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Postischemic Hypervascularity of the Infant Brain: Differential Diagnosis on Computed Tomography

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On noncontrast computed tomographic studies, four infants suffering severe ischemia demonstrated increased attenuation in a predominantly gray matter distribution. These areas enhanced homogenously after contrast infusion. Pathologically, marked capillary proliferation was found to occupy the areas of enhancement. This computed tomographic pattern lasted for months. It was associated with a poor prognosis for neurologic function.

Increased precontrast attenuation values on cranial computed tomography (CT) are usually associated with calcification or blood, either extra- or intravascular. Brain tumors can also be hyperdense on the basis of hypervascularity and tissue density. We report increased precontrast density corresponding to areas of marked capillary proliferation in infants after diffuse brain ischemia. These areas of increased attenuation are restricted to well defined anatomic structures, especially the deep gray matter, and show enhancement after contrast infusion. The pathologic features of this unusual lesion, termed "postischemic hypervascularity" were described in greater detail elsewhere [1]. On the basis of the pathologic changes, it was then postulated that the increased attenuation would become less pronounced after some months or years. Nevertheless, no regression was detected on CT performed as late as 6 months after the ischemic event. The 16 month follow-up CT in one case of postischemic hypervascularity suggests that the previous interpretation on the nature of the lesion was correct. It was believed to represent a transient, exaggerated endothelial response to severe hypoxic brain damage in areas of normally high capillary density. It has been seen only in infants, presumably because of their unique vascular plasticity. We discuss the CT aspects of postischemic hypervascularity and its differential diagnosis.

Materials, Methods, and Results

Four infants with postischemic hypervascularity were followed with serial CT scans, using either an EMI 1005 or 6000 scanners. Table 1 summarizes the varied causes of ischemia and the sites of hypervascularity. The CT scan of case 1 is representative (fig. 1). Areas of hypervascularity showed Hounsfield numbers (±1,000) 5–10 units higher than normal tissue, and enhanced by a further 5–10 units (table 2). In case 2, serial CT studies up to 4 months (2, 4, 12, and 16 weeks) showed the same pattern of increased attenuation that was further enhanced after contrast infusion. Compared with the previous studies, CT 16 months after the ischemic event (fig. 2) showed a relative decrease in the attenuation values, with only mild enhancement after contrast infusion. The clinical course of all infants was poor. One died 12 days after a CT study, and autopsy revealed that in areas corresponding to the CT abnormality, there was almost total replacement of the parenchyma by a dense network of capillaries, along with sparse microscopic calcium deposits (fig. 1). The three survivors suffered severe neurologic deficits, including spastic quadriparesis, deafness, and cortical blindness.

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TABLE 1: **Postischemic Hypervascularity: Summary of Cases**

Case No.	Cause of Ischemia	Site of Postischemic Hypervascularity
1	Meningitis at 9 months	Frontal lobes, basal ganglia
2	Premature, complicated delivery	Thalami
3	Term, umbilical knot meconium aspiration	Hippocampus, depths of sulci, meninges
4	Premature, prolonged apnea at 9 days	Meninges, subependymal

Discussion

Postischemic hypervascularity represents an organizing stage in the evolution of the traditional neuropathologic sequelae to brain ischemia in infants [2–4]. Serial CT scans reveal that the lesion tends to occur 1–2 weeks after an ischemic insult. The pathology of postischemic hypervascularity has been seldom described because severely asphyxiated infants usually either die in the immediate perinatal period and hypervascularity does not develop, or they continue to live for years afterwards, by which time it has given way to brain atrophy. CT permits recognition of this transient stage at a time when few patients come to autopsy.

Postischemic hypervascularity can be mistaken for hemorrhagic infarction, as occurred in case 1 before autopsy revealed the true nature of the lesion. Localizaton does not help in differentiation because both lesions can be restricted to similar anatomic areas. However, while hemorrhagic infarction can resemble postischemic hypervascularity on an initial scan (as enhancement associated with precontrast attenuation), its evolution in the clinical context provides a basis for distinction. Hemorrhagic infarction occurs within hours of ischemia, and the precontrast attenuation gradually fades as the blood is metabolized and reabsorbed. In contrast, hypervascularity does not appear until at least 7 days after ischemia, and tends to increase in intensity over the first few weeks as capillary proliferation proceeds. After several months, both the precontrast attenuation and the postcontrast enhancement decrease, as shown by our follow-up study 16 months after the ischemic event.

Postischemic hypervascularity differs from gray matter contrast enhancement, a pattern often recognized after ischemic infarction [5–7]. The latter correlates pathophysiologically with leakage across the blood-brain barrier, vasodilation, and possibly neovascularization [8, 9]. It usually occurs 7–21 days after infarction and disappears entirely by 3–6 months. It is not associated with any significant precontrast attenuation, unless the infarct is hemorrhagic. In contrast, postischemic hypervascularity is based on extreme neovascularization, is more lasting, and does exhibit precontrast increased attenuation. Postischemic hypervas-

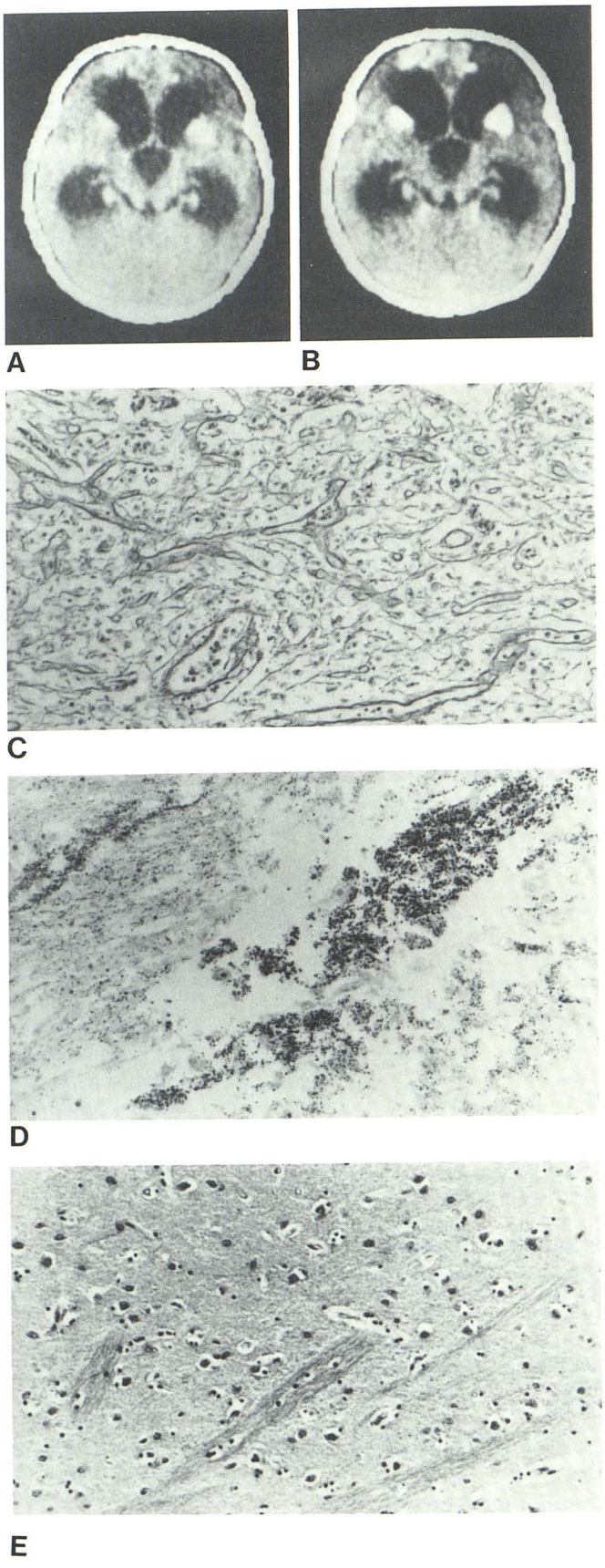
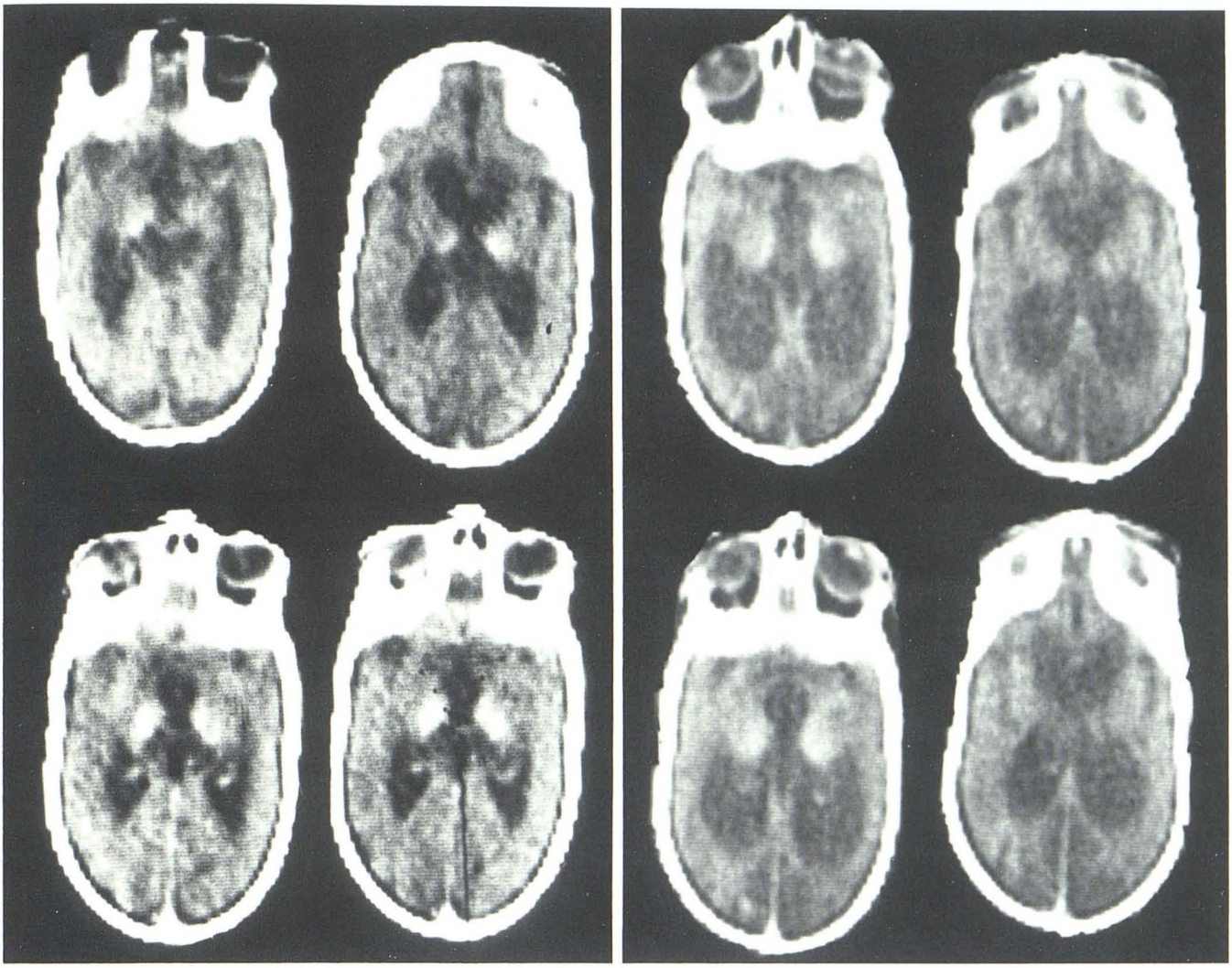


Fig. 1.—Case 1, 9-month-old boy. **A**, Precontrast scan 14 days after severe brain ischemia. Increased attenuation in head of caudate nuclei and frontal lobes. **B**, After contrast. Marked enhancement of same structures. **C** and **D**, Histology of caudate nucleus. Replacement of normal parenchyma (**E**, normal control) by neovascular network (**C**) and scattered areas of necrotic tissue with calcium deposition (**D**). Reticulin (**C** and **E**) and calcium (**D**) stains. (×100.) (**A** and **B** are reprinted from [1].



A B

Fig. 2.—Case A, Pre- (top) and post- (bottom) contrast CT scans with the same window level (50) and window width (100) at 3 (**A**) and 16 (**B**) months after perinatal brain hypoxia. High density of thalami, which enhanced after contrast infusion, had become less pronounced 16 months after hypoxic insult. (**A** is reprinted from [1]).

cularity is even less related to angiographic "luxury perfusion," a transient hyperemia due to local vasoparesis [10, 11].

Calcification is known to occur in restricted areas of the brain after ischemia, especially in the basal ganglia and dentate nuclei [12–14]. It might have accounted for some of the precontrast attenuation seen in postischemic hypervascularity, but it is likely that the hyperperfusion of these areas is primarily responsible, since highly vascular, noncalcified brain tumors such as microgliomas may have a similar appearance [15]. Moreover, calcification alone never enhances, as postischemic hypervascularity does.

The meninges may also be involved in the neovascular process of postischemic hypervascularity [2, 16]. The increased CT density of the meninges is similar to that which may be seen in meningitis or subarachnoid hemorrhage, but postischemic hypervascularity should be suspected in the context of the clinical presentation and of associated hypervascularity lesions. A normal lumbar puncture will confirm the nonhemorrhagic and noninfectious nature of the lesion as it did in our two cases with meningeal postischemic hypervascularity.

Examination of the attenuation values is necessary to establish that an area that appears abnormally dense on CT is not merely an area of normal density with an abnormally decreased surround [17]. This is particularly pertinent in infants where areas of brain edema or necrosis can be extensive [18–20].

Recognition of postischemic hypervascularity is important because of its probable prognostic significance. Although a

TABLE 2: **Hounsfield Numbers for Regions of Brain with Postischemic Hypervascularity versus Normals for Age using EMI 1005**

Anatomic Location	Case 3		Normal	
	Pre-	Postinfusion	Pre-	Postinfusion
Thalamus	40–43	45–52	29–32	34–37
Hippocampus	33–38	40–45	29–32	34–37
Brain stem	35–40	40–45	29–32	34–37
Periventricular	30–35	40–45	29–32	34–37
Falx cerebri	32–37	55–60	28–30	40–42
Uninvolved hemisphere	28–33	33–37	29–32	34–37

larger series with longer follow-up is needed, all of the patients we have seen so far with postischemic hypervascularity have sustained severe neurologic deficits.

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