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Research Paper

Surreptitious organophosphate poisoning presenting as metabolic and neurological illness - A case report and review

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ABSTRACT
In a predominantly agrarian country like India, organophosphates have been utilized as a pesticide since the twentieth century to increase food production. In recent years, due to their easy accessibility and debilitating effects on the body, their use as a suicidal poison has increased. While, organophosphates effects are highlighted in context to self-harm, they are often overlooked in view of long-term systemic side effects. We hereby, present a case report on chronic paltry amount surreptitious organophosphate poisoning that appeared as a case of metabolic and neurological illness.

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I. INTRODUCTION

Approximately 70 per cent of the rural livelihood in India depends on agriculture[1]. Since the Second World War, to feed the growing population worldwide numerous chemicals have been used to increase food production[2]. In India, chlorpyrifos (organophosphate) is the most commonly used insecticide[3]. Although, Organophosphates (OP) were listed as moderately hazardous to humans (class II) by the WHO, it accounts for 9.4% of the total insecticide usage[3]. It inhibits the action of acetylcholine esterase (AchE) enzyme[4]. AchE metabolizes acetylcholine, responsible for nerve impulse conduction. Acetylcholine acts through muscarinic and nicotinic receptors. Hence, it has acute and long-term effect on the neurological system[4]. Additionally, OP affects the glucose metabolism related pathways, lipid metabolism, heme synthesis and insulin resistance. It can be absorbed through the eyes, skin, respiratory tract and gastrointestinal tract[5].

While, organophosphates effects are highlighted in context to self-harm and suicides, they are often overlooked in view of long term systemic side effects.

II. CASE REPORT

A 40-year-old married businessman from an urban background presented to the medical emergency with complaints of incomprehensible speech, pedal oedema and pain in the legs, cellulitis of left leg, urinary-stool incontinence, black scaly skin, hair loss, inability to walk without support, immense weight gain (105 kgs), polydipsia (daily water consumption of 7-10 litres), dry eyes and lethargy. The patient had been exhibiting these symptoms for the last two years. While, since the past 7-8 months they had exacerbated to the extent of limiting his day-to-day activities. Further, his neuropsychological evaluation revealed severely impaired visuo-motor coordination, recognition, and memory.

Patient is a known case of bipolar disorder and has been on medication for the past 12 years. For the last two years he has been well maintained on Tab. Lithium carbonate 900 mg, Tab. Sodium Valproate 1700 mg, Tab. Risperidone 3 mg and Tab. Clonazepam 2 mg per day.
A thorough blood examination was done.

Table 1- Abnormalities were noted in the following parameters:

System	Test	Test value	Inference
Endocrine System	Blood glucose	582 mg% (60-100)	Uncontrolled Diabetes Mellitus
	HbA1C	12.7% (<5.7)	
Renal System	Blood urea	62 mg/dl (10 to 40)	Impaired renal function test
	Serum creatinine	1.6 mg/dl (0.50-1.00)	
Hepatic System	Ultrasound abdomen	Hepato-splenomegaly with Grade II fatty liver change	Deranged liver function
	Alkaline phosphatase	311 U/L	
Cardio-vascular System	Serum triglycerides	963 mg/dl (<150)	Dyslipidaemia
	LDL	189 mg/dl (<100)	
	Electrocardiogram	QTc	Deranged
Serum Levels	Vitamin D level	5 ng/ml (30-100)	Reduced
	Lithium level	2.15 mEq per litre (0.8 to 1.2)	Increased
	Uric acid level	7.9 mg% (3.5-7)	Hyperuricaemia

Patient was diagnosed with bipolar disorder, hypomania, diabetes mellitus type II, gout, obesity, hypothyroidism, and hypertension.

Consultation was done with various specialists: endocrinologist, nephrologist, gastroenterologist, medicine specialist, psychiatrist, neurologist, urologist, cardiologist, physical medicine and rehabilitation specialist, surgeon, and dietician. The patient was clinically stabilized.

During follow ups, his metabolic profile was controlled, weight reduced to 92.5 kgs and bipolar illness was in remission. However, he was incapable of maintaining simple conversations limited to few themes, follow simple instructions, perform activities involving multiple steps or logical reasoning and tasks like self-care and grooming. Other neurological issues that persisted included inability to concentrate and comprehend long conversations and required repetitive telling. His neuro-psychological assessments revealed moderately impaired verbal and performance IQ, severely impaired memory functions and visuo-spatial ability with an overall impression of moderate to severe cognitive deficit. These cognitive deficits limited his ability to perform tasks required for day-to-day life functioning.

Later, his son reported about surreptitious administration of a powder to the patient mixed in his meals for the past 1 year by his spouse. His blood and hair sample analysis were done to look for the presence of heavy metals and toxins.

Table 2- The report revealed high serum levels of following toxins:

Heavy metals	Test value
Strontium	77.17 µg/l (8-38)
Antimony	18.15 µg/l (0.0-18)

Table no. 3: Hair sample analysis report:

Heavy metals	Test value
Boron	1.19 (0.02-0.91)
Cobalt	0.006 (0.001-0.003)
Uranium	0.0578 (0.0170)
Barium	0.56 (0.00-0.26)
Nickel	0.11(0.000-0.002)
Strontium	0.54 (0.03-0.50)

Further legal proceedings were carried out by the family of the patient which led to the discovery of chlorpyriphos (OP) in their house.

Hence, the diagnosis was reviewed for organophosphate induced delayed onset neuropathy with diabetes and dyslipidemia. Once the administration of organophosphates was stopped there was a marked improvement seen in the metabolic parameters over 3 months, while a slow improvement was noted in the neuropathic symptoms.

III. DISCUSSION

Organophosphates are an essential measure for pest control in the agriculture and horticulture world. In India, OP like Chlorpyriphos, Parathion and Diazinon are widely used in farming. OP bind to the catalytic site of the Acetyl cholinesterase (Ach E) and irreversible inhibition of cholinesterase and pseudo cholinesterase (butyrylcholinesterase) enzymes. Hence, their exposure leads to acute cholinergic crisis and in the long term, impacts nerve conduction as well as neuro-muscular junction actions.

Because of Ach E involvement, OP affects the nicotinic receptors, muscarinic receptors and also the central nervous system. As the acetylcholine acts on the nervous system, exposure to it can lead to neurological debilitation depending on route of administration, total duration of contact and dose [(5-8)]:

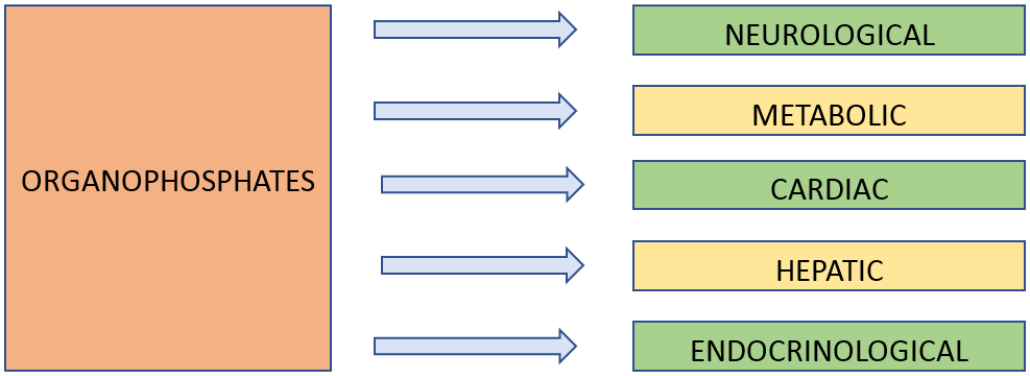
- *Acute cholinergic crisis:* Appears within a few minutes to hours of administration causing nicotinic and muscarinic effects.
- *Intermediate Syndrome:* Occurs 24–96 hours after exposure and resolves in 1–3 weeks. Involvement of the muscular system (respiratory, proximal and bulbar) is seen.
- *Organophosphate-induced delayed polyneuropathy:* OP exposure lasting for 2-4 weeks can lead to delayed neuropathy. Inhibition of neuronal esterase leads to distal muscle paresis, ataxia and cognitive disturbances. The recovery might take weeks to months after removing the offending agent[7].

Apart from causing neurological deficits, OP can also lead to hepatic dysfunction, defects in metabolic pathway, abnormal vitamin D3 metabolism, genotoxicity, and embryological teratogenicity.

Table 4- Organophosphate induced neuropsychiatric effects reported in various studies include:

Study	Neuropsychiatric effects reported
Peter JV, Sudarsan TI, Moran JL. Clinical features of organophosphate poisoning: A review of different classification systems and approaches.[9]	Impaired memory Confusion Irritability Lethargy Psychoses
Singh S et al : Neurological syndromes following organophosphate poisoning.[10]	Drowsiness Confusion Lethargy Anxiety Depression Fatigue Irritability
Levin HS et al: Anxiety associated with exposure to organophosphate compounds.[11]	Anxiety
Behan PD et al: Chronic fatigue syndrome as a delayed reaction to low dose organophosphate exposure.[12]	Chronic fatigue syndrome

Figure 1- Organophosphates can involve the following body systems:



Howell et al. (2016) has described the effect of OP exposure on lipid and glucose pathways. In-vitro study models in rat have shown, chlorpyrifos affects the hepatic metabolism and leads to impaired glucogenesis and gluconeogenesis. Additionally, raised intracellular lipid and triglyceride accumulation (de novo lipogenesis) was demonstrated[13].

In 2007, Vosough-Ghanbari et al., reported the effects of in-vivo exposure of malathion on islets of Langerhans cells in rats[14]. Increase in insulin, glucagon and C-peptides was observed. Insulin resistance and increased risk of diabetes was also inferred through this study.

Similarly, in our index case, the marked metabolic and neurological imbalance noted after the slow exposure of surreptitious OP was noted.

IV. CONCLUSION

Organophosphates are often associated with debilitating effects on human life in the context of suicide. Although, long-term systemic effects should also be considered in chronic cases which may present as metabolic or neurological illnesses that need extensive evaluation and management.

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CONFLICT OF INTEREST
None.
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