Motor Dysfunction as a Permanent Complication of Methanol Ingestion

Presentation of a Case With a Beneficial Response to Levodopa Treatment

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In a suicidal attempt by a 13-year-old white girl, methanol produced classical immediate symptoms and permanent damage to the central nervous system characterized by severe bilateral optic atrophy, rigidity, spasticity, and hypokinesis. Administration of levodopa has resulted in significant functional relief of the rigidity in this patient. It is suggested that this is the first case report in English describing permanent neurologic sequelae other than optic atrophy as a result of methanol ingestion. The physiologic basis is unknown. Further clinicopathologic correlation should be easily elucidated through reevaluation and longitudinal follow-up of other patients having ingested methanol.
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Key Words.—Methanol ingestion; adolescent suicide attempt; levodopa treatment; Parkinson syndrome; movement disorder; motor dysfunction.

THIS brief report details the case history of a young girl who developed rigidity, akinesia, tremor, and pyramidal tract signs following ingestion of methanol in a suicidal attempt. Permanent motor dysfunction due to methanol intoxication has not been previously reported in the English literature. Marked improvement in the motor disorder (rigidity) accompanied treatment with levodopa.

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Report of a Case

The patient, a 13-year, 10-month-old, depressed, white girl attempted suicide on the afternoon of June 11, 1969, by ingesting between 90 and 240 ml of a commercial windshield washer antifreeze (Wizard). This solution contained 60% methanol, 39.24% potassium phosphate, 0.25% wetting agent, and 0.25% green and yellow dye, but no heavy metals. Immediately following ingestion the patient vomited. Five hours later the family noted that she was unsteady, had slurred speech, but no other symptoms. She was taken to the Children's Mercy Hospital in Kansas City, Mo, that evening (nine hours after ingestion) where she was described as mildly drowsy, but fully oriented. At that time her vital signs were temperature, 98 F (36.7 C); blood pressure, 140/90 mm Hg; pulse rate, 80 beats per minute; respirations, 18 to 22 per minute; findings from her general physical examination were normal. During the initial eight hours in the hospital, she slept intermittently, took fluids orally, and conversed appropriately with the nurses attending her.

The following morning laboratory data showed that results of a urinalysis were nor-

Fig 1.—Rigidity and pain impaired passive extension of elbow and abduction of arm.

Fig 2.—After levodopa administered, patient could fully extend and flex her left arm 16 to 20 times per minute. Before therapy, she performed this maneuver only one or two times per minute.

mal; hematocrit reading, 42%; white blood cell count, 23,000 with 90% polymorphonuclear leukocytes; sodium, 140 mEq/liter; potassium, 3.1 mEq/liter; chloride, 104 mEq/liter; carbon dioxide content, 6.6mEq/liter; glucose, 147 mg/100 cc; calcium, 8.9 mEq/liter; and phosphate, 3.6 mEq/liter. At this time she was more lethargic but her vital signs were unchanged from admission with the exception of her respirations which were described as deep and somewhat irregular, varying from 18 to 30 per minute. Blood gases (arterial-capillary) confirmed the impression of a severe metabolic acidosis (pH = 7.107, arterial carbon dioxide pressure [P_{CO_2}] = 15.8 mm Hg). The patient was then transferred to an intensive care unit (ICU) where she was observed continuously with vital sign checks every 15 minutes, and blood gas determinations every two to four hours, and electrolyte counts at four- to six-hour intervals until recovery from the acute illness was complete. She was treated with intravenously administered fluids, including bicarbonate and ethanol. During the first 12 hours in the ICU, she was lethargic with acidotic respirations, but at no time did her blood pressure drop below 132/78 mm Hg or other vital signs change significantly. All electrolytes and results of blood chemistry studies remained normal except for the arterial pH and blood gases. The acidosis was corrected, and 20 hours after transfer to the ICU her arterial pH was 7.36 P_{CO_2} = 40.0 mm Hg, and carbon dioxide content 19.9 mEq/liter. Although initially sleepy and sometimes stuporous, she was always easily arousable and had normal pupillary responses. She was never cyanotic, had no difficulty handling oral secretions, and did not require vasopressor drugs, oxygen, intubation, or tracheostomy. By 36 hours after admission to the hospital, she was fully alert and following commands. Vital signs, arterial blood gases, and electrolytes were all normal. A blood methanol level obtained approximately 24 hours after ingestion and after ethanol infusion was 5 mg/100 cc.

Improvement was sustained, and on the fifth hospital day she was transferred to a regular ward. At that time bilateral optic neuritis with visual acuity of 20/200 OU was documented. She was discharged on the 16th hospital day. Four weeks after the ingestion and following discharge from the hospital, the patient noted progressive tightness in her neck and limb muscles, tremulousness, deterioration in handwriting, and difficulty walking. Neurological examination at the original hospital six weeks after ingestion revealed a broad-based, unsteady, stooped, propulsive gait. There was tremor of the head and hands and poverty of spontaneous movement.

During the following six months, both rigidity and spasticity increased and extension of the left arm became severely limited and painful. The patient's depression persisted with fre-

quently expressed death wishes and suicidal thoughts. Her visual acuity had not improved, and she had remained essentially blind. For these reasons she was referred to St. Louis Children's Hospital on Jan 24, 1970. Physical examination revealed a 14-year, 5-month-old adolescent girl who was overtly depressed. The general physical findings were normal. The optic discs were markedly pale and visual acuity was less than 20/400 OU. Visual fields consisted of crescentic, perimacular, superior altitudinal areas five degrees in width. Her facies was masked, and there was significant latency in motoric response and poverty of spontaneous movement. There was a severe plastic type of rigidity with moderate cogwheeling, most noticeable in the left arm and neck, somewhat less in the legs, and minimally in the right arm. A three to five per second intention tremor was present in the arms and neck and occurred at rest when the patient was tense. The left arm was carried in adduction at the shoulder with flexion at the elbow. Voluntary movements of this arm were slow and extension limited to 120°. Rigidity and pain impaired passive extension of the elbow and abduction of the arm as illustrated in Fig 1. Rapid alternating movements of the arms were performed slowly, especially on the left. Her gait was impoverished with short steps, wide-based, and she had difficulty in initiating movement. Deep tendon reflexes were normally active in the arms but increased in the lower extremities. The Hoffmann responses were absent, but there was a positive grasp response in the right foot; the right plantar response was clearly extensor and that on the left was questionable. Even though her affect was flat, she cried quite easily and the jaw jerk was 3+, suggesting a pseudobulbar palsy. The glabella response was positive. Results of sensory examination were normal, muscle strength was good, and there was no atrophy. Psychological testing revealed average intelligence.

Results of routine hemogram and urinalysis were normal as were blood chemistry studies including blood urea nitrogen, calcium, alkaline phosphatase, total serum protein with albumin/globulin ratio, protein bound iodine, and serum ceruloplasmin. The cerebrospinal fluid was colorless, acellular, and under normal pressure, and the protein was 25 mg/100 ml. Skull and chest roentgenograms were unremarkable and a pneumoencephalogram was entirely normal. The electroencephalogram using bipolar leads during the awake resting state demonstrated a low voltage fast tracing with bioccipital paroxysmal slow waves.

Ten days after admission treatment with 500 mg/day of levodopa was begun. The dosage was increased over the next seven days to 3 mg/24 hr. At this dose, there was striking improvement in her rigidity, tremor, and hypokinesia. Several attempts to increase the dosage were associated with anorexia, nausea, and vomiting. Amantidine hydrochloride was added, but it produced no further improvement and was discontinued.

Examination at discharge on March 4, 1970, after four weeks of continuous levodopa administration, revealed moderate decrease in the plastic rigidity with a marked improvement in ability to perform rapid alternating movements. She could fully extend and flex her left arm 16 to 20 times per minute, whereas she could perform this maneuver only 1 to 2 times per minute on admission. Such improvement is illustrated in Fig 2. Her gait was more rapid and less shuffling, her posture erect and facies no longer masked.

The patient has continued to receive 3 to 3.5 gm/day of levodopa with the improvement described maintained for a present total of eight months. During April 1970, she inadvertently stopped taking levodopa for two weeks during a school vacation period with prompt worsening of her condition to the pretreatment level of severity. Reinstitution of the drug again resulted in improvement. With levodopa her left arm is useful to her; without it, function is severely limited.

The patient's depression was treated with amitriptyline (Elavil), 150 mg/24 hr, for three weeks and then imipramine hydrochloride (Tofranil), 75 mg/day and amitriptyline, 50 mg at bedtime. The depression improved over the following four to six weeks, but attempts at decreasing dosage resulted in return of the depressive symptomatology.

Comment

Methanol has been an important industrial solvent for the past 100 years. During the 19th century, a few reports of adverse effects following methyl alcohol ingestion stimulated a spirited controversy as to whether the abnormalities were due to methanol or a contaminant. In 1923, Reif[1] presented unequivocal evidence that pure methanol could cause serious toxicity and death. Ree[2] published a historical review of this controversy in his classical paper on methanol poisoning in 1946.

The most extensive and well-studied experience in the United States occurred in 1951

n 323 cases of methanol intoxication pared over a five-day period in Atlanta. nett et al[3] studied both the acute and nic effects of methanol in these patients. ir report has become the definitive state- t regarding methanol poisoning in this try. Optic atrophy with associated vis- loss were the only permanent sequelae their patients who survived the acute ication. Coma and convulsions were mon during the acute phase, but no nces of either transient or permanent r abnormalities occurred. Their review ines the essential metabolic sequelae of anol ingestion. It emphasizes the sig- nt role of acidosis in causing acute al nervous system (CNS) depression death and reviews the evidence that olic products of methanol (especially aldehyde) are primarily responsible for retinal degeneration and subsequent op- trophy.

is our assumption that both the retinal focal neurologic sequelae observed in patient are secondary to methanol in- ation. Previous experiences (mentioned e) strongly support this assumption regard to the ocular abnormalities. ever, focal spasticity, rigidity, and dys- have rarely followed methanol poi- ing. Such symptoms exhibiting a delayed t have been attributed to a variety of es including acute and chronic heavy l intoxications, drugs, carbon monoxide oning, and hyperbaric oxygen.[4] In addi- , Plum and co-workers[5] have called at- ion to a similar clinical syndrome begin- g days to weeks after severe anoxia. In case, however, the carefully documented rvations during the acute intoxication ld seem to rule out possible etiologic ors such as heavy metals, hypotension, noxia. We have, therefore, concluded t the delayed focal neurologic abnormali- of this patient are a direct toxic effect of hanol or its catabolic by-products.

he German literature contains the only l incident whereby focal neurologic ns other than optic atrophy may have wed methanol intoxication. The case re- t by Riegel and Wolf[6] describes a 60- old man, seen 20 years following an ode of methanol ingestion, whose neuro- t abnormalities were said to be a result of that intoxication. He had focal cranial nerve deficits, optic atrophy and a Parkinson-like, extrapyramidal syndrome. In addition, Riegel and Wolf refer to case reports in the older literature[7,8] that describe neurologic abnormalities possibly secondary to methanol.

There are no consistent neuropathological findings of methanol poisoning reported in the literature. Pick and Bielschowsky[9] described "diffuse congestion and edema" in the postmortem findings of three cases. These findings were subsequently confirmed many times.[10-12] In a review by Bennett et al[3] of the Atlanta epidemic, they reported autopsy findings in 17 patients dying of acute methanol intoxication with the CNS abnormalities limited to "cerebral edema with meningeal and subarachnoid hemorrhage."

In 1965, Erlanson et al[13] reported the cases of four patients who had undergone neuropathologic study. Three died several days after ingesting methanol despite vigorous therapy including vasopressor drugs and positive pressure respiratory support. In all three the brain showed edema and diffuse grayish-red discoloration with large hemorrhages in the basal ganglia (especially putamen) and upper brain stem. The fourth patient, a 41-year-old woman, is of particular interest for she recovered from the acute intoxication without any significant anoxia and at no time required respiratory support or vasopressor drugs. She was apparently normal at the time of discharge and lost to follow-up until 1½ years later when she died of bronchopneumonia. Postmortem examination revealed multiple slit-shaped cysts restricted to the lateral parts of both putamina with glial proliferation noted microscopically. According to Erlanson et al[13] similar postmortem findings were described by Orthner[7] who considers them typical of methanol poisoning. Thus, although the motor abnormalities found in our patient represent a unique clinical sequelae of methanol intoxication, a possible neuropathologic substrate for such findings has been documented previously.

Interestingly, methanol intoxication in children is extremely rare, with no patient less than 19 years of age documented, although Bennett et al[3] state the age range of

patients in the Atlanta epidemic was 10 to 78 years. This, no doubt, reflects the usual reason for methanol ingestion as a substitute alcoholic beverage.

The beneficial effects to our patient of levodopa were gratifying. Substantial clinical improvement without adverse side effects has been maintained over seven months. The basis for this improvement, as in classic Parkinson's disease, is currently unknown, but attributed to effects on the dopaminergic neurons of the basal ganglia.

Knowledge of the potential dangers of methanol is increased by the observations noted in this report. Heretofore, only blindness has been recognized as a long-term effect of this poison. Careful reevaluation of patients known to have survived the acute stage of methanol intoxication, with or without visual sequela, may bring to light further evidence of this toxin's damaging effects on the brain.

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Nonproprietary and Trade Names of Drug

Levodopa—*Larodopa.*

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