Brief Communication

Late-onset polyneuropathy due to malathion intoxication

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Organophosphates are commonly used as agricultural insecticides. Poisoning with these agents may be accidental or suicidal. Intoxication occurs through absorption from skin or respiratory and gastrointestinal tracts. Organophosphates exert their toxicity by producing irreversible inhibition of the activity of circulating plasma cholinesterase. Acetyl cholinesterase is inhibited by phosphorylation. Firm binding of phosphate radicals between organophosphate and the active serine-containing enzymatic site causes this effect. Inhibition of acetyl cholinesterase results in accumulation of acetylcholine at the parasympathetic, sympathetic, and somatic sites of neurotransmission.[1] Symptoms of organophosphate intoxication are those of cholinergic stimulation and late neuropsychiatric manifestations including a subacute paralytic syndrome known as the intermediate syndrome.[2] Malathion is the most common agent in organophosphate intoxication. Lee et al[3] reported that, in malathion intoxication mechanical ventilation is required by 74% of patients, and only 22% of patients had features of intermediate syndrome. This report describes a case of organophosphate intoxication and the development of intermediate syndrome, an uncommon subacute complication of organophosphate intoxication.

A 27-year-old woman had been admitted to the hospital of Eskisehir Osmangazi University Medical Faculty after she attempted suicide by ingestion of Sentiom® (Malathion). Nausea and vomiting were the first symptoms before she was admitted to the hospital. On arrival to the emergency department, she had confusion and disorientation. Her vital signs were; blood pressure 120/70 mm Hg, pulse 102 beats/min, and respirations 30 breaths/min. Her pupils were miotic. On neurological examination, Glasgow coma scale score was 4-5. Cardiorespiratory and abdominal examinations were normal. There was a dense odor in her skin and breath. Laboratory findings were normal except white blood cells: 21.300/mm^3, creatine kinase: 226, creatine kinase, myocardial bound: 62. Electrocardiogram and chest x-rays were normal.

In the intensive care unit (ICU), after the gastric decontamination with lavage, charcoal via nasogastric tube was administered. Atropin and pralidoxime (500 mg every 6 hour for 2 days) were administered intravenously To avoid transdermal absorption of the toxin leading to secondary poisoning, cleaning of her body was performed routinely every hour. She developed a fluctuating level of consciousness. Profuse bronchorrhea continued despite atropinization and pralidoxime. Weakness of the respiratory muscle, bronchorrhea and bronchospasm lead to respiratory failure and mechanical ventilatory requirement. She remained ventilator dependent until the end of the second week. Antibiotherapy was planned for nosocomial pneumonia by culture-antibiogram results. Although hemodynamic parameters were generally in normal ranges, she sometimes required inotropic agents. In the third week, the trachea was extubated and she was breathing spontaneously in room air.

In the following days, hemodynamic and respiratory parameters were in normal ranges. Urinary incontinence had been realized after removal of urinary catheter. Consultation by urology department demonstrated detrusor over activity (hyperreflexia). She was also suffering from left leg pain. Electroneuromyelographic (ENMG) research demonstrated toxic neuropathic changes in the left peroneal and posterior tibial nerves. Ophthalmic examination demonstrated toxic optic neuropathy bilaterally, and a hemorrhage localized in the nasal part of the left eye. Steroid therapy was proposed for this pathology. She was discharged from hospital on day 36 with neurologic, urologic, and psychiatric follow up. She required a urinary catheter for 4 months after discharge from hospital. One year later, her left leg neuropathy and ophthalmic pathologies were still continuing. However, urodynamic research showed the detrusor over activity was within normal range. She gave her signed consent for her personal health information to be published without divulging personal identifiers.

Diagnosis of cholinergic agent intoxication may be easy due to history of exposure and specific odor in the skin and mouth. Severity of exposure causes some differences in symptoms on admission. Nausea and vomiting were the first symptoms in our case. These are the most common signs although exposure is small. Other gastrointestinal symptoms are salivation, diarrhea, and abdominal cramps. The usual cause of death from an organophosphate exposure is respiratory failure, resulting from weakness of the respiratory muscles and central depression of the respiratory drive.[1] Severe bronchorrhea and bronchospasm are also common symptoms that aggravate hypoxia. All these factors may lead the patient to mechanical ventilator requirement as in our case. Patients suffering from the pulmonary effects of poisoning are also susceptible to complications of prolonged intubations and mechanical ventilation. Central nervous system manifestations

may also lead to life threatening symptoms in organophosphate intoxication. These effects include restlessness, emotional lability, headache, tremor, ataxia, delirium, coma, seizures, cardiorespiratory depression, and death.[1] Besides the well-known acute cholinergic toxicity, mental status deterioration consistent with the intermediate syndrome may occur. Neuropsychiatric sequelae may be seen over the long-term period. Behavioral symptoms including depression, psychosis, aggression, irritability, and concentration problems have been reported late after organophosphate poisoning.[2] Our patient had confusion and disorientation in the first admission to the ICU. But there were no mental and psychiatric symptoms over the second week. Aside from acute neurological symptoms, organophosphates can cause several chronic neurological sequelae. The intermediate syndrome is confined to an abnormality of neuromuscular function in specific muscle groups: proximal limb muscles, neck flexors, motor cranial nerves, and respiratory muscles.[4] The pathophysiology of intermediate syndrome is due to organophosphate induced alteration in postjunctional acetylcholine receptors. Unlike the delayed polyneuropathy, intermediate syndrome occurs 24-48 hours after poisoning and carries a risk of death due to associated respiratory depression. Onset of delayed polyneuropathy occurs 2-4 weeks post-exposure. There is no effective treatment, and recovery is generally incomplete.[2] Although triarylphosphates, which are specific organophosphates carry a higher risk of peripheral neuropathy, malathion also can cause pathologic neuropathic changes.[4,5] Our patient required a urinary catheter due to neurogenic detrusor overactivity for 4 months after discharge from hospital. Overactive detrusor function indicates the presence of involuntary contractions. Neurologic changes above the brain stem that affect micturition generally result in involuntary bladder contractions. Komori et al[5] demonstrated that neurogenic bladder and spinal automatism may become obvious in malathion intoxication. They described an axonal degeneration, loss of large myelinated fibers, and increase in Schwann cell clusters in sural nerve biopsy. In our case, ENMG showed persistent neuropathic changes in the left peroneal and posterior tibial nerves one year later.

In summary, besides the well-known life threatening acute cholinergic toxicity like respiratory failure, organophosphates may cause late-onset polyneuropathy. These findings occur in an awake patient who appears to be recovering from the acute poisoning. The intermediate syndrome is quite uncommon. Onset of neurological symptoms may occur 2-4 weeks post-exposure. Close observation of the clinical symptoms is important in this period as far as the observation of early life threatening manifestations.

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