenichel GM. Hypoxic-ischemic encephalopathy in the newborn. *Arch Neurol* **1983**;40:261–266
16. DeReuck J, Chattha AS, Richardson EP. Pathogenesis and evolution of periventricular leukomalacia in infancy. *Arch Neurol* **1972**;27:229–236
17. Pape KE, Wigglesworth JS, eds. *Clinics in developmental medicine*, nos. 69/70. London: William Heinemann Medical, **1979**
18. Babcock DS, Ball W. Postasphyxial encephalopathy in full-term infants: ultrasound diagnosis. *Radiology* **1983**;148:417–423
19. Stannard MW, Jimenez JF. Sonographic recognition of multiple cystic encephalomalacia. *AJNR* **1983**;4:1111–1114, *AJR* **1983**; 141:1321–1324
20. Shackelford GD, Fulling KH, Glasier CM. Cysts of the subependymal germinal matrix: sonographic demonstration with pathologic correlation. *Radiology* **1983**;149:117–121