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ORGANOPHOSPHATE INDUCED DELAYED NEUROPATHY-A CASE REPORT

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ABSTRACT Organophoshate induced delayed polyneuropathy (OPIDP) is a rare clinical condition associated with ingestion of organophosphate.

Clinically the patient presents with distal lower limb weakness mainly along with paraesthesia and other symptoms of neuropathy. Nerve conduction study shows motor axonal neuropathy.Here, we are presenting a case of 23 years old INDIAN male who presented with pain and tingling sensations in lower limbs along with bilateral upper limb and lower limb paresis with difficulty in getting up and walking. He had history of Dichlorvos based organophosphate ingestion around 45 days before.

Electrophysiological study suggestive of Severe motor axonal polyneuropathy affecting all four limbs. No central nervous system signs were present.

KEYWORDS : Organophosphate, Polyneuropathy

INTRODUCTION:-

Organophosphate induced delayed polyneuropathy is a distal axonal polyneuropathy which occurs after ingestion of certain organophosphate insecticides. The neurotoxic effects of organophosphates have been well known since the dramatic outbreak of "Ginger Jake Paralysis", which crippled as manyas 50,000 in the USA in the 1930. Since then several other epidemics have occurred in different regions such as in Sri Lanka. In this epidemic area, adolescent Tamil girls attaining menarche or women right after childbirth were affected and developed polyneuropathy between fourteen and thirty days after gingilioil ingestion, following local customs and tradition.Recovery from OPIDP is considered to be generally poor. It is possible that several other factors such as the age of the patients, the difference in the chemical structure of the organophosphate and the duration of initial intoxication in some way contribute towards a favorable outcome.

Organophosphorus poisoning could be separated in three phases
(1)acute cholinergic effects,
(2)intermediate syndrome and
(3) organophosphate-induced delayed polyneuropathy

Case Report:-

A 23 years old INDIAN male patient, in an attempt to commit suicide, took an Dichlorvos based organophosphate insecticide for which he was admitted in private hospital for treatment of acute cholinergic syndrome with symptoms consisting of abdominal pain, salivation, diarrhea and lacrimation. He was treated for 15 days at hospital requiring mechanical ventilation and discharged without any symptoms. However after 10 days of discharge he started having paraesthesia and cramping pain followed by distal weakness in both lower limbs which he ignored at first but then after around 15 days when symptoms became intolerable he was admitted to Civil hospital,Ahmedabad. At this time he was already recovering the strength while keeping a motor deficit in lower limb. The neurological examination revealed hands amyotrophy and equine gait, distal motor deficit in lower limbs (3+/5+). The deep tendon reflexes were present and symmetrical. Cranial nerves were not involved. There was no loss of temperature discrimination and nociception in distal lower limbs.

Touch, vibration and proprioception were not involved.

MRI of spine was normal without any compression or demyelination. CSF- RM was normal without albumin-cytological dissociation. NCS suggestive of absent of CMAPs in B/L Lower limbs and upper limbs except severely reduced CMAPs in B/L ulnar nerves. Normal SNAPs in all tested nerves.

Absent F- wave latency in all tested nerves. These findings were consistent with motor axonalpolyneuropathy. He was treated with Gabapentin, Nortryptiline and thiamin along with daily physiotherapy. Which resulted in a partial control of pain and paraesthesia

DISCUSSION:-

Organophosphate esters are used as insecticides, petroleum additives, modifiers of plastics, lubricants,antioxidants and flame-retardants. They may be absorbed via skin or respiratory and gastrointestinal tracts. The liposolubility allows a penetration in the central and peripheral nervous systems. The organophosphorus associated with neuropathy are tri-o-cresylphosphate (TOCP), leptophos, mipafox, chlorphos, trichlorfon, malation, paration, metriphonate and metamidophos. The most dangerous OP ester is TOCP. The clinical sequence could be divided in three steps:

Type 1 syndrome: Excessive stimulation of muscarinic receptors is responsible for intense cholinergiceffects, which are always apparent within a day of exposure, often within hours. Cholinergic symptomsinclude bradycardia, diarrhea, vomiting, fasciculation, sweating, salivation and micturition.Excessive exposure causes emotional irritability,nervousness, fatigue, diminished alertness, cognitiveimpairment, coma and convulsion. The treatment in all cases is atropine in varying doses depending on the clinical state.

Type 2 syndrome (intermediate syndrome): It follows the intense cholinergic crisis of organophosphorus poisoning and occurs in up 20%-50% of casesdepending on the severity of poisoning, its duration,and on the type of organophosphorus compound.There are no associated autoimmune phenomena.Some authors propose that poor regulation of acetylcholine receptors (AChRs) could explain the syndrome and neurophysiological findings. Other symptomsoccur usually 24 to 96 hours after the poisoning on the recovery from the cholinergic crisis. The cardinal features comprise muscular weakness, affectingpredominantly the proximal limbs muscles and neckflexors. Cranial-nerve palsies are common. Unlike the delayed

polyneuropathy, this syndrome carries death risk due to associated respiratory depression. Theclinical courses may last from 5 to 18 days.

Type III syndrome (organophosphate induced delayed Polyuneuropathy- OPIDP):

many organophosphates (OPs) may cause a distal dying back axonopathy characterized by cramping muscle pain in legs, paresthesia, and motor shortcoming beginning10 days to 3 weeks after the initial exposure. OPIDPassociated signs include foot drop, wrist drop, weakness of theintrinsic hand muscles, Weakness in hip and knee flexors etc. The course is usuallysubacute and occurs within two weeks after the initialsymptoms. The OPIDP is a predominantly motor neuropathy.After ingesting Dichlorvos, our patient presented all signs and symptoms of the three phases of intoxication by organophosphate, a fact that shows that the quantity ingested was substantial. Rarely, some OPs produce delayed neurotoxicity with the onsetof clinicalsymptoms occurring one or two weeks after the exposure. This delayed effect is the result of phosphorylation of nervous tissue protein with resulting wallerian axonal degeneration.Fisher described a patient who was exposed toOPs and had no acute manifestations of OPs toxicity but developed polyradiculitis, cranial nerve involvement, elevated cerebral spinal fluid (CSF) protein level, and electromyography (EMG) pattern characteristics of the Guillain-Barré syndrome. OPIDP is an uncommon cause of polyneuropathy (PNP).

Therefore, during investigation of the causes of peripheral neuropathy it is important to reviewthe history of exposure to toxic substances. These intoxications should also be part of the differential diagnostic of paraparesis since the participation of CNS on the intoxication by OPs only becomes evidentafter several years of exposition to OPs.The pathogenesis of OPIDN involves the phosphorylation and inhibition of neuropathy target esterase(NTE). This enzyme is present in brain, spinal cordand peripheral nerve, as well as in non-neural tissuesand cells such as spleen, muscle and lymphocytes.The function of NTE is unknown. The ability to inhibit NTE does not necessarily characterize an OP as neurotoxic because some OPs inhibit the NTE but donot produce OPIDP. The OPIDN is predominantly motor weakness appears early and initially involves legs muscles before those of the hands. Despite the paucity of sensory complaints, objective evidence of the sensory loss is almost always present. Sensitive symptoms as well as paresthesia and hyperesthesia are frequent. Proximal weakness may be present in severe cases. In the present case, despite the initial seriousness, we did not observe clinical involvement of the proximalmuscles of the four limbs. The initiation was subacute with gradual worsening, increased in the second week.Patients with severe deficits may not recover completely. There may be residual claw hand deformity,persistent atrophy, and foot drop, as well as spasticity and ataxia.The most important differential diagnosis that should be considered in OPIDP include Guillain- Barré syndrome and acute disseminated encephalomyelitis.Electrodiagnostic studies of OPIDP demonstratean axonal neuropathy with acute and chronic denervation in distal andoccasionally proximal limb muscles. Despite symptoms being predominantly motor, diminished sensory potential amplitudes appear to be more sensitive than motor conduction changes in screening for OPIDP. Motor conduction studies are either normal or minimally slowed. The CSF is usually acellular, and protein levels are either normal or slightly elevated. Consequently, this examination procedure is not relevant for diagnosis. The eletrodiagnosis examination carried out in our patient indicated axonal neuropathy, involving motor nerves with signs of denervation.The incidence of pyramidal tract dysfunction is high but the presentation is delayed. Thus, our suggestion of the term Organophosphate Induced Delayed Polyneuropathy OPIDP seems more suitable. There is no specifictreatment for OPIDP. The use of thiamin is recommended by some authors but it does not alter the appearance of OPIDP. Hyperesthesia can becontrolled with the use of amitrptyline, carbamazepine and capsaicin, associated or not. Our patientrecovered slightly from hyperesthesic pain in plantar areas. Physiotherapy is also indicated in these cases. In a study carried out by Senanayde with twenty patients, the only form of treatment was physiotherapy, mainly walking exercises from two to six weeks during the initial period in hospital. The lower motor neuron signs and sensory findingsbegan to improve and almost completely disappeared at the end of one year.It is possible that several others factors such as age of patients, the difference in the chemical structure of OPs and the duration of initial intoxication had also, in some way, contributed towards the favorable outcome. After recovering from the acute effects the patients may develop spastic paraparesis. The follow up of thesepatients should be done over at least four weeks after the acute intoxication. Recovery in most cases is incomplete. Ingestion of organophosphate, either accidentalor suicidal should be considered in cases of neuropathy, even if the initial phases of intoxication are not clinically well defined.

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