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Flaccid paraplegia of organophosphate-induced delayed polyneuropathy leading to early spastic paraplegia. Case report

Porażenie poprzeczne wiotkie lub wywołana organofosforanem opóźniona polineuropatia prowadząca do wczesnego porażenia poprzecznego spastycznego. Opis przypadku

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Abstract

Organophosphate insecticides have been widely used for pest control. They have been readily used as a suicidal agent in developing countries. This paper reports the case of a middle aged male patient with acute organophosphate compound poisoning who in turn had acute cholinergic crisis and was put on ventilator. Within one week, he developed flaccid areflexic paraplegia with preserved sensation. Two weeks later, he had spasticity in both lower limbs with hyperreflexia. The reported case demonstrates the myelopathic presentation of organophosphate-induced delayed polyneuropathy.

Key words: organophosphate, poisoning, flaccid, spastic, paraplegia, polyneuropathy

Streszczenie

Instektycydy fosforoorganiczne znajdują zastosowanie na całym świecie jako środki zwalczania szkodników. Z uwagi na ich łatwą dostępność często sięgają po nie samobójcy, szczególnie w krajach rozwijających się. W niniejszej publikacji przedstawiono przypadek mężczyzny w średnim wieku, u którego wskutek ostrego zatrucia związkami organofosforanowymi doszło do przełomu cholinergicznego – pacjenta trzeba było podłączyć do respiratora. W ciągu tygodnia nastąpiło porażenie poprzeczne wiotkie kończyn dolnych z arefleksją, jednak z zachowaniem czucia. Dwa tygodnie później w obu kończynach wystąpiła spastyczność z nadwrażliwością odruchową. Omawiany w niniejszej pracy przypadek stanowi opis mielopatii w związku z opóźnioną polineuropatią wywołaną organofosforanem.

Słowa kluczowe: organofosforany, zatrucie, wiotkie, spastyczne, porażenie poprzeczne, polineuropatia

INTRODUCTION

Organophosphate (OP) insecticides are used for pest control all over the world. Poisoning with organophosphates is a global problem. According to World Health Organization, one million serious poisonings occur every year with additional two million people being hospitalised as a result of suicide attempts with these pesticides (Gunnell *et al.*, 2007). As they are readily available and accessible in developing countries like India, they have been used as a suicidal agent. Persons with OP compound poisoning have initial acute cholinergic crisis followed – in some cases – by the development of organophosphate-induced delayed polyneuropaty within two to five weeks. In this paper the case of a middle-aged male patient with acute OP compound poisoning who had acute cholinergic crisis and was put on ventilator is described. Within one week, he developed flaccid areflexic paraplegia with preserved sensation. Two weeks later, he had spasticity in both lower limbs with hyperreflexia. The reported case constitutes the myelopathic presentation of organophosphate-induced delayed polyneuropathy (OPIDP).

CASE REPORT

A 40-year-old man was brought to emergency department by his close relatives as he had consumed an OP compound preparation (chlorpyrifos 50%) six hours before. He was in an altered level of consciousness and one

could smell the OP compound odour from the patient's mouth and skin. His clothes were soiled with urine and faeces. He had profuse perspiration. There was no history of seizures. Prior to the consumption of the OP compound, he did not have medical comorbidity. During the examination his pulse rate was 124/minute, the blood pressure – 138/84 mm Hg. Systemic examination showed bilateral lung coarse crepitations. Neurologically, he was stuporous, his pupils were pinpoint-sized, but fundus examination was normal. There was a flexion of all limbs to painful stimulus with mute plantar response. The possibility of cholinergic toxicity was considered. His pseudocholinesterase level was 1420 U/L (with normal being 5650–11550 U/L). He was administered gastric lavage, atropine injection, pralidoxime injection, intravenous antibiotics and other supportive medical care. Due to a low level of consciousness and aspiration he was put on mechanical ventilator. Within four days, he started regaining his consciousness by the 6th day, he was found to have weakness in both lower limbs with medical research council grading of 0/5. Both lower limbs were hypotonic with areflexia. Sensations over the limbs were preserved and there was no sensory loss. He was unable to empty his bladder and as a result – was catheterised. Within next three weeks, the lower limbs became spastic with hyperreflexia, ill-sustained ankle clonus and extensor plantar responses. Complete haemogram, renal, hepatic and thyroid function tests were normal. Serum human immunodeficiency virus and VDRL (Venereal Disease Research Laboratory) tests showed negative results. Serum total creatine phosphokinase (CPK) levels were normal (110 U/L). The magnetic resonance imaging of the whole spine was normal. Nerve conduction study showed absent compound muscle action potential in bilateral peroneal and tibial nerves. The sensory nerve conduction studies were normal. Upper limb motor nerve conduction study was normal. The patient was treated with baclofen (orally, 30 mg in three divided doses per day) and received physiotherapy. At the time of discharge, he was bed-bound and dependent on all activities of daily life.

DISCUSSION

Organophosphate poisoning is the most common poisoning in India. Following the consumption of an OP compound, patients initially develop acute toxic effects due to cholinergic crisis as a result of widespread inhibition of the acetylcholinesterase enzyme. Excessive stimulation of muscarinic receptors by acetylcholine (Ach) that escapes degradation by acetylcholinesterase enzyme causes cholinergic crisis. Intermediate syndrome appears within 24 to 96 hours (1–4 days) following the OP compound poisoning. It is characterised by the appearance of muscular weakness affecting neck flexors and proximal muscles. The exact pathogenesis is neuromuscular junction dysfunction caused by downregulation of presynaptic and postsynaptic nicotinic receptors by excessive Ach and calcium respectively. Recovery occurs within 1 to 3 weeks (Samuel *et al.*, 1995). OPIDP occurs 7–20 days after OP compound exposure. It is pure motor or predominantly motor axonopathy affecting both peripheral and central nervous system. Patients usually complain about cramps in lower limbs, numbness and paraesthesia in distal lower limbs, followed by progressive weakness, and the depression of deep tendon reflexes in the lower limbs. Patients have weakness in the form of foot drop or even wrist drop. In severe cases, they may have quadriplegia with foot and wrist drop. OPIDP is a "dying-back" neuropathy which is symmetrical and motor-predominant. Nerve biopsy shows features suggestive of an axonal degeneration with secondary demyelination. As the peripheral neuropathy improves, the involvement of corticospinal tract becomes visible in the form of spasticity and hyperreflexia (Chatterjee and Sharma, 2003; Lotti and Moretto, 2005). The postulated pathomechanism in the causation of OPIDP involves the phosphorylation and ageing of an enzyme in axons termed neuropathy target esterase (NTE) (Jokanović *et al.*, 2011). The inhibition of NTE causes axonal degeneration with the loss of myelin and macrophage accumulation in nerves leading to motor axonal neuropathy. NTE inhibitors like phosphates cause OPIDP when more than 70% of the enzyme is inhibited. The inhibitor's affinity to the enzyme as well as the chemical structure and the residue attached to the enzyme determines the inhibitor ability to cause OPIDP (Jokanovic *et al.*, 2002).

Other mechanism is the aberrant phosphorylation of cytoskeletal proteins leading to axonal instability and degeneration (Abou-Donia, 2003).

There are earlier reports of delayed neuropathy with myelopathy following an OP compound poisoning. Chuang *et al.* (2002) reported a woman with delayed neuropathy (day 17) and myelopathy (18 months) following OP compound intoxication. Nand *et al.* (2007) reported a patient with chlorpyrifos-induced delayed neuropathy with hyperreflexia of both lower limbs. Thivakaran *et al.* (2012) reported chlorpyrifos-induced pure motor neuropathy and delayed myelopathy.

CONCLUSION

Our patient had OP compound toxicity (chlorpyrifos 50%) with flaccid paraplegia developed within one week and spastic paraplegia within 3–4 weeks. This case demonstrates the myelopathic presentation of OPIDP.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

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