Cerebral Blood Flow and Glucose Metabolism Measurements in a Patient Surviving One Year After Carbon Monoxide Intoxication

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A 29-yr-old woman was studied for 1 yr after acute carbon monoxide intoxication following an attempted suicide by inhalation of automobile exhaust fumes. The patient demonstrated impaired responsiveness to stimuli without any specific neurological deficits for 1 yr after carbon monoxide intoxication. Repeated brain magnetic resonance imaging consistently displayed only bilateral globus pallidus lesions, but no lesions in either deep white matter or cerebral cortex. Positron emission tomography measurements of regional cerebral blood flow, and glucose utilization rate were made in this patient at 6 mo and 1 yr following carbon monoxide intoxication. Impairment of both blood flow and glucose metabolism were found not only in the basal ganglia but also in morphologically normal frontal cortex. The decrease in glucose utilization in the frontal cortex was greater than that in the basal ganglia. During the period of 6 mo to 1 yr, blood flow and glucose metabolism in the basal ganglia recovered to the normal range. In the frontal cortex, however, blood flow and glucose metabolism remained approximately 20% lower than the normal mean values. This prolonged dysfunction in the frontal cortex may therefore be responsible for the impaired responsiveness of the subject.

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Carbon monoxide (CO) intoxication produces profound anemic hypoxia due to its 250 fold higher affinity for the ferrous haem of hemoglobin than oxygen (*1–3*). Survivors of acute CO intoxication often suffer from impaired responsiveness to stimuli, pyramidal and extrapyramidal deficits and other focal neurological disturbances (*4*). Bilateral lesions of the globus pallidus and hemispheric deep white matter are frequently observed on both computed tomographic (CT) and magnetic resonance (MR) images (*4–6*). The abnormalities in perfusion and metabolism in the brains of survivors of acute CO intoxication, however, have not been documented. In this report, repeated measurements with positron emission tomography (PET) of regional cerebral blood flow (rCBF) and glucose metabolism in a patient at 6 mo and 1 yr following acute CO intoxication are presented.

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CASE REPORT

Materials and Method

Regional CBF measurement was performed following a $H_2{}^{15}O$ bolus injection (30 mCi) into the cubital vein (*7*) using a HEADTOME IV (Shimadzu Co, Kyoto) positron emission tomograph, which has an effective resolution of 7 mm (*8*). Arterial blood sampling to estimate the arterial input function of the radiotracer into the brain was done by continuous withdrawal through a beta scintillation detector. After allowing for the decay of ^{15}O in the brain, 8 mCi of ^{18}F-2-fluoro-2-deoxy-D-glucose (FDG) were administered. Sequential PET scanning was started at the beginning of administration, after which fourteen 2-min scans followed by five 4-min scans were obtained. Manual arterial plasma samples were collected (every 15 sec during the first 2 min, every 30 sec for the following 3 min and then at increasing times) to define the input function. Rate constants defined by Sokoloff's model (*9*) were calculated from the dynamic images (*10*). Regional cerebral glucose utilization (rCMRGlu) was then estimated by employing the extension of the Sokoloff's equation (*11*) and using the calculated [^{18}F]FDG rate constants and a lumped constant of 0.52 (*12*). All emission data were corrected for tissue attenuation using transmission data measured by a ^{68}Ge-^{68}Ga external ring source.

MR scans were obtained using a 0.5 tesla superconductive MR system (SMT-50X, Shimadzu, Kyoto) with a quadrature head coil. All images were taken in the axial projection, parallel to the anterior commisure-posterior commisure (AC-PC) line, and were 6 mm thick covering a 25-cm field of view. The pulse sequence was 500/35/4 (TR/TE/excitations) by the gradient echo method for the T1-weighted image and 3000/35,90/1 by the double-spin echo method for the proton density-weighted and T2-weighted images.

The PET and MR studies were performed at 6 mo and 1 yr after CO intoxication, and the same scanning protocols were employed each time.

Case

A 29-yr-old woman was admitted following inhalation of automobile exhaust fumes in a suicide attempt. Although her

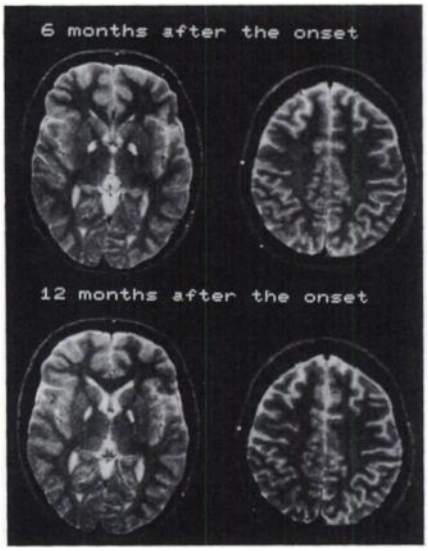

FIGURE 1. T2-weighted axial MR images obtained at 45 (upper left) and 80 mm (upper right) above and parallel to orbitomeatal line at 6 mo after CO exposure. High intensity in the bilateral globus pallidus was evident. No detectable deep white matter demyelination was found. At 12 mo after CO intoxication, there were no remarkable changes in corresponding MR images (lower left and lower right).

arterial carboxy hemoglobin concentration was not measured, she was diagnosed as suffering from CO intoxication circumstantially. On admission, she showed symptoms of impaired responsiveness, but showed no focal neurological deficits. Systemic arterial blood pressure, electrocardiographic and hematological examinations were normal. Although she was under psychiatric therapy, antidepressant therapy and hyperbaric oxygen therapy for 5 mo after the suicide attempt, her low spontaneity and slow responsiveness did not change during that period.

Brain MR at 6 mo after the intoxication indicated symmetrical high intensity only in the bilateral globus pallidus on the T2-weighted image. No signal changes in deep white matter, cortical gray matter or the hippocampus were seen. The repeat MR study at 12 mo after the intoxication showed no remarkable changes (Fig. 1).

Regional CBF and glucose utilization rates in the serial PET studies are summarized in Table 1. Mean values from nine age-matched normals (one female, eight males) obtained using the same PET protocol are also listed in Table 1. The first PET examination revealed 41% and 32% decreases in rCBF in the basal ganglia, including the globus pallidus and frontal cortex, respectively, compared to normal mean. In the follow-up study, blood flow in the basal ganglia recovered to a value 10% lower than the normal, but frontal cortex blood flow was still 20% lower than the normal value. Glucose utilization rates in the frontal cortex were most severely decreased among brain structures in the repeated examination although morphological lesions were detected only in the globus pallidus and not in the frontal cortex. No decrease in rCBF or rCMRGlu was evident in centrum semiovale in the repeat PET study. Figure 2 illustrates rCBF and rCMRGlu images obtained at 6 and 12 mo after CO intoxication.

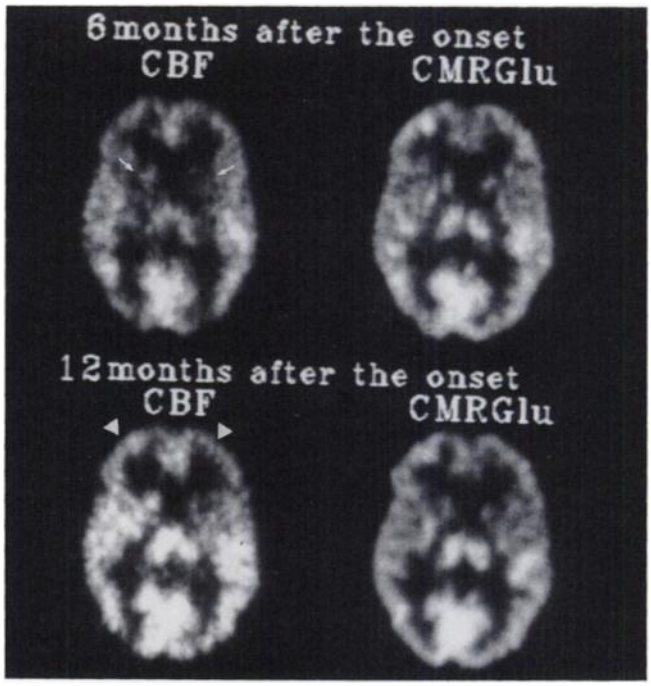

FIGURE 2. PET rCBF and rCMRGlu images corresponding to MR images at 6 mo (upper raw) and 12 mo (bottom raw) after CO intoxication. Decreased CBF in the bilateral basal ganglia at 6 mo (small arrow) recovered to normal range at 12 mo after intoxication. The most severe decline in rCBF was found in bilateral frontal cortex at 12 mo after CO exposure (arrow head). Temporal and occipital cortex as well as thalamus showed no significant changes during this period (left column). Hypometabolism of glucose was found predominantly in bilateral basal ganglia and frontal cortex. In the follow-up study, no significant changes of rCMRGlu were evident. Glucose utilization in the frontal cortex was still 22% lower than the normal mean.

DISCUSSION

After exposure to CO, various levels of impaired consciousness and subsequent slow responsiveness to stimuli are characteristics of CO encephalopathy. Many patients suffer from longstanding neuropsychiatric deficits and occasionally relapse to severe mental deterioration and fatal coma (*4*). Neuropathologic studies have revealed that lesions in the globus pallidus and deep white matter are

TABLE 1
Values of rCBF and rCMRGlu at 6 and 12 Months After Carbon Monoxide Intoxication

	CBF (ml/100 ml/min)			CMRGlu (mg/100 ml/min)		
	Normal	6 mo	12 mo	Normal	6 mo	12 mo
Cortex mean	52.2 ± 9.9	40.6	50.4	6.19 ± 0.65	5.68	5.81
Frontal cortex	48.6 ± 8.0	33.1	39.1	6.40 ± 0.70	4.50	5.02
Basal ganglia	59.3 ± 12.9	35.0	53.7	6.20 ± 0.61	5.09	5.46
Centrum semiovale	26.4 ± 5.3	23.4	24.3	3.22 ± 0.28	3.14	2.63

frequently found in an autopsied brain of CO encephalopathy (*1*). With the use of CT (*5*) and, more recently, MRI (*6*), these morphological changes are well documented. In particular, MRI detected lesions in the spongy cerebral cortex, necrotic lesions in the hippocampus and globus pallidus, as well as demyelination in white matter (*6*).

To date, only a preliminary study of rCMRGlu in six survivors of CO intoxication has been reported (*13*). Global cortical hypometabolism of glucose utilization with a 15%–30% decrease was reported. This case also showed regional decreases in rCBF and rCMRGlu, predominantly in the frontal cortex. Although the pathogenesis of CO encephalopathy is not clearly established, flow-metabolism disturbances detected in the PET measurements definitely extended beyond the morphological lesions observed in the MR images. Prolonged slow response and impaired spontaneity observed in the present case might be induced by dysfunction of the frontal cortex. The measurement of flow and metabolism in patients with various severities of CO encephalopathy may provide prognostic information as well as improve the understanding of CO encephalopathy.

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