Organophosphate Compound Poisoning – An Unusual Presentation as Guillain Barre Syndrome

Sir,

Organophosphate (OP) poisoning can present with a variety of clinical manifestations in a time-bound fashion. It can present acutely (acute toxicity related to cholinergic activity), subacutely (intermediate syndrome [IMS]), or delayed (OP-induced delayed neuropathy [OPIND][1] or chronic OP-induced neuropsychiatric disorder [COPIND]).[1,2] Acute or subacute presentation of OP poisoning in the form of Guillain Barre syndrome (GBS) is rarely described in the literature.[3-5] The proposed mechanisms of OP-induced GBS involve phosphorylation of myelin and axon of the peripheral nerve;[4] however, the exact mechanism is not known. In this case, we present an extremely rare trigger of GBS due to OP poisoning.

A 39-year-old female was admitted in the emergency department (ED) at 06:00 PM on March 8, 2023 in a private hospital as she had ingested 50 ml OP substance (phenthoate 50% Emulsified concentrate (EC)) in the form of fertilized liquid at nearly 05:15 PM at her house. The patient presented with complaints of excessive salivation, tearing, vomiting, diarrhea, and agitated behavior and one episode of seizure. Immediately on arrival in ED, the patient was treated with gastric lavage (after 1 h), atropine, oxime, and levetiracetam. The patient required immediate intubation and mechanical ventilation for respiratory distress, and she was referred to New Civil Hospital, Surat (NCH), for further management. In the intensive care unit (ICU) at NCH, examination revealed conscious but disoriented patient with bilateral wheeze and crepitation on respiratory examination, without focal neurologic deficits. Investigations revealed low levels of serum cholinesterase (3000 U/L), which continued to be low for the next 2 days (3200 and 2800 U/L) and then started rising gradually. Other investigations including Complete Blood Count (CBC), Liver Function Test (LFT), Renal Function Test (RFT), Thyroid Function Test (TFT), electrolytes, urinalysis, X-ray chest, Arterial Blood Gas Analysis (ABG), ECG, 2D Echo, and Pro-B-type Natriuretic Peptide (ProBNP) (to rule out heart failure) were in normal limits. Patient was treated with atropine and oxime for 5 days, levetiracetam, and supportive treatment. The patient gradually improved, was extubated on March 17, 2023 and was shifted to general ward, where she was able to eat, speak, and walk unaided. However, in the next 2–3 days, the patient developed new weakness of bilateral lower and then upper limbs and, subsequently, dysarthria and dysphagia without any twitching or cramps in muscles. At this point, the patient was fully conscious, cooperative, and well oriented to time, place, and person. Examination revealed lower motor neuron (LMN) bulbar palsy, hypotonia, and grade 2 power in all four extremities, with absent deep tendon reflexes and planters. Sensory system was intact. No fasciculation was noticed. The patient was again intubated for new respiratory distress and was shifted to ICU. Presumptive diagnosis of OPIND along with all other differential diagnoses for acute flaccid paralysis were considered. However, nerve conduction study (NCS) showed pure motor axonal polyradiculoneuropathy affecting all four limbs [see supplementary files], while cerebrospinal fluid (CSF) analysis showed cytoalbuminological dissociation (cells 5/mm^3, protein 264 mg%). History, clinical examination, and relevant investigations suggested diagnosis of GBS (Acute Motor

Axonal Polyneuroradiculopathy (AMAN) variant). The patient was treated with five cycles of plasmapheresis on alternate days. She improved slowly over the next 15 days, in form that respiratory distress, dysarthria, and dysphagia improved and, she was extubated and she started taking orally. However, there is only a subtle improvement in weakness of all four limbs, and recent examination revealed power of grade 3 in all four limbs, making her unable to ambulate unaided.

Discussion

Self-poisoning with OP insecticides is a common clinical scenario.[6] OP poisoning presents with signs and symptoms consistent with cholinergic excess in acute settings with multiorgan involvement. Various neurologic manifestations have been reported in association with OP poisoning. Each complication occurs at a specific time following poisoning, which includes acute toxicity, IMS, and OPIND. Other rare neurologic manifestations of OP poisoning described in literature are COPIND, focal weakness of specific muscle groups at sites of dermal exposure, cranial nerve palsies, supranuclear gaze palsy, isolated laryngeal paralysis, diaphragmatic paralysis, ototoxicity, GBS, and sphincter involvement.[7]

Acute toxicity (type I paralysis) is characterized by weakness, fasciculations, cramps, and twitching and occurs acutely with the cholinergic symptoms, while IMS[8,9] (type II paralysis) typically occurs within 24–96 h probably due to prolonged downregulation of Ach receptors. Inadequate oxime therapy is characterized by weakness of muscles involving respiratory, proximal limbs, neck flexors, and oropharynx. With appropriate supportive treatment and mechanical ventilation, complete recovery is expected in 5–18 days.

OPIND[1] (type III paralysis) manifests as subacute distal dying-back predominantly motor axonopathy characterized by cramping muscle pain in the legs, paresthesia, and distal muscle weakness beginning 10 days to 3 weeks after the initial exposure to OP.[10] Clinical manifestations include foot drop, weakness of the intrinsic hand muscles, absent ankle jerks, and weakness of hip and knee flexors.[10] Postulated mechanisms involve phosphorylation or aging of neuropathy target esterases (NTEs), and electromyography (EMG) shows denervation patterns.[1,10]

In our case, the patient presented with predominantly proximal muscles weakness with cranial nerve involvement, and evaluation detected cytoalbuminological dissociation in CSF and polyradiculitis pattern in NCS, favoring diagnosis of GBS. Moreover, our patient responded to plasmapharesis to some extent in the form of improvement in muscle weakness, especially respiratory ones. Postulated mechanism of occurrence of GBS is that it could occur due to phosphorylation of nervous tissue protein with resulting Wallerian axonal degeneration[11] or due to inhibition of an enzyme called NTE,[12] and it is not prevented by treatment with atropine and oximes as it is not related to cholinergic excess. We propose a mechanism of GBS that it could be related to the development of ganglioside-like autoantibody following OP poisoning, which may bind to paranodal myelin, nodes of Ranvier, and neuromuscular junction, resulting in destruction of myelin protein sheathing and the axons themselves to various degrees. However, this needs to be studied further.

Various differential diagnoses were considered like acute intermittent porphyria, botulinum toxicity, poliomyelitis, human immunodeficiency virus (HIV) neuropathy, and acute myelopathy, which were ruled out based on clinical history, examination, and relevant investigations. OPIDN has been previously reported as GBS because of its rapid progression after a latent period and systemic involvement.[13] Although the current consensus is that OPIDN is distinct from GBS, in a scenario like OP poisoning, it becomes very important to distinguish between OPIND and GBS, as the latter could be a life-threatening condition if not recognized and treated timely. The distinguishing features between the two are different time of onset, group of extremity muscle (proximal vs. distal) involvement, and electrophysiology study, especially the late response (F wave), which is delayed or absent in GBS [Table 1].

Despite timely diagnosis, intervention, and rehabilitation, the patient has subtle improvement in muscle power and is barely able to ambulate unaided at 2-month follow-up, which could be due to underlying AMAN variant of GBS. However, the outcome of GBS due to OP poisoning is more often unfavorable among the cases described in literature[3,4,14] with a few exceptions,[5] which may suggest the possibility of OP poisoning-related unique etiopathogenesis.

Table 1: Distinguishing features between OPIND and GBS

Characteristics	OPIND	GBS
Time of onset	10 days to 3 weeks	10 days to 4 weeks: 26 days,[3] 14 days,[4] 2 days,[5] 10 days,[14] 12 days [our case]
Extremity muscle involved	Distal > > proximal	Proximal > distal
Lower cranial nerve involvement	Rare	Common
Respiratory muscle weakness	Rare	Common
Cytoalbuminological dissociation	Not seen	Common
NCS	Denervation potential	Prolonged or absent late response, reduced velocity or compound motor action potential
Treatment	Conservative	Intravenous immunoglobulins versus plasmapharesis

GBS=Guillain Barre syndrome, OPIND=Organophosphate-induced delayed neuropathy

Our case serves to highlight an unusual presentation of OP poisoning and an unusual trigger of GBS, consequent to a noninfectious condition in the form of OP poisoning, thereby adding to the etiological repertoire. Because of their widespread use in agricultural areas, practicing physicians must be aware of the possibility that certain OP compounds can cause delayed neurotoxicity, and hence must consider differential diagnosis of GBS of delayed onset.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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