Delayed Neuropathy Due to Organophosphate Insecticide Injection in an Attempt to Commit Suicide

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Abstract Organophosphates (OPs) are commonly used as pesticides throughout the world. Exposures to OPs cause a significant number of poisonings and deaths every year. Organophosphate-induced delayed polyneuropathy is a sensory-motor distal axonopathy which usually occurs after exposure of certain OP insecticides. Neuropathies due to ingestion of OPs have rarely been reported in the literature. Moreover, until now, there is no report of a patient developing organophosphorus injection-induced delayed neuropathy in the literature. We report a patient with serious organophosphorus-induced delayed neuropathy due to malathion injection. The patient was a 32-year-old

female who self-injected undetermined amounts of malathion over the median nerve trace on the forearm crease in a suicide attempt which resulted in peripheral neuropathy.

Keywords Delayed neuropathy · Organophosphate injection · Treatment

Introduction

Organophosphates (OPs) are potent inhibitors of acetylcholinesterase; for that reason, poisoning by OP insecticides cause cholinergic toxicity. Exposure may occur transdermally, via the respiratory tree or from the gastrointestinal tract. The most common source of exposure is pesticide use in the agricultural industry, although cases of intentional poisoning may also occur [15].

OP intoxication occurs in three phases: first an acute syndrome with prominent neuromuscular weakness and autonomic features is observed; then, an intermediate syndrome follows the intense cholinergic crisis of OPs poisoning, depending on the severity of poisoning, its duration, and on the type of OP compound; and, finally, a delayed peripheral neuropathy comes about. Onset of the peripheral neuropathy is usually several weeks following exposure and it may be progressive and severe. The reason for this delayed effect is the phosphorylation of nervous tissue proteins resulting in Wallerian axonal degeneration [10, 12, 15, 16].

Diagnosis of organophosphate-induced neuropathy rests on recognition of an appropriate exposure in a patient with progressive motor deficit greater than sensory neuropathy. Electrodiagnostic studies demonstrate an axonal neuropathy. There are no specific features and nerve biopsy reveals axonal degeneration with secondary demyelination [10, 15].

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The clinical picture of the toxic neuropathy may be characterized by a distal paresis in the lower limbs associated with sensitive symptoms. Involvement of the central nervous system may occur. Pyramidal tract dysfunction may be observed later in the upper limbs [16].

We present a 32-year-old female patient who self-injected malathion over the median nerve trace on the forearm crease in a suicide attempt which resulted in delayed peripheral neuropathy. Four months after the injury, the patient underwent an operation in which segmental excision of the affected median nerve was performed, and the nerve was repaired with a sural nerve graft, and tendon transfers were also performed in the same session.

Case Report

A 32-year-old female patient was admitted to our hospital complaining of pain, swelling on the left arm, forearm, and hand. The patient attempted suicide by injecting undetermined amounts of a commercial formulation of malathion over the left median nerve trace on the forearm crease 2 days before.

Physical examination revealed swelling, tenderness, erythema, and warmth in 1/3 of the upper part of the left arm to the dorsum of the hand. The elbow movements were restricted due to pain. Peripheral arteries were palpable. No findings related to the systemic organophosphate toxicity were determined.

Blood count revealed elevated white blood cell counts ($24,100/\text{mm}^3$). Erythrocyte sedimentation rate was 39 mm/h. CRP was 20 mg/dl (usual value 0–1 mg/dl).

On venous USG, normal flow pattern was observed in the axillary, brachial, cephalic, basilic, ulnar, and radial veins.

On the basis of clinical and laboratory findings, a final diagnosis of cellulitis was made. Treatment with cephazolin Na 3×1 g/day, gentamicin 1×160 mg/day, Flagyl 2×500 mg/day, and acetylsalicylic acid 1×300 mg/day were started. Additionally, topical eau de Goulard applications were applied and the arm was elevated.

During the psychiatric examination, the patient reflected depressive mood characterized by crying, complaining about sleeplessness, hopelessness, and irritability. There was also loss of appetite. However, she did not report any hallucinations and suicidal attitudes. Also, no delusions were found. Her story revealed two other prior suicide attempts, in one of which she jumped off 10 years ago, and in the other attempt, which was 6 years ago, she took oral insecticide. With these findings, a final diagnosis of depression was made. Sertraline 50 mg/day and risperidone 0.5 mg/day were prescribed.

Four days after the initiation of treatment, local suppuration occurred. Following local suppuration, swelling

and tenderness of the involved sites regressed rapidly. The culture-antibiogram result was negative.

Ten days after the initiation of treatment, her symptoms waned, and the previously abnormal results on laboratory tests significantly improved.

After regression of her symptoms, she was discharged from the hospital. The patient was lost to follow-up for 2 months. Two months later, she was admitted again to our hospital with a second-degree burn injury on the pulp of the index finger, and complaint of sensory loss of thumb, index and middle finger, and inability to oppose the thumb and flex the thumb and index finger (Fig. 1). Physical examination revealed thenar atrophy, sensory loss of the median-nerve-innervated areas and motor deficit on the thumb and index finger. On the MP joint of the thumb, she was able to accomplish 30° of flexion and 30° of extension, and the active range of motion on the IP joint of the thumb was zero. On the MP joint of the index finger, she was able to accomplish 50° of flexion but extension was 0° , active range of motion on the PIP and DIP joint were zero. The active and passive range of motion in middle, ring, and small finger were within normal ranges.

Electromyography (EMG) and nerve conduction studies revealed that the patient had sensorimotor peripheral neuropathy. It also revealed loss of motor unit action potentials in mAPB and mFCR. No motor conduction velocities of the nervus medianus were detected. The left ulnar nerve sensory and motor conduction studies and needle EMG findings were within normal ranges. These findings were consistent with total axonal degeneration of the left median nerve on the elbow level.

Four months after the injury, the patient was operated under general anesthesia. The fibrotic segment of the median nerve was resected. A 10-cm-long nerve gap was repaired with three segmented sural nerve grafts. Musculus brachioradialis was transferred to the flexor pollicis longus tendon and musculus extensor carpi radialis longus to the flexor digitorum profundus tendon of the index finger.

Figure 1 Appearance of the patient's left arm on second admission. Note the second-degree burn injury on the pulp of the index finger.

Figure 2 On the lower half of the picture, the peripheral nerve was quite normal; but the upper part showed extensive fibrosis, resulted in distortion of the nerve and axonal loss (hematoxylin–eosin $\times 200$).

Histopathological examination revealed endoneurial and perineurial fibrosis and axonal loss (Figs. 2 and 3).

The patient's postoperative course was uneventful. There was evidence of nerve healing after 8 months of follow-up on the needle EMG and nerve conduction studies (Fig. 4).

Discussion

Peripheral neuropathy and polyneuropathy are terms that describe syndromes caused by diffuse lesions of peripheral nerves, and usually manifested by weakness, sensory loss, and impairment of reflexes. The diagnosis is most often based on the clinical picture and confirmed by electrodiagnostic techniques, most commonly by electromyography (EMG) and nerve conduction studies [9].

Figure 3 The same area was highlighted with Masson trichrome, intense green staining showed fibrosis (Masson trichrome $\times 200$).

Figure 4 Appearance of the patient's left arm postoperatively. Note the ability to flex the thumb and index finger.

Neuropathy may be categorized by presentation such as motor or sensory symptoms, electrodiagnostic features, and neuroanatomical location within the peripheral nerve such as demyelinating or axonal neuropathy, ion channel neuropathy, neuromuscular transmission or location such as cranial or peripheral neuropathy [1].

Toxic neuropathy refers to those presentations that are caused by drug ingestion, drug or chemical abuse, or industrial chemical exposure from the workplace or from the environment. Organophosphate-induced delayed neuropathy is an uncommon clinical condition. It occurs in association with the ingestion of great amounts of organophosphate after the stimulation of cholinergic receptor. Although acute effects of organophosphate intoxication appear to be directly related to cholinergic over-activity, the pathophysiology of the following neuropathy is less clear and is not related to

cholinesterase inhibition. OP-induced neuropathy is thought to be due to inhibition of the neuropathy target esterase (NTE) [5, 6, 10, 15].

According to the literature, most of the suicides committed through OPs take place by ingestion of the substance. Injection-type suicides are rare. Systemic toxicity is rarely reported in these cases. Although, local complications at the site of the injection such as necrosis, abscess formation, and cellulitis had been reported, delayed neuropathy has not been reported before. Our patient is the first reported case who has developed delayed neuropathy in the literature [8, 12, 16].

In our case, since other peripheral nerves are not affected, the damage observed in median nerve is considered to be caused by the local toxicity of OP. In an experimental study carried out by Lotti M et al., intra-arterial injection of diisopropyl phosphorofluoridate into only one leg of hens caused a high NTE inhibition in the sciatic nerve of the injected leg, but not in other parts of the nervous system. A unilateral neuropathy with typical histopathological lesions developed in the injected leg [2]. The history of our patient as regards nerve injection injury was not characteristic. Needle placement did not incite an immediate electric-like shock sensation down the extremity. Consequently, upon injection of the injected agent, the patient did not complain about severe radiating pain and paresthesias [4, 11, 13]. Instead, she reported a mild pain radiating around the injectional site, and not along the course of the affected nerve. So, it was concluded that neuropathy was due to local toxicity of OP and not to the injury caused by injection.

Additional treatment following acute treatment of OP poisoning is usually not needed. There is no known effective treatment of the organophosphate-induced delayed neuropathy. Only supportive and symptomatic care is available [9, 15]. Care of a patient with such a condition is carried out as in a case with a nerve lesion in continuity. According to the guidelines established for any patient with a nerve lesion in continuity, surgery is indicated for those who have not improved within 4 months [3, 7, 14]. If, as seen in our case, the subject has attempted suicide, it is advisable to prescribe antidepressant and/or antipsychotics after psychiatric examination, and to perform long psychiatric follow-up.

References

1. Brannagan TH III, Weimer LH, Latov N. Acquired neuropathies. In: Rowland LP, editor. *Merritt's neurology*. 11th ed. New York: Lippincot Williams & Wilkins; 2005. p. 748–67.
2. Caroli S, Lotti M, Masutti A. Intra-arterial injection of diisopropylfluorophosphate or phenylmethanesulphonyl fluoride produces unilateral neuropathy or protection, respectively, in hens. *Biochem Pharmacol*. 1984;33(20):3213–7. doi:10.1016/0006-2952(84)90079-0.
3. Frykman GK, Wolf A, Coyle T. An algorithm for management of peripheral nerve injuries. *Orthop Clin North Am*. 1981;12(2):239–44.
4. Gentili F, Hudson AR, Hunter D. Clinical and experimental aspects of injection injuries of peripheral nerves. *Can J Neurol Sci*. 1980;7(2):143–51.
5. Glynn P. A mechanism for organophosphate-induced delayed neuropathy. *Toxicol Lett*. 2006;162(1):94–7. doi:10.1016/j.toxlet.2005.10.012.
6. Glynn P. Axonal degeneration and neuropathy target esterase. *Arch Hig Rada Toksikol*. 2007;58(3):355–8. Review. doi:10.2478/v10004-007-0029-z.
7. Gutowski KA. Peripheral nerves and tendon transfers. In: *Hand II. Selected Readings in Plastic Surgery*; 2003;9(33). p. 1–55.
8. Hadimioğlu N, Dosemeci L, Arici G, Ramazanoglu A. Systemic organophosphate poisoning following the percutaneous injection of insecticide. Case report. *Skin Pharmacol Appl Skin Physiol*. 2002;15(3):195–9. doi:10.1159/000063548.
9. Latov N. General considerations. In: Rowland LP, editor. *Merritt's neurology*. 11th ed. New York: Lippincot Williams & Wilkins; 2005. p. 735–7.
10. Lotti M, Moretto A. Organophosphate-induced delayed polyneuropathy. *Toxicol Rev*. 2005;24(1):37–49.
11. Mackinnon SE, Hudson AR, Gentili F, Kline DG, Hunter D. Peripheral nerve injection injury with steroid agents. *Plast Reconstr Surg*. 1982;69(3):482–90. doi:10.1097/00006534-198203000-00014.
12. Moretto A, Lotti M. Poisoning by organophosphorus insecticides and sensory neuropathy. *J Neurosurg Psychiatry*. 1998;64(4):463–8.
13. Ochs G, Schenk M, Struppler A. Painful dysesthesias following peripheral nerve injury. A clinical and electrophysiological study. *Brain Res*. 1989;496(1–2):228–40. doi:10.1016/0006-8993(89)91070-6.
14. Omer GE. Timing of tendon transfers in peripheral nerve injury. *Hand Clin*. 1988;4(2):317–22. Review, May.
15. Sorenson EJ, Smith GA. Toxic neuropathy. In: Bromberg MB, Smith AG, editors. *Handbook of peripheral neuropathy*. New York: Taylor & Francis; 2005. p. 351–75. Review. doi:10.2165/00139709-200524010-00003.
16. Vasconcellos LF, Leite AC, Nascimento OJ. Organophosphate induced delayed neuropathy: case report. *Arq Neuropsiquiatr*. 2002;60(4):1003–7. doi:10.1590/S0004-282X2002000600022.