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Early CT Findings of Global Central Nervous System Hypoperfusion

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The early computed tomographic (CT) findings of acute global central nervous system hypoperfusion were studied in 10 patients. The findings could be characterized as: (1) diffuse mass effect with effacement of the cerebral sulci and of the brainstem cisterns (nine patients); (2) global decrease in the cortical gray-matter density from edema, causing loss of the normal gray-white matter differentiation (six patients); (3) low-density lesions of the basal ganglia bilaterally (five patients); and (4) decreased gray-matter density in watershed distributions bilaterally (two patients). Subsequent contrast-enhanced scans in three of the 10 patients demonstrated selective enhancement of the cerebral cortex or the basal ganglia or both. The CT findings seen in this study predicted a poor outcome; nine of the 10 patients died from the insult. The abnormal CT findings can be ascribed to increased vulnerability of the cerebral cortex and basal ganglia to hypotensive episodes. This vulnerability is due to the large metabolic demand of these regions and their characteristic local cerebral blood flow.

Computed tomography (CT) is of major importance in the evaluation of acute insult to the brain, including early focal infarctions [1–5]. Acute damage from global central nervous system (CNS) hypoperfusion differs from that of focal infarction, but has been given little attention in the CT literature. At our institution, patients are often brought in comatose or obtunded, with no indication of the cause or duration of symptoms. In these clinically confusing situations, recognition of the early CT findings of global CNS hypoperfusion would be useful in confirming that significant diffuse neurologic damage has occurred and would help direct further evaluation and management. We retrospectively assessed the early CT findings of global CNS hypoperfusion in 10 patients.

Materials and Methods

During a 22 month period, 10 patients at our institution demonstrated early CT findings of global CNS hypoperfusion, subsequently proved by means of autopsy or their clinical course. The CNS hypoperfusion was caused by various pathologic states: four patients had had an acute cardiopulmonary arrest, five patients had been found comatose and hypotensive, and one patient had become comatose during hemodialysis. Our patients ranged in age from 2 months to 72 years. Six patients were male and four were female.

All the CT studies were performed using a GE 8800 scanner with contiguous 1 cm slices. In all 10 patients, the initial CT scans were obtained without contrast material. In six of the 10, the initial CT scan was obtained within 24 hr of hospital admission; in the other four, it was 2–5 days after admission. Seven follow-up scans were obtained in four patients 3–17 days after the initial study; three patients had contrast-enhanced studies. We used 150 ml of 60% iothalamate (Conray, Mallinckrodt, St. Louis) for the contrast material. Electroencephalograms (EEGs) were obtained for seven patients. Autopsies were performed on five patients, three by the county coroner and two in our institution.

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TABLE 1: **Summary of Findings in Acute Global CNS Hypoperfusion**

Clinical Diagnosis: Case No. (age, gender)	Clinical History	EEG Findings	Time from Insult to CT	Contrast-Enhanced CT?	CT Findings				Days to Death
					Sulci and Brainstem Cisterns Effaced?	Diffuse Cortical Density	Basal Ganglia Density	Cortical Watershed Density	
Brain death:									
1 (62,F)	Cardiopulmonary arrest; recurrent ventricular tachycardia	Not done	4 hr	No	Yes	–	–	Normal	3
9 (26,F)	On hemodialysis due to recent trauma	Not done	Same day	No	Yes	Normal	Normal	Normal	1
Persistent vegetative state:									
2 (59,M)	Cardiopulmonary arrest	Alpha coma	5 days	No	Yes	–	–	Normal	5
3 (39,M)	Alcoholic; found pulseless in street	BS	2 days	No	Yes	–	–	Normal	19
		ES	16 days	Yes	No	+	+	Normal	
5 (64,M)	Found comatose on hospital ward	Alpha coma	Same day	No	No	Normal	Normal	Normal	31
			3 days	No	No	–	Normal	Normal	
			20 days	No	No	Normal	Normal	Normal	
			20 days	Yes	No	+	Normal	Normal	
Persistent coma:									
4 (63,M)	Alcoholic; found comatose on doorstep	Alpha coma	2½ days	No	No	Normal	Normal	–	13
			5 days	No	Yes	Normal	Normal	–	
6 (79,F)	Pneumomediastinum and hypotension from car accident	Not done	Same day	No	Yes	Normal	Normal	–	1
7 (52,F)	Hypotension	ES	Same day	No	Yes	–	–	Normal	2
8 (2m,M)*	Cardiopulmonary arrest	BS	4 days	No	Yes	–	Normal	Normal	4
10 (21,F)†	Drug overdose	Diffuse slowing	2 days	No	Yes	Normal	–	Normal	Recovered
			14 days	No	No	Normal	Normal	Normal	
			17 days	Yes	No	Normal	+	Normal	

Note.—– = abnormal low density on unenhanced CT scan; + = abnormal high density on contrast-enhanced CT scan; BS = burst suppresssion; ES = electrocerebral silence.
* In case 8, the patient's age is given in months (m), not in years.
† In case 10, the coma persisted only until the patient recovered.

Results

The nonenhanced CT scans of our patients illustrated acute abnormalities characterized by one or more of the following patterns (table 1): (1) diffuse mass effect evidenced by effacement of the cerebral sulci and of the brainstem cisterns; (2) global decrease in cortical gray-matter density, causing loss of the normal gray-white matter differentiation; (3) decreased density of the basal ganglia bilaterally; and (4) decreased cortical gray-matter density in watershed distributions bilaterally.

The most common CT finding was diffuse mass effect evidenced by effacement of the sulci and brainstem cisterns. This was present in nine of the 10 patients and seen on the initial CT scan in eight of these nine patients (figs. 1 and 2). The ninth patient had prominent sulci when scanned less than 3 hr after admission, at which time only low-density areas in the peripheral watershed regions were demonstrated. A repeat study 5 days later showed the low-density watershed areas (infarcts) and diffuse sulcal effacement.

Diffuse, decreased density of gray matter causing loss of the normal gray-white matter differentiation on CT was seen in six of the 10 patients (figs. 1 and 2). In one patient, this finding was not observed until the second CT study 3 days after admission. In one patient, an infant with cardiopulmonary arrest, the decrease in gray-matter attenuation was so great that an actual reversal was observed in the normal relation of gray-white matter density (fig. 3).

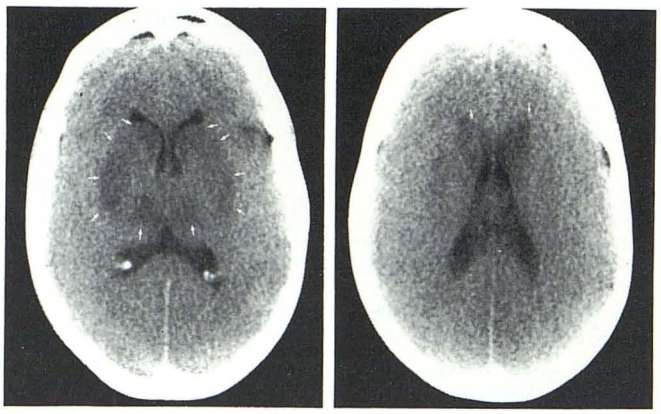


Fig. 1.—Case 1, 62-year-old woman with cardiopulmonary arrest secondary to recurrent ventricular tachycardia. CT scans 4 hr after arrest. Diffuse cerebral sulcal effacement and bilateral low-density lesions (*arrows*) in lenticular nuclei, thalami, and head of caudates. Gray-white differentiation is diminished.

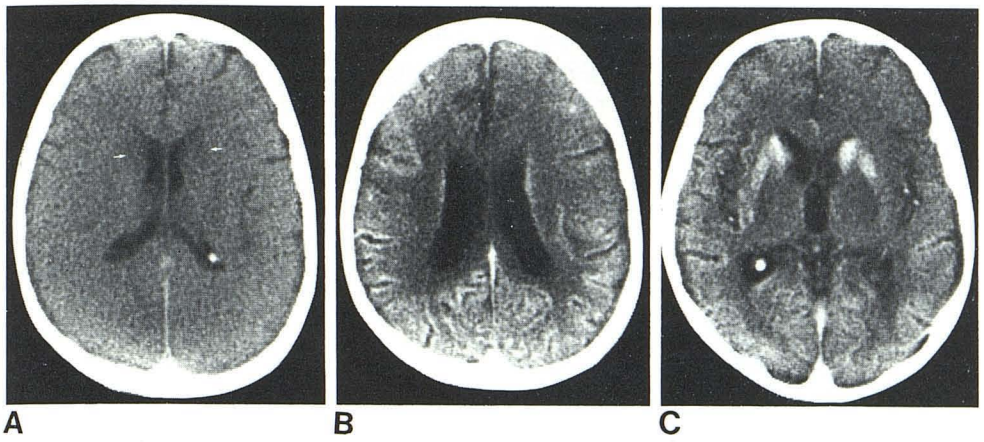


Fig. 2.—Case 3, 39-year-old alcoholic man found pulseless on street. **A**, Unenhanced CT scan 2 days after admission. Subtle areas of low density in caudate bilaterally (*arrows*), effaced sulci, and loss of normal differentiation of gray-white matter (cf. fig. 6). **B** and **C**, Contrast-enhanced CT scans 14 days later. Marked, diffuse enhancement of deep cortex and of basal ganglia. Sulci have returned to normal.

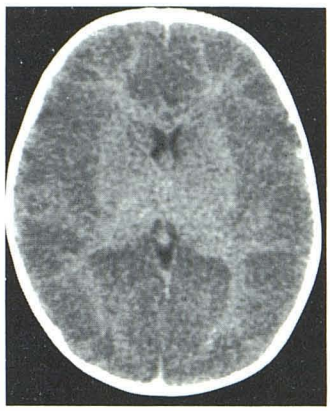
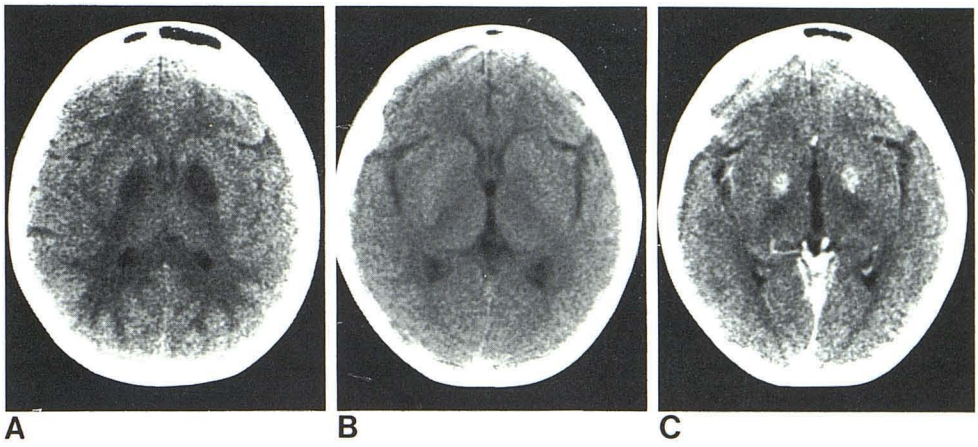


Fig. 3.—Case 8, 2-month-old boy with cardiopulmonary arrest. CT scan 4 days after arrest indicates diffuse, severe, cortical, gray-matter edema. Gray matter actually is lower in density than white matter. Sulci and basilar cisterns are effaced.

Fig. 4.—Case 10, 21-year-old woman with drug overdose who survived. **A**, Initial CT scan 2 days after admission. Large, bilateral, low-density lesions centered in globus pallidus. Generalized swelling with sulcal effacement is visible. Posterior white matter is abnormally low in density. **B**, 12 days later without contrast enhancement. Mass effect and low density in basal ganglia and subcortical white matter have apparently resolved. **C**, Contrast-enhanced scan 17 days after admission. Marked enhancement of globus pallidus bilaterally compatible with subacute infarctions.



Bilateral, low-density lesions of the basal ganglia were seen on the initial CT scan in five patients (fig. 1); this finding was sometimes subtle (fig. 2), sometimes striking (fig. 4).

Finally, two patients demonstrated abnormal areas of low density in the peripheral watershed distribution bilaterally. CT scans for both patients were obtained within 4 hr of hospital admission (figs. 5 and 6).

Of the three patients who received intravenous contrast material on follow-up CT scanning, one showed abnormal high density of the basal ganglia (fig. 4), another abnormal high density of the deep layers of the cortex, and the third abnormal high density of both areas (fig. 2). In cases 5 and 10, follow-up nonenhanced CT scans obtained just before the follow-up contrast-enhanced scans confirmed that the areas of high density represented abnormal enhancement rather than diastrophic calcification. Although the third patient (case 3, fig. 2) did not undergo noncontrast scanning at follow-up, we assume, based on this experience, that the high-density areas also represented abnormal enhancement. In all three patients, the areas of abnormal high

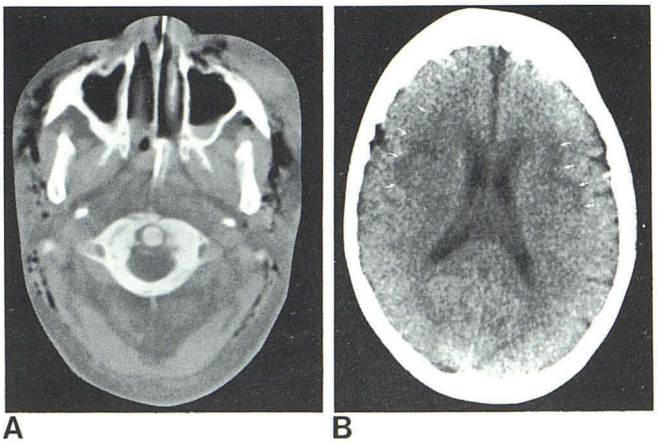


Fig. 5.—Case 6, 79-year-old woman with pneumomediastinum and secondary hypotension resulting from car accident. **A**, Initial CT scan on day of accident. Abundant subcutaneous emphysema from dissecting pneumomediastinum. **B**, Another level. Subtle, low-density areas (*arrows*) in watershed regions bilaterally. Sulci are effaced, especially if patient's age is considered.

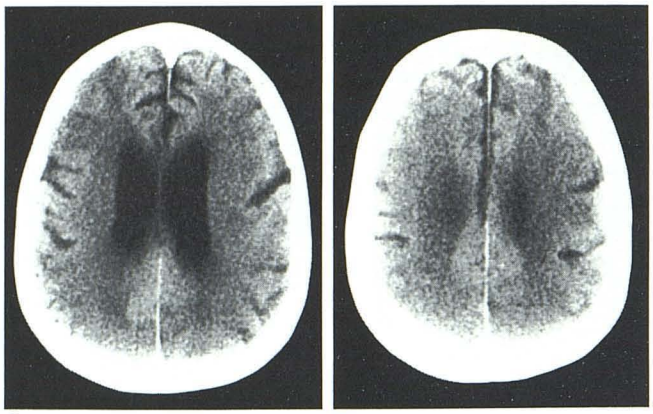


Fig. 6.—Case 4, 63-year-old alcoholic man found hypotensive on doorstep. Unenhanced scans 2½ hr after admission. Bilateral, low-density areas in watershed distribution involving both cortex and subcortical white matter. In noninvolved cortex, note normal differentiation of gray-white matter and preservation of sulci.

density corresponded to the abnormal, low-density areas of the cortex and basal ganglia on the early noncontrast CT scans. No areas of abnormal calcification were shown on any of the 13 noncontrast CT scans in our study.

One patient (case 10) showed abnormal low density in the cerebral white matter instead of in the cortical gray matter (fig 4). Diffuse mass effect with sulcal effacement and low density in the basal ganglia were also noted in this patient.

Clinically, the patients did poorly. Nine of the 10 patients died within 31 days of the inciting event. These patients had poor prognostic neurologic pictures, that is, persistent vegetative state, persistent coma, or clinical brain death (table 1).

Six of the seven patients who had EEGs died; they had exhibited alpha coma, burst suppression, and electrocerebral silence. One patient with an initial burst suppression pattern on EEG progressed to electrocerebral silence. The patient who subsequently recovered had shown only diffuse slowing. This patient had been hospitalized in a coma from a probable drug overdose complicated by hypotension and hypoxia; she showed unexpected neurologic improvement within 48 hr with residual short-term memory impairment and bradykinesia.

Autopsy confirmed the diagnosis of anoxic brain damage in four of the five in whom it was performed. Anoxic changes were found in the cerebral cortex in four, in the putamen and thalamus in one, and in the cerebellar cortex in two. In the fifth patient, one of the three coroner's cases, the brain was thought to be normal; but only limited superficial samples were taken (CT scans had indicated deep watershed infarcts).

Discussion

In this study, CT demonstrated the findings of acute global CNS hypoperfusion by showing mass effect and low density, predominately localized to the basal ganglia and cerebral cortex. These findings were often subtle. The EEGs were compatible with diffuse cortical damage. Autopsies, when performed, verified the diagnosis of anoxic brain damage. The pathophysiology of CNS hypoperfusion helps clarify the early findings seen on CT scans.

Tissue anoxia is the primary cause of CNS ischemic damage. Lowered oxygen tension, which occurs within minutes in hypoperfused brain cells, initially affects the mitochondrial system. Inadequate production of adenosine triphosphate disrupts the sodium-potassium pump and, in turn, the homeostatic properties of the cell membrane. Experiments in cats [6, 7] have demonstrated an influx of sodium and water from the extracellular to the intracellular compartments, with an overall increase in the water content of 2%–3% within 4 hr of an ischemic insult. This early intracellular edema is also called cytotoxic edema [8]. Such cellular swelling manifests itself on CT scans as a subtle mass effect, while the minimally increased water content may cause areas of decreased density. Both changes are subtle, but can be detected with current-generation CT scanners [1]. The blood-brain barrier remains intact during this early phase of tissue anoxia [7, 9].

In our patients, the predilection of the pathologic and therefore of the CT changes for the basal ganglia, cerebral cortex, and watershed regions may be explained by considering the local cerebral blood flow to these areas with respect to their metabolic demand. Areas of either very high metabolic activity or relatively limited local cerebral blood flow may be expected to undergo selective necrosis at times of hypoperfusion and therefore to demonstrate CT changes.

An experimental primate model [10] demonstrated the selective vulnerability of gray matter to ischemic necrosis from controlled, progressive hypoperfusion. During the hypoperfusion, the local cerebral blood flow to different regions was measured, and these measurements were correlated with the pathologic findings. For equivalent degrees of local hypoperfusion, the gray matter of the basal ganglia was the most vulnerable, followed by that of the cortex. The white matter showed necrosis only at more severe levels of local hypoperfusion. Presumably this differential vulnerability, at equivalent degrees of local hypoperfusion, reflects the greater metabolic demand of the basal ganglia and of the cortical gray matter compared with that of the white matter.

Results from other animal studies [11, 12] have also shown increased susceptibility of the gray matter to necrosis after hypotensive episodes, but in these studies the basal ganglia were apparently less vulnerable than the cortical gray matter. However, local cerebral blood flow to these different areas was not measured.

In addition to normal regional variations in metabolic demand, there are normal regional differences in local cerebral blood flow. Watershed areas, which include boundary zones between two or three major cerebral artery distributions and end-arterial terminal zones, are relatively underperfused and are therefore more vulnerable to damage during periods of hypotension [13]. Aside from the cortical "watersheds," boundary zones of perfusion include the head of the caudate, the putamen, and the adjacent internal capsule [13].

The head of the caudate and the putamen are especially

at risk during periods of low perfusion, in view of their high metabolic activity and their location in the boundary zones of perfusion. The CT pattern of bilateral low-density lesions of the basal ganglia occurs with numerous conditions, including carbon monoxide poisoning, hypoglycemia, cyanide poisoning, barbiturate overdose, trauma, and hydrogen sulfide poisoning [14–18]. All of the these entities induce metabolic insult, hypotension, or both.

The deep white matter also contains relatively hypoperfused boundary zones. Studies employing postmortem injection of radiographic contrast material have shown that the periventricular white matter lying 3–10 mm from the bodies of the lateral ventricles is relatively hypoperfused [19]. This area is a boundary zone between the ventriculopetal medullary branches of the major cerebral arteries and the ventriculofugal striate arteries. The subcortical arcuate white matter (which is more peripheral) is better perfused by virtue of extensive small-vessel anastomoses.

The CT literature is sparse on the changes found in CNS hypoperfusion [20, 21]. However, an autopsy study [22] of 11 patients who died from severe episodes of systemic hypotension demonstrated selective necrosis of the cerebral cortex with varied involvement of the basal ganglia. This study distinguished one group of patients having discrete cortical necrosis occurring only in the watershed regions from another group having ischemic damage involving the entire cerebral cortex. Every patient in the latter group also had bilateral ischemic damage of the basal ganglia. This study suggested that the watershed distribution of cortical necrosis was due to a precipitous drop in systemic blood pressure and that the diffuse cortical and basal ganglia damage was due to less severe but more sustained periods of hypotension. In our study, both patterns of cortical involvement were seen on the CT scans. However, a similar, temporal correlation with hypotension could not be found.

The survivor in our series bears special mention. This was the only patient demonstrating diffuse low density in the white matter with sparing of the cortical gray matter; she also had bilateral low-density lesions of the basal ganglia. Hypoxic-ischemic leukoencephalopathy is an unusual but recognized sequela of hypotensive episodes [23]. Prolonged, but not severe, hypoxia may allow for the sparing of the gray matter. The rarity of this lesion suggests that another factor besides hypoxia per se is required to produce hypoxic-ischemic leukoencephalopathy. The degree of systemic metabolic acidosis appears to correlate with the development of these white-matter lesions [23, 24]. Drug overdose with prolonged depression of both circulation and oxygenation and the resultant metabolic acidosis is a common cause of hypoxic-ischemic leukoencephalopathy [23]. The survivor probably had such a case, which resulted in bilateral basal ganglia infarcts and reversible white-matter edema. Her subsequent recovery was unexpected both clinically and radiologically, although her EEG pattern was less ominous than that of our other patients.

The abnormal CT findings in our study correlate well with the pathophysiologic and autopsy data. The cellular swelling in the cerebral cortex causes sulcal effacement and diminution of the basilar cisterns. Increased water content in the cortical gray matter decreases its CT density, thereby obliterating the normally small difference in contrast between the gray and white matter. Increased water content also causes the low-density lesions in the basal ganglia. The selective enhancement of only the cortex and basal ganglia on subsequent contrast-enhanced scans demonstrates that breakdown of the blood-brain barrier eventually occurs and supports the concept of selective necrosis in hypoperfused states.

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