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ORGANOPHOSPHATE POISONING PRESENTING WITH DELAYED CHOLINERGIC CRISIS AND INTERMEDIATE SYNDROME-A CASE REPORT

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ABSTRACT

Organophosphate poisoning for suicidal intent is common in Indian rural areas. Hence, it is important for the caregivers to be able to manage such cases accurately in order to prevent complications. The patient reported here is a 22 years old male who ingested organophosphate insecticide, Monocrotophos, leading to cholinergic crisis with Intermediate syndrome manifested as respiratory depression evidenced by weakness of respiratory muscles and neck flexors, tachypnea and continuous drop in oxygen saturation in spite of appropriate intervention. This case report highlights that patients with severe organophosphate poisoning presenting with delayed cholinergic manifestations can have simultaneous occurrence of Intermediate syndrome. This report also aims to alert physicians that early diagnosis and prompt treatment is key to managing such difficult cases in spite atypical presentation and limited resources. Therefore, it is our recommendation that health care providers should be aware of such presentation, complications and their manifestations to facilitate effective management.

Introduction:

Acute organophosphate poisoning is a significant cause of morbidity and mortality in developing countries including India. Although no exact estimates are available from India, hospital based studies suggest that it is the commonest poisoning in India with nearly half of the cases requiring hospital admission. Most of these poisonings are usually with a suicidal intent [(1)(2)(3)(4)]. According to WHO, one million serious accidental and two million suicidal poisonings due to insecticides occur worldwide, every year, of which 200,000 die and most of these deaths occur in developing countries[(5)].

The Toxic effects of organophosphate insecticide poisoning can manifest three different phases namely:

- Acute cholinergic crisis: It is a medical emergency and can last from 24 hours to 72 hours. It occurs as a result of accumulation of acetylcholine at muscarinic and nicotinic sites. The excess acetylcholine at these receptors leads to their initial stimulation with subsequent exhaustion. At muscarinic sites it leads to increased salivation, sweating, tearing, bronchorrhea, bronchospasm. Increased gastrointestinal motility results in vomiting and diarrhea. Miosis and blurred vision are typical ophthalmic features. At nicotinic sites it results in muscle fasciculation and flaccid paralysis. CNS manifestations include headache, giddiness, drowsiness, and coma. Death can occur as a result of respiratory failure, which may be central, peripheral or both or following fatal cardiac arrhythmias.
- Intermediate syndrome (IMS): Develops12 hours to 96 hours post-exposure due to prolonged action of acetylcholine on nicotinic receptors. Intermediate syndrome has been found to be associated more with certain OP compounds, like diazinon, dimethoate, ethyl parathion, fenthion, methyl parathion, methamidaphos and monocrotophos. Clinical Features includes inability to lift neck (pathognomic), inability to sit up, ophthalmoparesis, facial weakness, swallowing difficulty, limb weakness (proximal >distal) and areflexia.
- OP-induced delayed neuropathy (OPIDN): Typically observed with Triorthocresyl phosphate (TOCP) and Tricresyl phosphate (TCP) but can develop with other compounds too. It is a pure motor axonal neuropathy with wrist and foot drop. It is probably due to depression of neuropathy target esterase in the nervous system.

Case Report:

The patient was admitted to Deben Mahato Sadar Hospital, Purulia for five weeks and discharged with improved status. The details of clinical manifestations are as described:

A Twenty two years old male patient from Purulia town ingested unquantifiable amounts of Monocrotophos in an attempt to commit suicide on 12th December 2017. This act of poison consumption was unnoticed by the family members as patient did not develop any noticeable symptoms. After two days, patient developed profuse diarrhea with multiple episodes of vomiting along with shortness of breath for which he was brought to Emergency room of Deben Mahato Sadar Hospital, Purulia on 14th December 2017.

On physical examination his Blood Pressure was 80/60 mmHg, Pulse Rate was 70/min, Respiratory Rate was 15/min, Temperature was 37.9°C and Oxygen Saturation was 30% but eventually was 80% with 6lts/min flow of oxygen through nasal prongs. He had decreased breath sounds with few rhonchi all over chest, pupils were bilaterally constricted and not reacting to light. Patient was unable to lift neck and had paradoxical abdominal muscles movement. Glasgow Coma Scale (GCS) was 3/15. He was shifted to critical care unit with assessment of severe organophosphorous poisoning with acute cholinergic crisis and Intermediate syndrome with presumptive diagnosis of Type II Respiratory Failure.

On Investigation Hemoglobin was 11.8 gm/dl, white blood cell count was 17,900/dl (DC:Nuetrophils-91, Lymphocytes-6, Eosinophils-3, Basophils-0, Monocytes-0), Hematocrit was 31%, Platelet count 178,000/dl, Erythrocyte Sedimentation rate 15/hr Random Blood Sugar 80mg/dl, Bleeding time 2min 35sec, Clotting time 3min 50sec and ECG showed prolonged Q-Tc interval (51ms). However, Arterial blood gas values, Liver and Renal function tests and Serum Electrolytes were in normal range. Patient was started with 2mg atropine (IV bolus) stat followed by 2mg every 10 minutes till signs of atropinization was achieved. Thereafter, an infusion of 3mg of atropine in 0.9% normal saline was started per hour. He was later intubated and put on ventilatory support due to failure to maintain oxygen saturation. Bedside surgical tracheostomy was performed after 4 days of intubation in view of requirement of prolonged mechanical ventilation. Meanwhile, patient developed Generalized Tonic Clonic seizure on day 10 while still on ventilatory support. He was started on midazolam, but later shifted to dexmedetomidine owing to further respiratory depression caused by midazolam.

Treatment administered includes:

• Antidotes:	Loading Dose	Maintenance Dose	Duration
Atropine	6mg	3mg with 0.9% normal saline (@ 0.06mg/kg/hr)	8 days
Pralidoxime	1.8 gm. (@30mg/kg)	500mg/hr. (@8-10mg/kg)	3 days

- **Antibiotics:**
- Inj. Meropenam 1gm 8 hourly
- Inj. Levofloxacin 500mg once daily
- Ulcer Prophylaxis: Inj. Pantoprazole 40mg 12 hourly

- **Sedation:**
- Inj. Midazolam 40mg @ 4ml/hr (discontinued after 2 days)
- Inj. Dexmedetomidine 100mg @ 5ml/hr.

- **Supportive:**
- Nutrition: Ryle's Tube feeding was started after 96hrs.
- Thrombo-Embolic prophylaxis with thrombo-elastic stocking.
- Glycemic control: monitoring of capillary blood glucose thrice daily with target of 140-180 mg/dl.
- Urine output hourly charting.
- Suction of Endotracheal tube every 2 hours.
- Inj. Metoclopramide 10 mg 8 hourly after starting of RT feed.

Subsequently Atropine and Pralidoxime were spaced and discontinued. Antibiotics were given for four weeks in order to treat ventilator associated pneumonia. Dexmedetomidine was continued for about 10 days and then stopped after improvement of seizure. Finally, at the end of fifth week he was discharged after thorough psychiatric evaluation and counseling.

Discussion:

First termed by Wadia et al [6] in 1974 as 'Type II paralysis' and characterized by respiratory muscle paralysis following the acute cholinergic phase. This terminology was later altered by Senanayake and Karalliedde [7] in 1987 to 'Intermediate Syndrome' as it arises between the period of early cholinergic syndrome and the late onset peripheral neuropathy. It is estimated 20-60% of those patients with organophosphophate poisoning will develop intermediate syndrome [8] [9]. In the case reported here, majority of complications described in literatures were observed [10][11][12][13]. The knowledge of risk of intermediate syndrome is important for patient management, because those who have apparently recovered from the acute cholinergic toxicity may later suffer from acute respiratory failure 3-4 days later. Therefore, close monitoring and observation is required during this period [14].However, one of the rare and noteworthy finding of this case was simultaneous onset of cholinergic symptoms and respiratory paralysis making it difficult to diagnose and treat. Some authors beleive that the syndrome only occurs after severe cases of acute toxicity [15][16][17] but Khan et al. (2001) found that the syndrome occurred in 22% of those with mild poisoning and 17% of those with moderate poisoning [18]. One of the challenging situations in our case was development of central nervous system manifestations i.e. seizure after 10 days. Such delayed manifestations are reported to occur due to aging of Acetylcholinesterase enzyme, poor rephosphorylation and decreased synthesis of new enzymes. Seizures were managed by midazolam, which further accentuated respiratory depression, thus hampering recovery. As a result, midazolam was replaced by dexmedetomidine after 2 days. Data from India suggests IMS as the main cause of morbidity and mortality from organophosphate poisoning [18]. The effect of intermediate syndrome may last for 2–18 days [11][12][13]. However, in this case it took more than 25 days for complete resolution. This may be attributed to delayed onset cholinergic symptoms leading to delayed hospitalization. In Intermediate Syndrome, characteristically, muscles of the neck, proximal limb, and the eyes, bulbar and respiratory groups are affected. In our patient respiratory muscle groups were affected leading to respiratory failure but other group of muscles were not affected. Another problem encountered by us was lack of confirmatory tests like RBC cholinesterase level, making it difficult to plan the treatment i.e. titration of antidotes. Dose of antidotes were titrated based of clinical evaluation of patient. Besides this, prolonged mechanical ventilation lead to complication i.e. Ventilator associated pneumonia, which marred the recovery. However, appropriate antibiotic cover along with supportive management helped us combat this obstacle.

In conclusion, from this case report we would like to highlight that patients with severe organophosphate poisoning can present with delayed cholinergic manifestations with simultaneous occurrence of Intermediate syndrome. Also, this kind of presentation may need large dosage of atropine administration and thorough evaluation of clinical features to titrate the dose and discontinue it. This case report is an example that early diagnosis and prompt treatment is key to manage such difficult cases in spite atypical presentation and limited resources. Therefore, it is our recommendation that health care providers should be aware of such presentation and their manifestations as well as its complications in order to facilitate effective management.

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