Axonal Polyneuropathy After Acute Dimethylamine Borane Intoxication

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**Objective:** To study a patient with axonal polyneuropathy due to acute dimethylamine borane (DMAB) intoxication.

**Patient:** Confusion and drowsiness in the acute stage, followed by cognitive impairments and polyneuropathy, are reported in a chemical factory worker after acute exposure to DMAB.

**Results:** Nerve conduction studies indicated axonal polyneuropathy, particularly in the motor nerves. Sural nerve biopsy studies 3 months later revealed an axonal degeneration with a mild decrease of fiber density in the large myelinated fibers. Quantitative sensory testing also disclosed an impairment of pinprick, temperature, and touch sensations. Cutaneous nerve biopsy studies 9 months later demonstrated a moderate loss of epidermal nerves. During the follow-up period of 1.5 years, the clinical features and serial nerve conduction studies showed a steady improvement.

**Conclusions:** Since DMAB is a new product and has been widely used recently in the manufacturing of semiconductors and electronics, we conclude that DMAB intoxication may produce motor-predominant axonal polyneuropathy and that the establishment of a threshold limit value is warranted.

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**Dimethylamine Borane (DMAB), (CH₃)₂NH·BH₃**, also called boron-dimethylamine complex, is a white, solid substance with an amine odor at room temperature and may release a flammable gas in contact with water or form unstable peroxides after a prolonged exposure to the air.¹,² Dimethylamine borane is widely used in the manufacturing of high-temperature printed circuit boards, thin metal film, floppy disks, semiconductors, and power transistors.²,³

The DMAB products contain more than 97% DMAB and dimethylamine. Dimethylamine borane may decompose to dimethylamine, particularly at temperatures higher than 34°C.¹ Excessive exposure to DMAB may cause damage to the central nervous system.¹,² For DMAB, the median lethal dose in rats is 59 mg/kg by oral administration.¹,³ In this study, we report the clinical manifestations and nerve conduction studies (NCS), quantitative sensory test (QST), and pathologic findings of the sural nerve and cutaneous nerve after acute exposure to DMAB.

**REPORT OF A CASE**

In March 2004, a 38-year-old man working at a chemical factory as a DMAB production operator developed distal limb numbness and muscle weakness after an accident.⁴ Five weeks prior to hospital admission, liquid DMAB blew out of the pipe when a filter door had not been closed tightly. Because the patient did not wear protective gear except for a pair of gloves, the liquid DMAB clung to his entire body. He quickly took off his clothes and cleaned the exposed skin with water. However, his eyes were irritated and painful. Ten hours later, dizziness, tightness of the mouth and throat, and swelling of the tongue were noted and he was drowsy and confused with a Glasgow Coma Scale score of E3V4M6. The mouth and throat were injected, but his vital signs were normal. The results of laboratory tests, including complete blood cell counts and levels of electrolytes, aspartate aminotransferase, glucose, and creatinine, were normal.

Five days after DMAB exposure, he developed numbness and weakness in the distal limbs, slurred speech, difficulty swallowing, and poor attention. Neurological examinations showed hypoactive tendon reflexes, decreased sensation in all sensory modalities, and weakness in the 4 distal limbs. Brain magnetic resonance imaging and computed tomographic results were normal, although the electroencephalogram showed a mildly diffuse slowing. Results of a toxicological screen, including mercury, lead, and arsenic concentrations, were normal. Nerve conduction studies and electromyography on March 22, 2004, showed an axonal polyneuropathy with...
predominant motor nerve involvement. Motor NCS disclosed markedly decreased amplitudes of compound muscle action potentials in the bilateral median, ulnar, peroneal, and tibial nerves; mildly prolonged distal latencies of compound muscle action potentials in the right median nerve; and decreased nerve conduction velocities in the right ulnar and bilateral peroneal and tibial nerves. Sensory NCS showed mildly decreased amplitudes of sensory nerve action potentials in the right ulnar nerve and a slowing of sensory nerve conduction velocities in the bilateral sural nerves. The electromyography studies demonstrated marked fibrillations and positive waves in the biceps, abductor pollicis brevis, vastus medialis, and gastrocnemius muscles.

Immediately after exposure, the patient quit the job and had regular follow-ups for at least 1.5 years. Five weeks later, the patient still had a glove-and-stocking–like sensory impairment. There was a generalized absence of tendon reflexes, muscle weakness in the distal limbs, and muscle wasting in both hands and feet. The muscle strength grades, according to the Medical Research Council of Great Britain, were 3/5 in the abductor pollicis brevis, 4/5 in the extensor digitorum communis and biceps muscles, 2/5 in the tibialis anterior and gastrocnemius muscles, and 4/5 in the quadriceps muscle.

Six weeks later, he still showed a dull mental response and impaired concentration. Two and a half months later, a neuropsychological examination was performed using a Chinese test and results of this demonstrated a normal full IQ (89), with a verbal IQ of 89 and a performance IQ of 94. However, there were cognitive impairments in the verbal and nonverbal learning memory and attention functions, such as focusing, tracing, divided attention, working, and semantic category retrieval.

Three months later, sensory impairment had improved in both hands, but motor and sensory impairments in the distal lower limbs still persisted. Repeated NCS on June 8, 2004, showed no definite improvement but an electromyography study revealed a reinnervation pattern in the tibialis anterior muscle. Measures of the QST, including pinprick, temperature, pressure pain, blunt-sharp discrimination, and light-touch detection, were obtained 3 months after exposure, using the standard QST methods of our laboratory. The QST showed a prominent impairment in pinprick, temperature, and touch sensations, particularly in both feet.

With informed consent, a sural nerve biopsy specimen was obtained 3 months after DMAB exposure and studied as previously described. Light microscopic examinations showed a reduction of fiber density involving both large and small myelinated fibers. Some degenerating fibers with a disrupted myelin sheath (Figure 1A) and clusters of small myelinated fibers were noted. Electron microscopic examinations revealed an axonal degeneration with vacuoles and derangement of microtubules and neurofilaments in some fibers (Figure 1B). The histograms of the myelinated fibers showed a decrease

![Figure 1](image1.png)

**Figure 1.** Microscopic examination of the sural nerve biopsy specimen. A, Light microscopic examination showing some degenerating fibers with disruption of the myelin sheath (arrows) and a reduction of fiber density (toluidine blue, original magnification ×400 before reduction). B, Electron microscopic examination demonstrating an axonal degeneration with vacuoles in the myelinated fibers.

![Figure 2](image2.png)

**Figure 2.** Histograms of myelinated nerve fiber diameters showing a mild decrease in the large myelinated fibers. A, Patient. B, Control.

![Figure 3](image3.png)

**Figure 3.** The skin section was immunostained with protein gene product 9.5. The representative section shows marked depletion of epidermal nerves. There is only a fragmented nerve in the subepidermal region (arrow) (original magnification ×400).
staining as previously described. Skin innervation was evaluated using 0.5M Tris buffer (pH 7.6) and processed for immunostaining with antibodies against nerve fibers. Samples were fixed with 4% paraformaldehyde and sections of 50 µm were treated with 0.5% Triton X-100 in 1% normal goat serum to permeabilize the tissue. The immunostained sections were observed in the subepidermal regions of the skin.

A skin biopsy was performed 6 months after acute DMAB intoxication, following the established procedures and after informed consent was obtained. Skin samples were fixed with 4% paraformaldehyde and sections of 50 µm were treated with 0.5% Triton X-100 in 1% normal goat serum to permeabilize the tissue. The immunostained sections were observed in the subepidermal regions of the skin.

One year later, muscle strength in the distal limbs had improved, particularly in both hands, and tendon reflexes returned to normal in the upper limbs. In addition, the sensory functions also recovered except for pinprick, temperature, and touch sensations in the distal feet. Follow-up NCS on April 27, 2005, showed a prominent improvement. One and a half years later, the muscle strength was still abnormal with a grade of 4/5 in the bilateral tibialis anterior and gastrocnemius muscles, and the sensory functions were also impaired in both feet, particularly pinprick and temperature sensations, but vibration and position sensations were normal. The QST also confirmed an abnormality in pinprick, temperature, and touch sensations. The tendon reflexes were nearly normal in both knee and ankle jerks. A follow-up nerve conduction velocity study on November 9, 2005, showed further improvement, except for a decreased amplitude of compound muscle action potentials in the right tibial nerve.

The serial motor NCS and sensory NCS are summarized in Table 1 and Table 2.

<table>
<thead>
<tr>
<th>Time</th>
<th>Median Nerve</th>
<th>Ulnar Nerve</th>
<th>Peroneal Nerve</th>
<th>Tibial Nerve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>DL, ms</td>
<td>Amp, µV</td>
<td>NCV, m/s</td>
<td>DL, ms</td>
</tr>
<tr>
<td>March 22, 2004</td>
<td>R 3.8</td>
<td>1.8</td>
<td>51.8</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>L 3.8</td>
<td>1.8</td>
<td>51.8</td>
<td>3.8</td>
</tr>
<tr>
<td>June 8, 2004</td>
<td>R 3.8</td>
<td>1.8</td>
<td>51.8</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>L 3.8</td>
<td>1.8</td>
<td>51.8</td>
<td>4.4</td>
</tr>
<tr>
<td>April 27, 2005</td>
<td>R 3.8</td>
<td>1.8</td>
<td>51.8</td>
<td>4.4</td>
</tr>
<tr>
<td>November 9, 2005</td>
<td>R 3.8</td>
<td>1.8</td>
<td>51.8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Control mean (SD) (n = 40) 3.0 (0.4) 10.9 (2.4) 60.5 (4.0) 2.6 (0.4) 9.1 (1.8) 60.5 (4.2) 4.2 (0.5) 5.9 (2.5) 51.1 (3.2) 5.3 (1.0) 9.8 (2.9) 50.5 (3.4)

Abbreviations: Amp, amplitude; DL, distal latency; DMAB, dimethylamine borane; L, left; NCV, nerve conduction velocity; R, right.

*Abnormal if the data are beyond the mean (3 SDs) or the amplitude is 10 µV or lower in the peroneal nerves and 3.0 mV or lower in the tibial nerves.
The present data indicate that an acute exposure to DMAB may induce an axonal polyneuropathy. The confusion and the abnormalities seen in the electroencephalogram and neuropsychological tests also suggest an involvement of the central nervous system. In acute DMAB poisoning or exposure to dimethylamine vapor or diborane, corneal irritation, tongue swelling, discomfort in the esophagus and throat, epigastralgia, vomiting, diarrhea, and pulmonary edema can occur.

Neurotoxic effects to the peripheral nervous system began in the distal limbs a few days after DMAB exposure. The sensory impairments seemed to occur in a glove-and-stockin-like pattern. Muscle weakness was more marked in both legs and feet. The data indicated a dying-back polyneuropathy similar to the majority of other toxic polyneuropathies. Clinical improvements gradually began 2 to 3 months after exposure. One year later, muscle strength and sensory functions were still abnormal in the distal feet, compatible with the improvement in both motor and sensory NCS.

The NCS findings included marked abnormalities in the motor nerves. In contrast to marked motor NCS abnormalities, sensory NCS abnormalities were relatively mild. However, the cutaneous nerve studies also showed a moderate degree of involvement in the sensory nerve fibers, which correlated well with the clinical manifestations and the results of the QST. The electromyography study showed an active denervation pattern in the subacute stage and partial reinnervation 3 months later. These data indicated an axonal degeneration, which was compatible with primary axonal degeneration found in the sural nerve biopsy specimen. The results of pathologic studies of DMAB-induced axonal polyneuropathy are more like those of triorthocresyl phosphate and diborane, which show paranodal swelling. However, the selective involvement of large myelinated fibers in the sural nerve biopsy specimen is very similar to the majority of other toxic polyneuropathies, such as triorthocresyl phosphate, n-hexane, and carbon disulfide neuropathies.

Since DMAB is widely used in modern industry, intoxication may occur in many occupational settings. The threshold limit values of DMAB have not been established. The pathogenetic mechanisms of the neurological impairments remain unclear. Otherwise, an avoidance of excessive and accidental exposure at the workplace and education about the potential hazards to workers should be emphasized.

REFERENCES


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