Case Report

Reversible parkinsonism: a rare presentation of dual poisoning

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Introduction

The organophosphate insecticides (OPI) are chemical substances that act by inhibiting the acetyl cholinesterase enzyme (AChE) activity. In the acute phases of organophosphate poisoning, symptoms include muscarinic actions such as miosis, hypersalivation, and nicotinic actions such as muscle weakness and fasciculations. After the initial remission of these acute cholinergic crises, there is an intermediate phase of neuropathy and muscle weakness (intermediate syndrome). Delayed polyneuropathies emerge later, and finally a phase involving the appearance of neuropsychiatric manifestations is possible. But, very rarely it may produce extrapyramidal symptoms. Cypermethrin is a class II synthetic pyrethroid pesticide and crosses the blood brain barrier and exerts neurotoxicity in the central nervous system. Cypermethrin-mediated neurotoxicity is contributed by its ability to induce free radical generation. Since oxidative stress critically contributes to the nigrostriatal dopaminergic neurodegeneration, cypermethrin could be considered as one of the most relevant pesticides, which possibly implicates in Parkinson's disease pathogenesis.

Case report

A 36-year-old female patient presented with history of headache, giddiness and nausea following brief accidental inhalation exposure of an organophosphate insecticide (OPI) compound, (cypermethrin 5% and chlorpyrifos 50%). She was treated with atropine, pralidoxime, 2 gm IV bolus followed by 500 mg/hr. infusion for 48 hrs.

On examination, she was conscious but disoriented. Vitals were stable. Pupils were bilaterally pin point. The systemic examination was normal. Her biochemical values including arterial blood gas analysis were normal. Her ECG and chest X-ray were normal. Only the serum cholinesterase level was very low (2190 IU/L); normal value being 4000 IU/L to 11000 IU/L.

From the day 8 onward, the patient rapidly developed extrapyramidal manifestations. There was rigidity and bradykinesia, mask like face with decreased blinking rate, slow saccades, broken pursuits, monotonous speech, rest tremors, and cogwheel rigidity. The deep tendon reflexes were brisk in both upper limbs. The knee and ankle jerk in the left lower limb were absent with bilateral mute plantar response. Power of all the four limbs was grade 3/5 and fasciculations were present. Pupils were persistently pin point. MRI brain was done which showed hyperintense signal in bilateral caudate nucleus, putamen and pulvinar of thalamus in T2 and FLAIR images. CSF examination showed 2 cells, all lymphocytes; protein was 392 mg/dl and sugar 84 mg/dl against a corresponding blood sugar of 103 mg/dl. CSF IgM for Japanese encephalitis was negative. Slit lamp examination for Kayser Fleischer ring was negative. EEG showed generalized slowing and there was no interictal or periodic discharge. She was treated with oral amantadine 100 mg bid and trihexyphenidyl 2 mg tid. Her condition gradually improved. Follow-up MRI brain done after 6 months did not show any abnormality.

Discussion

In organophosphate insecticide (OPI) poisoning, there is spectrum of delayed neurological manifestations like intermediate syndrome, organophosphorus induced neuropsychiatric disturbances, etc. Each one has specific features and the period of occurrence from ingestion of organophosphate compound (OPC). Intermediate syndrome (IMS) presents in 1-4 days after ingestion of OPC as weakness of proximal muscles, neck muscles, extra ocular muscles and involvement of cranial nerves. Organophosphorus induced neuropsychiatric disturbance (OPIND) manifests 2-3 weeks after ingestion of OPC as weakness of distal muscle, with or without sensory involvement[1].

Only 0.5% of organophosphate poisoning patients develop neurotoxic manifestations in the form of extrapyramidal syndromes such as parkinsonism[2]. The first report of parkinsonism following OPI exposure was in 1978 by Davis et al[3]. In 1999 Bhatt et al reported five patients with OPI-induced parkinsonism, among whom four cases occurred following inhalational exposure to OPI[1]. The phosphate-containing OPI compounds such as chlorpyriphos appear to exhibit more neurotoxicity than other compounds[4]. The exact latent period before onset of parkinsonism following OPI exposure is uncertain and varies in different reports. After an acute cholinergic crisis, patients may develop parkinsonism symptoms including rigidity, tremors, bradykinesia, and masked face. Eighty-one per cent of patients with extrapyramidal syndrome developed the symptoms within 2 weeks of their poisoning[2,4]. Seventy-seven per cent of patients with extrapyramidal symptoms recovered, and 71% of the patients recovered without anti-parkinsonian drug treatments[2,4]. The duration of extrapyramidal symptoms ranges from seven days to two months[2]. The mechanisms of extrapyramidal parkinsonism, however, remain unclear[2,5]. The excessive acetylcholine activity due to prolonged and irreversible inhibition of acetyl cholinesterase during OPI poisoning may alter the dopamine activity within the basal ganglia and substantia nigra, resulting in the exposed person exhibiting parkinsonism-like features[2,6].

One study was undertaken to investigate the effects of cypermethrin on dopamine transporter (DAT), vesicular monoamine transporter 2 (VMAT 2). Dopamine transporter (DAT) and vesicular monoamine transporter 2 (VMAT 2) regulate dopamine level in the nigrostriatal dopaminergic neurons. DAT mediates the removal of dopamine from the synapse to the intracellular space for recycling and metabolism. VMAT 2, on the other hand, transports cytoplasmic dopamine into vesicles for storage and release and protects it from oxidation. DAT or VMAT 2 dysfunctions or their abnormal expressions lead to dopamine oxidation, thereby free radical generation, one of the major causes of the nigrostriatal neurodegeneration[6,7]. Higher ratio of DAT/VMAT 2 is observed in the terminals of dopaminergic neurons in pesticide-induced PD phenotype[7]. The decreased VMAT 2 level directly reflects loss of the ability of dopaminergic neurons to protect against cypermethrin-induced neurotoxicity after prolonged exposure, as VMAT 2 is well known to protect dopaminergic neurons through vesicular sequestration of toxic metabolites[7]. The reduced VMAT 2 is not an unusual phenomenon, as it is involved in the transportation of dopamine into vesicles for storage, release and to protect from auto-oxidation. The reduced VMAT 2 could also be explained by the fact that cypermethrin reduced the level of dopamine[7].

The imaging findings in OPI-induced parkinsonism vary from normal appearance to symmetric signal changes in the basal ganglia. OPI-induced acute parkinsonism is a reversible phenomenon. There are reports of recovery from OPI-induced parkinsonism without any treatment. Treatment can be undertaken if the symptoms are prolonged and distressing. The selection of the suitable drug for the management of OPI-induced parkinsonism is also a challenging task. The drugs reported to be effective in case reports of OPI-induced parkinsonism are bromocriptine, benzhexol, amantadine, and biperidine. Levodopa was not effective in the treatment of OPI-induced parkinsonism.

Fig 1a

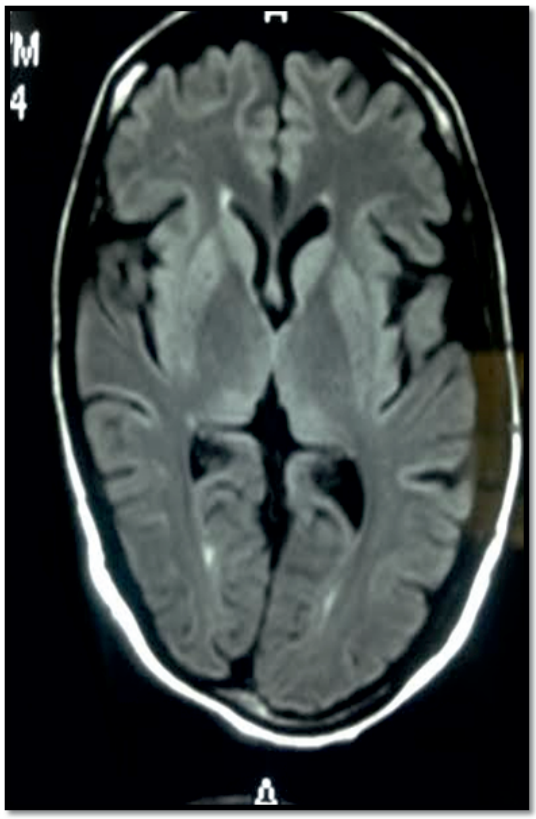

Fig 1b

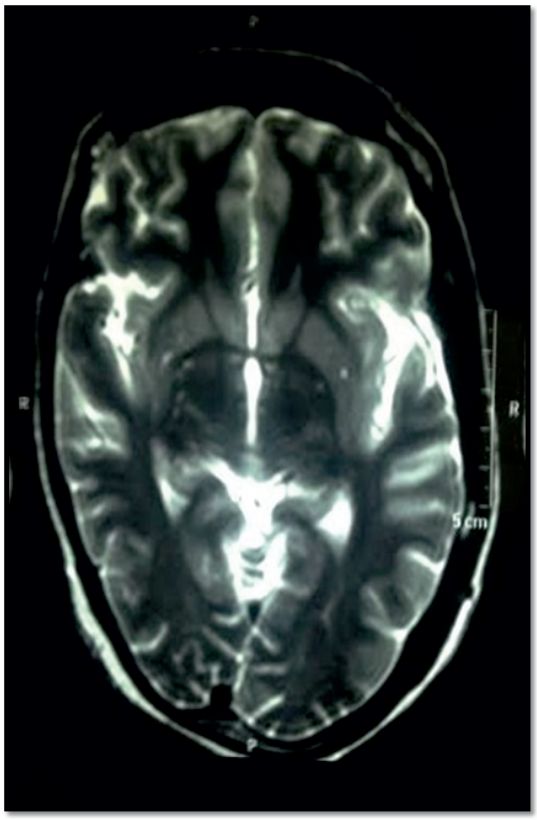

Figure 1a & 1b: MRI Brain:-T2 & FLAIR images showing a hyper intensity signal in bilateral caudate nucleus, putamen and pulvinar of thalamus

Fig 2a

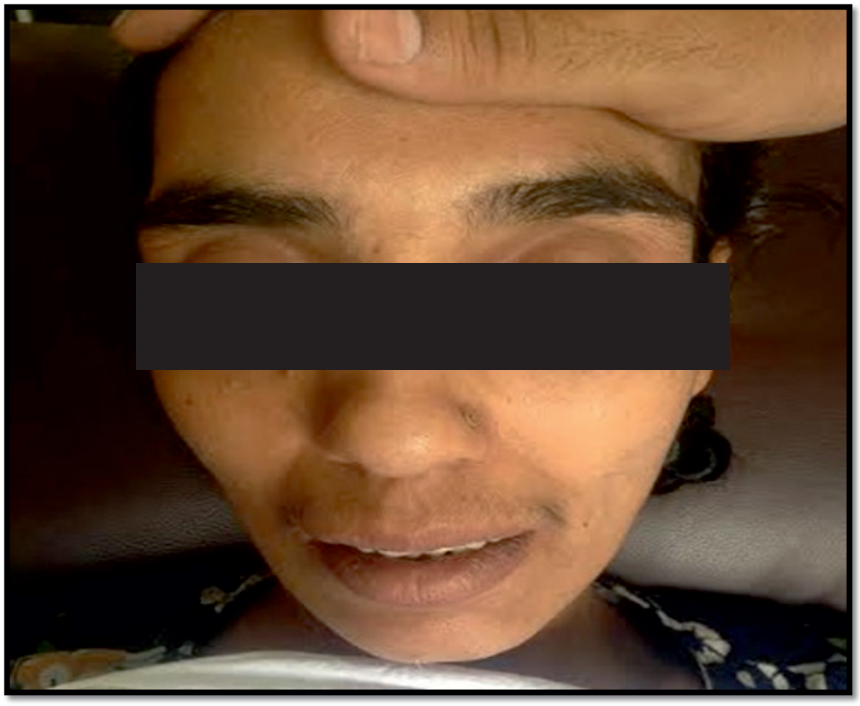

Fig 2b

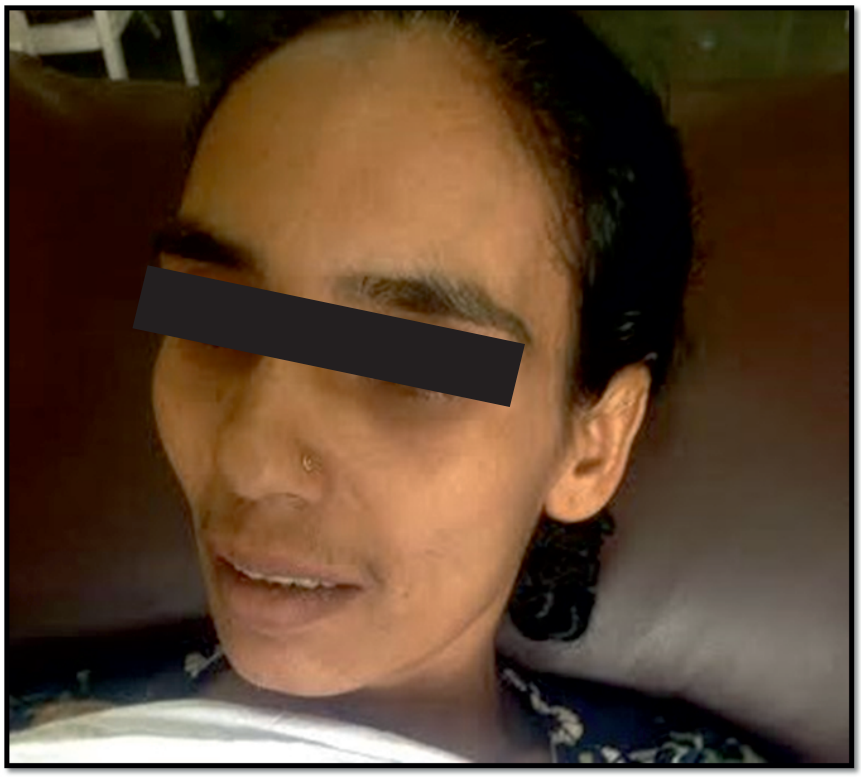

Fig 2c

Figure 2a, 2b & 2c showing mask like face

Source of support: Nil

Conflict of interest: Nil

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