Child Neurology Open
October - December 2015: 1-3

DOI: 10.1177/2329048X15618970
cno.sagepub.com
SAGE

Delayed Effects of Transcutaneous Organophosphate Poisoning in Four Children

Milen Pavlovic, MD, PhD[1], David Neubauer, MD, PhD[2], and Asma A. Al-Tawari, MD, PhD[1]

Abstract

Contamination or transcutaneous absorption of organophosphates (OP) is rare and there exist only few reports of such manner of poisoning. We report four children from the same family in whom temporal proximity of the disease onset, a detailed interrogation of parents and exclusion of other clinical differentials, led to the diagnosis of transcutaneous intoxication with organophosphates (diazinon). The contamination occurred during the game with a freshly used poison can. Uncommon clinical picture was marked by delayed signs predominantly reflecting certain nicotinic effects (muscle weakness, cramps) along with subtle neuropathic features occurring throughout a few weeks after initial event. Our illustrative cases can further contribute to the better awareness and understanding of variable spectrum of transcutaneous route of OP poisoning.

Keywords

organophosphates, delayed, neuropathy

Received August 20, 2015. Received revised October 4, 2015. Accepted for publication October 26, 2015.

Organophosphates intoxication produce a spectrum of muscarinic, nicotinic, and cholinergic neurosymptoms involving both central and peripheral nervous systems in well-described time base patterns.[1,2] However, sometimes the history of exposure cannot be initially so evident, especially in children and in cases with delayed manifestations. Transcutaneous absorption of organophosphate is rare in comparison to organophosphate ingestion, and there exist only few such reports.[3-5]

We report 4 children from the same family in whom, only after thorough interrogation of parents and exclusion of other differentials, the diagnosis of transcutaneous intoxication with organophosphate was made.

Case Reports

Case 1 was a 6-year-old, previously healthy girl from the family of 7 siblings of consanguineous parents living in a rural area of Kuwait. For the last 10 days, she complained for pain in muscles of lower limbs, clumsiness, and difficult walking. There was no history of precedent infection. On examination, she had limping gait and symmetrically painful muscles on palpation, without signs of trauma. Distal muscles limb weakness appeared more pronounced than proximal one. However, she had preserved deep tendon reflexes and sphincter control, and sensory appeared intact. Whole blood count, liver, renal, electrolyte profiles, creatine kinase enzyme, erythrocyte sedimentation rate, C-reactive protein, and cerebrospinal fluid investigations (cell and protein counts) were normal. Serologic tests for viruses and stool culture for polio were negative. Due to presumed Guillain-Barre syndrome, she received immunoglobulins intravenously with mild improvement afterward.

Case 2 was her elder 10-year-old brother who came 4 days later to the same hospital with nearly same symptoms and signs, however pain in the muscles was less severe. Cases 3 and 4 were 2 other brothers (8 years and 12 years old) who after another 2 days were admitted for the same problems, then all 4 were transferred from the local hospital to our Neuropediatric Unit.

[1] Al-Sabah Hospital, Shuwaikh Medical, Kuwait
[2] University Children's Hospital Ljubljana, Ljubljana, Slovenia

Corresponding Author:
Milen Pavlovic, MD, PhD, Al-Sabah Hospital, Shuwaikh Medical, Kuwait.
Email: mpavlov34@gmail.com

Table 1. Summary of Clinical Features of Presented Patients.

Demographic/Clinical/ Electrophysiological Findings	Patient 1	Patient 2	Patient 3	Patient 4
Sex	F	M	M	M
Age	6 years	10 years	8 years	12 years
Onset of neuropathic symptoms	10 days	12 days	14 days	14 days
Severity and distribution of weakness	Light, LL>UL	Light, LL>UL	Not present	Not present
Muscle strength	3	4	4 -5	4 -5
Deep tendon reflexes	+	+	+	+
Sensation (light touch, deep proprioception)	+	+	+	+
Nerve conduction studies			Not done	Not done
Motor nerve	CV/TL/A	CV/TL/A		
Left peroneal	45.0/2.2/5.2	48.0/2.2/5.7		
Left posterior tibial	49/2.1/9.0	50/2.3/11.8		
Right peroneal	48/2.4/6.0	51/2.6/6.9		
Sensory nerve	CV/A	CV/A		
Left sural	45.0/21.5	47.0/22.5		
Repetitive nerve stimulation[a]	N	N		

Abbreviations: ADM, abductor digigit minimi; UL/LL, upper/lower limb; CV, conduction velocity (m/s), TL, terminal latency (ms); A, amplitude (M wave); mV, motor nerve, amplitude of action potential; μV, sensory nerve; N, normal.
[a]Decrement study were done in the right ADM/right nasalis/left nasalis. Decrement (first-fourth response: 1.0/0/0% at frequency 3 Hz). After 15-second contraction: potentiation-%, decrement- %; after 60-second rest: decrement-%.

On admission, 18 days after the first symptoms, the girl was still complaining of severe pain in the lower limb muscles, also generated by light touch of the extremities, and she was clumsy. The 3 affected brothers complained of only mild, movement-related muscular pain and had mild gait disturbance. The 3 other siblings of the same family (a 14-year-old girl and two boys of 2 and 3 years) were unaffected.

As an exposure to a common environmental agent (toxin or drug) was the most probable explanation, the parents (who first denied) were specifically asked for any possible poisons in the house. The father then remembered that he was using a pesticide inside the house to get rid of cockroaches and brought one empty can to us. It proved to be diacidol 60% (IUPAC) containing 60% of diazinon, a colorless thiophosphoric acid ester—a nonsystemic organophosphate used to control cockroaches, ants, and flees in residential buildings. However, the father insisted that the insecticide was used just before they left the house for a week, for a trip to Saudi Arabia, and that upon return they cleaned the house completely.

With enigma why not all family members were affected, we additionally asked about the circumstances. Finally, the father remembered that the 4 affected children were playing football with the can of diacidol in the garden for an hour before their trip. He also told us that all affected children had had mild abdominal cramps and diarrheal symptoms during the trip.

Unfortunately, hand-on toxicology service was not available at that time and tests to determine cholinesterase activity in red blood cells and/or serum pseudo cholinesterase were not possible.[6]

Being aware of this stumbling point in the diagnostic process, and complaints of leg pain provoked by touch, suggestive of a sensory neuropathy, we performed electromyography/nerve conduction study (EMG/NCV) studies in 2 most affected siblings (cases 1 and 2). The results were reported as unremarkable. However, we started gabapentin reaching the therapeutical dose of 30 mg/kg/d, and the symptoms improved. On discharge, only the girl was still complaining of mild pain in the muscles. On follow-up after 6 months, no lasting effects of poisoning remained in these children. Table 1 summarizes the clinical features of the presented patients.

Discussion

The clustering of cases in a temporal proximity in a family evoked a challenging pathway in search for a common cause. The diagnosis of Guillain-Barre syndrome, as first suspected in the girl, became less probable when the brother (case 2) was admitted for the same problems. Viral, autoimmune, or metabolic myopathies seemed unlikely as complete blood counts, creatine kinase, liver enzymes, renal and electrolyte profiles were normal, and serology tests were negative.

Once toxin exposure became evident, organophosphate-induced delayed polyneuropathy was considered. Organophosphate-induced delayed polyneuropathy is a rare neurotoxicity effect, occurring 1 to 5 weeks following acute cholinergic crisis or after a period of mild or no clinical features, resulting in muscle weakness, pain, and paresthesiae.[2,6,7] Although the mechanism is not well understood, organophosphate-induced delayed polyneuropathy is considered not to be due to the effects on acetylcholinesterase itself but to the inhibition of an enzyme in the nervous system, called neuropathy target esterase.

In regard to this possibility, initial diarrheal symptoms and abdominal cramps could be interpreted as mild muscarinic effect of organophosphate. Indeed, one study confirmed that only pinpoint pupils and diarrhea are enough for early triage in pediatric exposure to insecticides.[8] However, further course of otherwise not straightforward symptoms were actually

dominated by nicotinic effects (muscle weakness and cramps) and subtle neuropathic signs (sensitivity to touch).

The neuropathy in organophosphate-induced delayed polyneuropathy is commonly described as motor predominant, and if sensory symptoms are present, they are always milder than the motor component.[7] In our cases, EMG/NCV studies were normal. However, the small sensory nerves involved in organophosphate neuropathy can also give rise to normal results, thus by no means excluding its presence.[9]

Clinical signs of organophosphate-induced delayed polyneuropathy in children are otherwise rarely reported, and are much milder than in adults, as it appeared also in our cases.[6] Given that the volume of exposure was not perfectly clear, we postulate that the condition in our cases was due to short-lasting contact, low exposure level, and not on the body parts where almost complete absorption occurs, that is, scrotum and axilla.[10] In view of possible additional inhalation route, as the house has been sprayed, the reported history was not supportive.

Regarding potential therapies for neuropathic pain as described in this setting, we have chosen gabapentin with subsequent improvement in symptoms. In an earlier similar study in adult cases,[11] carbamazepine was successfully used. However, owing to its ability to inhibit neuronal hyperactivity along the pain pathways and less side effects, currently gabapentin, along with pregabaline, has become mainstay of treatment for various neuropathic pain syndromes and in these cases a reasonable choice.[12]

So far, only 1 study has been reported specifically related to diazinon-related family poisoning by combined inhaled and cutaneous route, however, with severe symptoms and course.[13]

One might reasonably argue whether there was another, unknown environmental toxic agent (heavy metal, drug) to induce described temporal pattern of events. Under the circumstances described, the authors stand for the answer grounded on disclosed contact and subsequent transcutaneous organophosphate absorption, carefully excluding other differentials. In conclusion, we believe that our illustrative cases can further contribute to the better awareness and understanding of variable spectrum of transcutaneous route of organophosphate poisoning.

Author Contributions

MP, DN, and AAT contributed equally to this work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Rastogi SK, Tripathi S, Ravishanker D. A study of neurologic symptoms on exposure to organophosphate pesticides in the children of agricultural workers. *Indian J Occup Environ Med*. 2010;14(2):54-57.
2. Peter JV, Sudarsan TI, Moran JL.Clinical features of organophosphate poisoning: A review of different classification systems and approaches. *Indian J Crit Care Med*. 2014;18(11): 735-745.
3. Sadaka Y, Broides A, Tzion RL, Lifshitz M. Organophosphate acetylcholine esterase inhibitor poisoning from a home-made shampoo. *J Emerg Trauma Shock*. 2011;4(3):433-434.
4. Senthilkumaran S, SathyaPrabhu K, Balamurugan N, Thirumalaikolundusubramanian P. Deadly drop–cholinergic syndrome from wearing a laundered uniform. *Pediatr Emerg Care*. 2012;28(1): 57-58.
5. Halle A, Sloas DD. Percutaneous organophosphate poisoning. *South Med J*. 1987;80(9):1179-1181.
6. Jokanovic M, Stukalov PV, Kosanovic M. Organophosphate induced delayed polyneuropathy. *Curr Drug Target CNS Neural Disord*. 2002;1(6):593-602.
7. Kumar S. Clinical characteristics of organophosphate-induced delayed polyneuropathy. *Neurol India*. 2004;52(1):128-129.
8. Bond GR, Pieche S, Sonicki Z, et al. A clinical decision aid for triage of children younger than 5 years and with organophosphate or carbamate insecticide exposure in developing countries. *Ann Emerg Med*. 2008;52(6):617-622.
9. Roach ES, Abramson JS. Lawless MR Self-injurious behavior in acquired Sensory neuropathy. *Neuropediatrics*. 1985;16(3): 159-161.
10. Maibach HI, Feldman RJ, Milby TH, Serat WF. Regional variation in percutaneous penetration in man. Pesticides. *Arch Environ Health*. 1971;23(3):208-211.
11. Vasilescu C, Alexianu M, Dan A. Delayed neuropathy after organophosphorus insecticide (Dipterex) poisoning: a clinical, electrophysiological and nerve biopsy study. *J Neurol Neurosurg Psychiatry*. 1984;47(5):543-548.
12. Bialer M. Why are antiepileptic drugs used for nonepileptic conditions? *Epilepsia*. 2012;53(suppl 7):26-33.
13. Dahlgren JG, Takhar HS, Ruffalo CA, Zwass M. Health effects of diazinon on a family. *J Toxicol Clin Toxicol*. 2004;42(5):579-591.