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Paraoccupational Exposure to Mixed Solvents

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ABSTRACT

Exposure to solvent vapors resulted in a sensory neuropathy and mild encephalopathy in a 44-yr-old female cook. The route of exposure was unusual: a ventilation system cross-connection between her restaurant and an adjacent upholstery shop. Possible "paraoccupational" exposures should be sought in cases of neurologic or other unexplained symptoms possibly caused by toxic substances. The role of solvent mixtures in the genesis of nervous system disorders is reviewed.

Exposure of persons to toxic materials within the work place or from adjacent sources may contribute to the development of certain neurologic disorders. Syndromes of "paraoccupational illness" have been seen in persons living or working near plants handling toxic

substances or in families of workers who are indirectly exposed to toxic dust carried home on workers' clothing. Persons living near lead, zinc, and copper smelters have been shown to have increased absorption of heavy metals emitted by the smelters [1-3] and to suffer neuropsychologic damage [2, 4]. Children of workers employed in secondary lead smelters and in battery plants have been found to have excessive lead absorption and even overt lead poisoning following exposure to lead dust carried home on parents' clothing [5-7]. Furthermore, family members of workers employed in the beryllium and asbestos industries have been found to have developed berylliosis [8] and mesothelioma [9] from similar paraoccupational exposures. This report describes the development of sensory neuropathy and mild encephalopathy in a woman with unwitting recurrent paraoccupational exposure to a mixture of volatile solvents.

CASE HISTORY

The patient, a 44-yr-old woman, began work as a cook in a family-owned restaurant in October 1975. In February 1976 she began to notice unusual odors in the vicinity of her work area and stove where she spent 10 to 15 h per day preparing food. At this time she also began to notice headaches, dizziness, difficulty in coordination, nausea, and diarrhea. These symptoms persisted until April 1977 when she began to notice, in addition, intermittent burning paresthesiae of the face, hands, legs, and back. She also noted during this period persistent fatigue, lethargy, and feelings of depression and anxiety.

She ceased working in the restaurant in April 1977, and medical evaluations described below were performed during the subsequent 2 yr. After removal from exposure, she noted a gradual reduction in the frequency of episodes of burning paresthesiae and did not experience further symptoms of nausea, headache, dizziness, or diarrhea. Difficulty in coordination persisted. The depressive symptoms continued despite psychotherapy and several drug-treatment regimens. She did not experience significant muscle weakness during the course of her illness. She also denies having had any numbness or loss of sensation in her extremities. There is a negative history of excessive alcohol consumption, diabetes, or trauma to her extremities. There is no family history of neurologic disease.

Neurologic Examinations

Serial neurologic examinations performed between 1977 and 1979 revealed no abnormality in cranial nerve function, tendon reflexes, or tests of coordination. Vibration sensation was variably reduced in the legs. Sensation to pinprick was reduced in a patchy distribution over

TABLE 1. Result

Nerve parameter
Right Median N. Motor C.V. (M/s)
Right Peroneal N. Motor C.V. (M/s)
Right Sural N. Sensory C.V. (M/
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TABLE 1. Results of Nerve Conduction Studies

Nerve parameter	Study 1 (8-15-77)	Control values	Study 2 (6-30-78)
Right Median N.			
Motor C.V. (M/s)	55	57.2 ± 2.0	64
Right Peroneal N.			
Motor C.V. (M/s)	44	51.0 ± 4.7	54
Right Sural N.			
Sensory C.V. (M/s)	Absent	51.0	45.5
Amplitude (uv)	Absent	39.0	14

the forearms and legs. Sensation of position was normal. Clinical laboratory testing revealed normal hematologic studies and 2-h postprandial blood glucose determinations. An electroencephalogram in 1977 showed no abnormalities although obvious disturbances in mental status were not detected. Formal neuropsychological testing revealed marked deficits in sustained attention, particularly for visual motor responses.

Electrodiagnostic Peripheral Nerve Studies

Electrodiagnostic peripheral nerve studies were performed in August 1977 and in June 1978. These studies (Table 1) show evidence of a mild sensory neuropathy as evidenced by absent sural nerve potentials and slowed median and peroneal motor nerve conduction velocity, which were noted in the first examination, and improvement of the subsequent examination performed 9 months after removal from exposure. Electromyographic signs of denervation and motor unit regeneration were noted during the last examination in the muscles of the lower extremities. These consisted of reduced interference pattern in the extensor digitorum brevis, gastrocnemius, and hamstring muscles, increased number of polyphasic potentials with increased insertional activity and bizarre high frequency discharges in the extensor digitorum brevis muscle.

Environmental Studies

Investigations were performed to document the source of the unusual odor detected in the patient's work area. The odors were found to arise from an upholstery shop which was located in the same building and which shared a common ventilation system with the restaurant. The odor was identified as caused by an aerosol lacquer used in the

upholstery operation. It appeared that the ventilation system hood, which operated over the stove where the patient cooked, was conveying fumes to the area where the patient worked. The lacquer compound was analyzed and found to contain a mixture of 7% resin solids, 43% solvents, and 50% propellent. The solvent was a mixture of esters, ketones, alcohols, and hydrocarbons. Among these were toluene, methyl isobutyl ketone, and ethyl acetate. An air sample was taken over a period of 10 min during which 3 min of spraying with the lacquer took place. The effect was a noticeably strong odor. Ethyl acetate, methyl ethyl ketone, and isopropyl alcohol were identified as well as other nonspecified hydrocarbons.

An on-site visit focused on potential air exchange routes between the upholstery shop and the restaurant. Two basic direct air paths were identified. One was the single heating and ventilation system which served both the restaurant and the upholstery shop. The single central heating unit and fan system serving both tenants encouraged mixing of air from one side of the building to the other during normal fan operation. A second possible route of air transfer between sides of the building was the return duct system which had back-to-back openings on the bottom of the wall separating the two business establishments. The openings connected immediately below the floor to form a single return duct. Under normal fan operation, both return ducts were maintained at negative pressure to both rooms, causing air to be drawn continually into the return vent from each room to the fans, mixed, and returned to the supply ducts when the ventilation fan was on. However, at the time the odors were most noticeable, a ventilation hood system over the stove was in place, producing a negative pressure in the kitchen area. The heat of the stove added to the negative draft effect, drawing air containing vapors from the solvents into the restaurant kitchen.

DISCUSSION

An indirect route, paraoccupational, of toxic exposure leading to the development of a peripheral neuropathy and a mild encephalopathy is described in this report. The association of central nervous system symptoms with acute exposure to solvents is well recognized [24]. That the symptoms and signs in the patient resolved almost completely after removal from exposure to the solvents is consistent with the findings of previous studies of solvent-induced neuropathy [10, 13].

Exposure to mixtures of volatile industrial solvents is extremely frequent in industry. Reports of peripheral neuropathy following exposure to solvents are not uncommon [9, 18]. The term "mixed solvent neuropathy" may be used to describe the syndrome characterized by insidious distal, symmetrical sensory, and motor impairment following exposure to mixtures of industrial solvents in which a specific

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neurotoxic chemical is not identified. Both inhalation and percutaneous absorption appear to be important routes of exposure. Although specific substances are undoubtedly responsible for the neurologic insult, the complexity of the exposure often makes identification of the particular offending agents impossible.

Substances commonly contained in such mixtures include toluene, xylene, butyl acetate, methyl isobutyl ketone, n-heptanone, isobutyl alcohol, nitropropane, isopropyl acetate, isobutyl isobutyrite, isopropanol, pentane, heptane, and acetone [9, 18, 19]. Some of these substances were found in the environment of this case. Although isolated case reports have indicated that agents from this group may have neurotoxic potential, clear evidence linking specific substances with neurotoxic effects is lacking. In contrast, several other solvents, used singly or in combination in industry, have been shown definitively to cause peripheral and central nervous system damage: methyl n-butyl ketone [10, 11], n-hexane [12, 13], trichlorethylene [14, 15], carbon disulfide [16], and ethanol [19]. These agents with known neurotoxic effects may be present in solvent mixtures as contaminants and may not be listed in the product's chemical formulation. Since potentiation of the neurotoxic effect of a solvent (methyl butyl ketone) by another solvent (methyl ethyl ketone) has been demonstrated [20], it appears likely that the neurotoxic potential of certain constituents of solvent mixtures may be enhanced by metabolic interactions. Thus formulations whose individual constituents have relatively little neurotoxicity may exhibit significant effects when these constituents are combined.

Many solvents, including toluene, are associated with acute symptoms of lightheadedness, difficulty in coordination, and occasionally nausea. The acute symptoms, experienced by this patient when first noticing unusual odors in February 1976, were quite likely due to acute solvent toxicity. The associated systemic symptoms of fatigue, lethargy, and signs of encephalopathy detected on neuropsychological tests are symptoms also seen in persons with peripheral neuropathy associated with chronic solvent exposure.

In a recent study of Finnish automobile painters exposed to a mixture of solvents, Seppalainen and associates [9] found evidence of impaired nerve conduction velocity. Environmental measurements revealed exposure to a mixture of solvents including toluene, methyl isobutyl ketone, and butyl acetate, substances to which our patient was exposed. In that study and others, electrodiagnostic peripheral nerve testing has been shown to be particularly useful in the evaluation of toxic peripheral neuropathies [9, 10, 13, 14, 16, 17, 21-23]. Such studies were quite helpful in our case in providing an objective measure of peripheral nerve function that was seen to improve after cessation of neurotoxin exposure.

A nerve biopsy was not performed in our case but the observations of Means et al. [25] are helpful in explaining the pathophysiology of the course of her illness and recovery. They studied light and electron microscopic pathology of sural nerve biopsy specimens as well

as the central and peripheral nervous system from an autopsy of a patient who abused solvents. Isolated teased nerve fibers showed prominent focal paranodal axonal swellings. Segmental demyelination was infrequent; the predominant abnormality was retraction and thinning of the myelin sheath surrounding the nodes of Ranvier. Electron microscopy revealed neurofilament accumulation in the myelinated axons. Changes in anterior horn cells were taken as evidence of the "dying back" process characteristic of solvent neuropathies [11, 26, 27]. Although some deterioration in peripheral nerve function, an apparent delayed effect, may be seen within a few months after removal from exposure, reevaluation 1 yr later consistently shows improvement in nerve conduction parameters. Complete recovery may not ever occur after axonal degeneration. Sensory nerve conduction velocities measured in the sural nerves of the patient revealed slowing consistent with axonal changes. These changes were most striking, although relative differences in motor conduction velocities between 1977 and the later studies of 1979 provide further evidence of peripheral neuropathy.

This report emphasizes the important observation that toxic exposure may emanate from beyond the immediate work environment, thus requiring an extensive search to identify the source. The result of such exposure by our patient was neurotoxic effects of mixed solvents in the form of neuropathology and mild encephalopathy.

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