MR Imaging of "Spray Heads": Toluene Abuse via Aerosol Paint Inhalation

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PURPOSE: Three male patients with a history of spray-paint inhalation are presented. **METHODS:** Spin-echo MR was used to evaluate the central nervous system changes secondary to toluene inhalation delivered via spray-paint fumes. **RESULTS:** The remarkable findings included the loss of cerebral and cerebellar gray-white matter discrimination, scattered multifocal deep white matter lesions, and gross generalized atrophy of the cerebrum, the cerebellum, and the corpus callosum. **CONCLUSION:** Although the observed changes are nonspecific, combined with a positive history the diagnosis of inhalation toluene abuse can be made on the basis of consistent MR findings.

Index terms: Brain, effects of toxic substances on; Brain, magnetic resonance

AJNR 14:1195–1199, Sep/Oct 1993

Toluene is an important component of organic solvents. It is present in a wide variety of products, including spray paints and glues. Its toxicity has long been implicated as a cause of acute and chronic neurologic and behavioral effects. The colloquial term "spray head" comes from bizarre behavioral changes associated with chronic toluene abuse resulting from the inhalation of spray-paint fumes. Previous investigations using computed tomography (CT) combined with gross necropsy findings have described diffuse cortical atrophy in toluene inhalant abusers. The magnetic resonance (MR) findings presented in this article indicate that the neurotoxicity associated with toluene abuse may be more variable in appearance and more extensive than previously described.

Materials and Methods

Three Latin American men (mean age = 30 years) who had a history of sniffing spray paint had MR imaging studies between November 1988 and January 1992 (Table 1). In all patients, the cranial MR imaging studies were performed on a GE Signa 1.5-T magnet by the use of standard spin-echo pulse sequence technique. T1-weighted (500/26/1, TR/TE/excitations) and T2-weighted (2000/80) conventional spin-echo images were obtained with a section thickness of 5 mm. The matrix size was 256 × 192 in all acquisitions. The average thickness index of the corpus callosum was measured by the method of Simon et al (1, 2) and was based on the T1-weighted midsagittal image. CT scans were also obtained in all cases. In addition, two cases had electroencephalography (EEG) studies.

Results

The CT scans showed generalized cerebral atrophy and ventricular dilation in all cases. The EEG evaluation was normal in one patient; however, the other patient who underwent EEG showed diffuse slow-wave activity.

The abnormal MR findings were as follows: (*a*) generalized cerebral and/or cerebellar atrophy on both T1- and T2-weighted images (n = 3), (*b*) atrophy of the corpus callosum (n = 3) (the measurements-at-average index ranged from 3.9 to 4.1 mm; normal range 5–7.2 mm); (*c*) loss of gray-white matter discrimination on T2-weighted images (n = 3); (*d*) multifocal high signal intensity (above that of the background) in the cerebral white matter (n = 3) (Figs. 1 and 2); and (*e*) symmetric hypointensity of the thalami on T2-weighted acquisitions (Fig. 2) (Table 1).

Discussion

Central and peripheral nervous system insult secondary to drug and alcohol abuse has been

Received April 16, 1992; revision requested June 26; final revision received October 12 and accepted October 14.

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AJNR 14:1195–1199, Sep/Oct 1993 0195-6108/93/1405-1195

TABLE 1: Clinicoradiologic findings in three patients with a history of toluene abuse[a]

Patient No.	Sex/Age	Major clinical findings	Length of toluene use	Other drug use history	EEG	CT	MR		
							Atrophy	Loss of G/W Discrimination	Multifocal white matter hyperintensity
1	M/28	Generalized seizure activity, "doll's eyes," ataxia, dementia	1 yr	None	Diffuse slow-wave activity	Generalized cerebral and cerebellar atrophy	Cerebral, cerebellar, CC	+	Cerebral hemispheres
2	M/34	Increased extremity weakness, vertigo with episodes of falling, nausea and vomiting, positive asterixis, resting tremor, hyperreflexive deep tendon reflexes, ataxia, dementia	12 yr	None	Normal	Generalized cerebral and cerebellar atrophy	Cerebral, cerebellar, CC	+	Cerebral hemispheres
3	M/28	Acute renal failure, urinalysis positive for THC and cocaine, no neurologic abnormality	Multiyear	Alcohol, cocaine, and marijuana	Not done	Generalized cerebral and cerebellar atrophy	Cerebral, cerebellar, CC	+	Cerebral hemispheres

[a] Abbreviations: CC, corpus callosum; G/W, gray/white; THC, tetrahydrocannabinol.

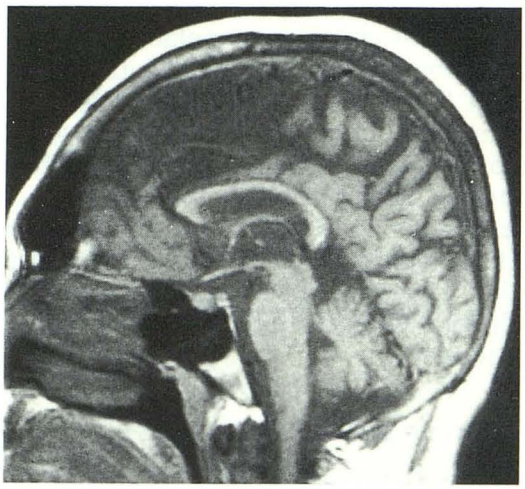
Fig. 1. Patient 1. Twenty-eight-year old man with a 1-year history of inhaled toluene abuse.

A, Sagittal T1-weighted (500/20) spin-echo image demonstrating marked corpus callosum atrophy.

B, Coronal T1-weighted (500/20) spin-echo image showing frank cerebellar atrophy indicated by the enlarged cerebellar sulci.

C, Axial T2-weighted (2500/80) spin-echo image showing generalized atrophy, loss of the gray-white matter discrimination, and irregular hyperintense areas in the parietooccipital white matter bilaterally.

D, Axial T2-weighted (2500/80) spin-echo image revealing a loss of gray-white matter discrimination in the cerebellar region.



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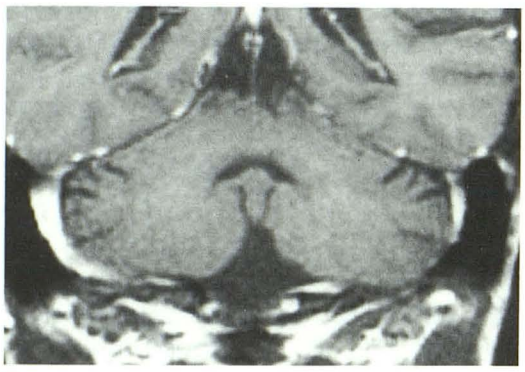

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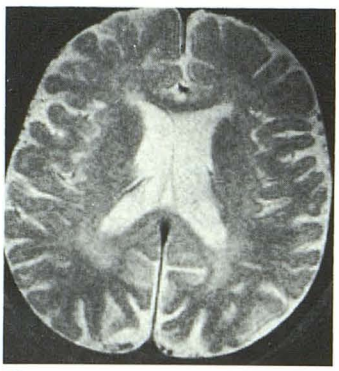

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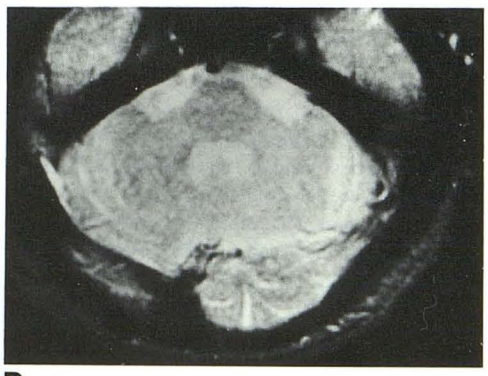

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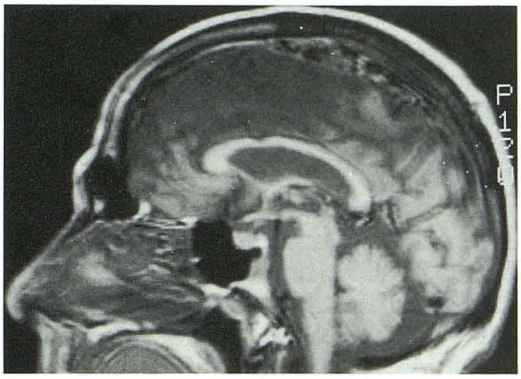

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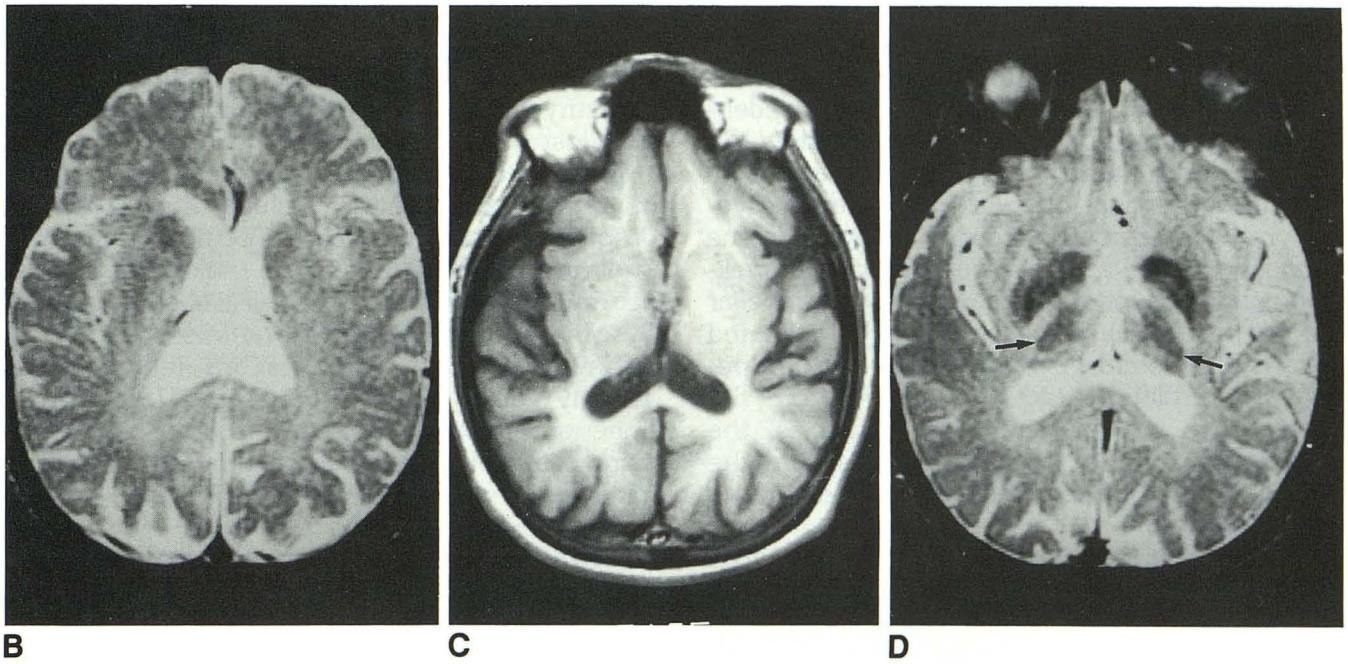

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Fig. 2. Patient 2. Thirty-four-year-old man with a 12-year history of inhaled toluene abuse.

A, Sagittal T1-weighted (500/20) spin-echo image showing marked callosal atrophy.

B, Axial T2-weighted (2500/80) spin-echo image revealing diffuse hyperintensity of the hemispheric white matter, including the corpus callosum, with resultant loss of the gray-white matter discrimination.

C, Axial T1-weighted (500/20) spin-echo image through the level of the thalami showing moderate generalized atrophy.

D, Axial T2-weighted (2500/80) spin-echo image demonstrating the diffuse hyperintensity of the white matter and the striking hypointensity of the thalami bilaterally (*arrows*).

well documented (3, 4). However, less attention has been given to the potential neurotoxicity caused by toluene in adolescents and young adults. Grabski (5) reported in 1961 the first case that showed permanent cerebellar degeneration on the basis of clinical findings from long-term toluene inhalation.

Toluene ($C_6H_4CH_3$) is a hydrocarbon solvent that is insoluble in water. When inhaled, toluene is absorbed by the lung and bound to lipoproteins. Some 70% to 80% is metabolized in the liver by oxidation to benzoic acid, is then conjugated with glycine to form hippuric acid, and is subsequently eliminated in this form through the kidneys. The mechanism of toluene neurotoxicity is not clearly understood. Laboratory studies have shown that toluene concentrations in fatty tissues are 80 times higher than those found in blood.

Clinically, the toxicity effects of toluene can be divided into two stages. The acute effects include feelings of euphoria, disinhibition, exhilaration, tinnitus, dizziness, and difficulty in visual focusing. These effects last for approximately 30 to 45 minutes after exposure. Other features include sneezing and coughing, nausea and vomiting, diarrhea, diffuse somatic pain, tremor, paraesthesia, and epileptic fits (6, 7). During this acute stage, there is usually no permanent observable structural damage to central nervous system neurons. However, chronic inhalation of toluene can cause multifocal permanent central nervous system injury accompanied by neural dysfunction (8). In the main, chronic toxicity presents as a cerebellar syndrome with findings of nystagmus, gait abnormality, ataxia, and tremor in the limbs (5, 9). Peripheral neuropathy, optic atrophy, and hearing impairment have also been reported (6, 10). In cases of chronic intoxication, the patient typically manifests headache, dizziness, insomnia, and nervous irritability. Besides neurotoxicity, tol-

uene also causes damage to the kidneys, liver, gastrointestinal system, and heart (6, 11). The severity of acute clinical symptoms partly relates to the levels of toluene in blood. A concentration of approximately 5.0 $\mu g/g$ (toluene in blood) will classically show severe patient symptoms that encompass generalized lack of coordination. Higher levels in blood may cause coma, and over 20 $\mu g/g$ may result in fatal intoxication (6).

Neuropathologic changes of toluene abuse include diffuse demyelination in the cerebral, cerebellar, and subcortical white matter; degeneration and gliosis of ascending and descending long fiber tracts, peripheral nerves, and fibers of the corpus callosum; and generalized cerebral, cerebellar, and corpus callosum atrophy. In gross brain specimens, scattered, ill-defined myelin pallor is identified in the periventricular deep white matter (12). The pathologic changes are primarily caused by neuronal and axonal loss with associated demyelination. In experimental animal studies, toluene intoxication results in diffuse cerebral demyelination and a reduction in the number of cerebellar Purkinje cells (13). Degeneration of myelinated fibers is also found in the ventromedial and peripheral ventrolateral tracts of the spinal cord, the medulla, the inferior cerebellar peduncles, the white matter of the cerebellar vermis, and the peripheral nerves in rat models of toluene intoxication (14).

In the early stages, the radiologic abnormalities secondary to toluene abuse include a widening of the basal cisterns with enlargement of the ventricular system and cortical sulci, compatible with generalized atrophy. Pneumoencephalography has been used in the past to evaluate the size of the ventricles, cisterns, and cortical sulci. Juntunen et al reported that 64% of 37 cases studied with pneumoencephalography showed changes suggesting atrophy (15). On CT, the major findings were ventricular enlargement with widening of the cortical sulci and basal cisterns, consistent with cerebral and cerebellar atrophy (8, 9, 16). There was a significant correlation between the clinical cerebellar symptoms and measurements of the width of cerebellar sulci and the superior cerebellar cistern on CT scans (9). Ikeda and Tsukagoshi (17) recently reported one case of toluene sniffing evaluated by MR that showed generalized atrophy of the cerebrum and cerebellum, as well as the corpus callosum, and abnormal hyperintensity in the internal capsule on T2-weighted acquisitions. In this study, the clinical and MR data not only confirmed these findings, but they also revealed a loss of gray-white matter discrimination, an associated generalized and multifocal increase in periventricular white matter signal intensity, and a reduction in size of the corpus callosum in cases of toluene abuse (12, 17, 18). Filley et al (18) showed that there was a strong correlation between the clinical dementia and the white matter changes.

According to the method of Simon et al, the corpus callosum can be somewhat quantitatively measured in vivo on the basis of the midsagittal section (1, 2). The mean corpus callosum thickness index in healthy subjects was 6.06 mm (standard deviation, 0.63 mm; range, 5 to 7.2 mm). All of the current patients with toluene abuse (range, 3.9 to 4.1 mm) fell below this normal range. The reason for the corpus callosum atrophy is still not clear, but it probably relates to demyelination and perhaps gliosis and frank fiber loss.

The differential diagnosis of these MR findings of toluene abuse should include other forms of drug abuse such as cocaine. The neuroradiologic findings of cocaine abuse are mainly those of a neurovascular nature: cerebral ischemia caused by cerebral vasculitis, cerebral vasospasm, and thrombosis. Other complications (eg, cerebral atrophy) can be found in some cases (19). Positive urine and blood tests can usually clarify the diagnosis of other specific drug abuse if it is being taken at or near the time of the imaging examination. In some patients who have a history of multisubstance drug abuse, it may be difficult to distinguish between findings, as was seen in patient 3. However, the MR findings of this patient revealed findings similar to those seen in the other two cases rather than those typical of isolated cocaine abuse. Acquired immunodeficiency syndrome is another possibility that may present with atrophy and single or multifocal areas of high signal intensity on T2-weighted MR images in subcortical regions (20). Its rapid progression coupled with a positive blood test for human immunodeficiency virus can usually confirm the diagnosis in this circumstance.

The cause and nature of the MR signal hypointensity seen symmetrically within the thalami on T2-weighted acquisitions in one of the three cases presented here are of uncertain etiology. Theoretically, they seem to relate to an increase in magnetic susceptibility such as might be seen in calcification or perhaps iron deposition (21). Normally, iron deposition in the brain may be seen with MR at certain specific cerebral locations such as the basal ganglia, the red nuclei, and the substantia nigra. Abnormal degrees and locations of iron deposition have been demonstrated on high-field MR acquisitions in certain disease states

that include neuraxonal dystrophy or Hallervorden-Spatz disease, Parkinson disease (22) Shy-Drayer syndrome, and multiple sclerosis (1, 2, 23), and in children after severe ischemic-anoxic events (24). The true cause of this abnormal accumulation and MR appearance in toluene abuse remains to be clarified. In addition, although metabolic diseases might be expected to cause hyperintense alteration of MR signal within the cerebrum on T2-weighted acquisitions, hypointensity does not seem to be a major feature of such diseases. In cases in which hypointensity is present, it seems to be caused by associated calcification (25). No calcium deposits were seen in the thalami on CT examination in our one patient who had hypointense thalami on T2-weighted MR images.

EEG abnormalities have been reported in fewer than half of the cases of toluene abuse consisting of intermittent θ and δ activity and focal or diffuse slow-wave activity (6–9). In the two patients presented here who had EEG studies, one case showed diffuse slow-wave activity, whereas the other was normal. After treatment, repeat EEG examinations in some cases may revert to normal (6, 7).

In summary, the MR findings in chronic toluene abuse consist of generalized cerebral, cerebellar, and corpus callosum atrophy, a loss of the gray-white matter discrimination associated with diffuse and multifocal hyperintensity of the cerebral white matter on T2-weighted acquisitions, and occasional hypointensity of the thalami on T2-weighted studies. Although longitudinal studies would be necessary to prove this hypothesis, the severity of the MR changes is quite likely largely irreversible and signifies the severe nature of chronic toluene toxicity in the central nervous system. Further clinicoradiologic studies are required to evaluate the precise relationship of the MR findings to the signs and symptoms in a larger number of cases, the time course from the initiation of toluene abuse to the onset of imaging findings, and the mechanism of the hypointensity of the thalami on T2-weighted images.

Acknowledgments

We thank Joanne Murray for the preparation of the manuscript and Cono Farias for the photographic reproductions.

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