Suspected Endotoxin Poisoning In Two Intravenous Methamphetamine Users

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The effects of methamphetamine used as a recreational drug include central nervous system stimulation that can induce euphoria, increased alertness, intensity of emotions, anorexia, and increased sexuality.[1]

In toxic doses methamphetamine induces agitation, anxiety, hallucinations, delirium, seizures, and even death. Hyperthermia can result from drug-induced central nervous system abnormalities, muscular hyperactivity, or seizures. Cardiovascular complaints include chest pain, palpitations, and dyspnea,[2,3] and dysrhythmias, tachycardia, hypertension, and myocardial ischemia are not uncommon.[4,5]

We report the cases of two patients who arrived and were admitted to our hospital at the same time, both manifesting some of the above-described effects, but whose conditions were accompanied by some abnormalities not usually seen with methamphetamine. These effects included hypotension, pulmonary edema with hypoxia, and an initial leukopenia followed by leukocytosis. These manifestations might be more easily explained by hypothesizing that an endotoxin was a contaminant in the drug used.

Case Reports

Case 1

A 19-year-old woman was using intravenous methamphetamine. She was sharing her drug and needle with her girlfriend. Later the patients revealed that both used the drug directly out of the plastic bag in which it was purchased, without using their own extenders. Within 10 minutes after injection, the 19-year-old had myalgias, chills, and abdominal pain. Subsequently she was transported by ambulance to Stanislaus Medical Center. In the emergency department the following values were recorded: oral temperature 103.5°F, pulse 120 beats per minute, respirations 30/min, and blood pressure 70/30 mmHg. The patient, while alert and oriented on examination, was pale and diaphoretic and had fresh needle marks bilaterally in the antecubital areas. A pulmonary examination found bilateral inspiratory and expiratory wheezes without end-inspiratory rales. Only tachycardia was found on a cardiac examination. Pulse oximetry showed a saturation of 93 percent on room air. A chest radiograph was read as normal.

Laboratory studies disclosed the following values: white-cell count was 2600/μL with 52 percent segmented neutrophils, 25 percent band cells, and 23 percent lymphocytes. Urinalysis showed her white-cell count was 100–125/hpf with few bacteria. A urine toxicology screening test was positive only for methamphetamine. Urine and blood cultures (aerobic and anaerobic, two sets) showed no growth at 72 hours and 6 days, respectively.

Hospital Course

The patient was admitted to the intensive care unit and given intravenous ceftizoxime sodium and nafcillin sodium. Vigorous fluid administration was used to support blood pressure. Intravenous methylprednisolone was also given.

Within 24 hours the patient was stable and afebrile. At this time her white-cell count was 19,900/μL with 70 percent segmented neutrophils, 17 percent band cells, and 13 percent lymphocytes. Antibiotics were continued, and she was transferred from the intensive care unit. Methylprednisolone and intravenous antibiotics were discontinued on day 3, and oral trimethoprim-sulfamethoxazole therapy was begun without sequelae. On day 4 she remained afebrile and her white-cell count was 7500/μL. She was discharged at this time and prescribed oral antibiotics; subsequently, she was lost to follow-up.

Case 2

A 24-year-old woman was sharing needle and intravenous methamphetamine with the woman described above and was transported to the emer-

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gency department in the same ambulance. She also had chills, nausea, myalgias, and abdominal pain within 10 minutes of injection. Her oral temperature was 103.2°F, pulse 130 beats per minute, respirations 30/min, blood pressure 68/40 mmHg. She was an oriented, diaphoretic woman in some respiratory distress and had rigors. A cardiovascular examination found only tachycardia, and a pulmonary examination revealed generalized inspiratory and expiratory wheezes without end-inspiratory rales. She also had several fresh needle marks on both arms. Pulse oximeter showed a saturation of 88 percent on room air. A chest radiograph showed bilateral pulmonary infiltrates consistent with pulmonary edema.

Laboratory studies disclosed the following values: white-cell count 2500/μL, with 55 percent segmented neutrophils, 33 percent band cells, 11 percent lymphocytes, and 1 percent monocytes. White-cell count on a urinalysis was 15–20/hpf with no bacteria. A urine toxicology screening test was positive only for methamphetamine. Urine and blood cultures (aerobic and anaerobic, two sets) remained without growth at 72 hours and 6 days, respectively.

Hospital Course

The patient was admitted to the intensive care unit and given vigorous fluid support. Methylprednisolone and intravenous ceftizoxime sodium and nafcillin sodium therapies were administered. Because she had a history of pulmonary embolus, heparin was given initially but then discontinued when the ventilation-perfusion scan found a low probability for emboli.

Laboratory studies from day 2 disclosed a white-cell count of 19,200/μL, with 70 percent segmented neutrophils, 17 percent band cells, 12 percent lymphocytes, and 1 percent monocytes. The patient remained in the intensive care unit until day 3 when her respiratory status had stabilized enough for transfer to the progressive care unit. The intravenous antibiotics and methylprednisolone were discontinued, and oral trimethoprim-sulfamethoxazole therapy was given without fever return. She was discharged on day 4 and lost to follow-up.

Discussion

The similarity of signs and symptoms of these two cases is remarkable. Both patients had initial leukopenia, fever, rigors, and hypotension. Both had respiratory compromise, one severe with a chest radiograph consistent with pulmonary edema, the other with clinical wheezing and pulse oximetry levels that could be called hypoxic in this young patient without history of lung disease. Both had leukocytosis the following day (though both were receiving steroids). Blood cultures and urine cultures in both patients had no growth. Both women rapidly improved considering their initial clinical conditions.

On the day of admission, the mother of one of the patients brought in the bag containing some of the substance injected. When analyzed by gas chromatography, the substance was pure methamphetamine. A toxicology screening test to search for more than 30 substances and drugs of abuse could find none of the traditionally used "cutting" substances, including quinine, quinidine, and strychnine. Cultures of the bag for bacteria, fungi, and acid-fast bacilli remained negative.

Effects of Endotoxin in Humans

Endotoxemia in humans is usually the result of gram-negative sepsis. Studies of the effects of synthesized *Escherichia coli* endotoxin have shown that endotoxin causes an increase in temperature, an elevated white-cell count, increases in blood cortisol and β-endorphin levels and plasma histamine levels.[6] Extensive research also implicates various host-effector molecules, such as tumor necrosis factor and others.

An important sequela of septic shock is cardiovascular dysfunction,[7,8] in which endotoxin is implicated as a major mediator. Administration of endotoxin to healthy subjects causes a depression of left ventricular function,[9] which along with increases in permeability of the vascular system, particularly in the lung,[10] leads to the effects of lowered systemic vascular resistance, hypotension, and pulmonary edema. All of these effects were reversible in test subjects.[9]

Methamphetamine Synthesis

Methamphetamine is relatively easy to synthesize in a crude laboratory,[11-13] and can be produced as a relatively pure product that is sold on the streets. Contamination by nonstimulant organic and inorganic substances is certainly possible,[14] however, and probably occurs during the final steps of conversion and drying, as the chemicals involved in synthesis would most likely preclude organis-

mal contamination. Other areas of possible contamination might include the packaging and distribution process, the syringe and needle, and the method of preparation for injection.

Implications

We postulate that the drug or drug-using paraphernalia used by these two women was probably contaminated with an endotoxin. The possibility of one patient being ill before the injection and passing it to the other patient through the shared needle seems unlikely. The initial leukopenia is difficult to explain except by postulating that initial responses overwhelmed the patients' immune systems, much like advanced sepsis. It would appear that whatever organism from which the endotoxin originated was somehow eliminated, but the toxin was not exposed to sufficient denaturing conditions, leaving it physiologically active.

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