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Pulmonary Thromboembolism in Organophosphorus Poisoning – A Rare Complication

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Abstract

Organophosphate based insecticides constitute the cause of a large number of mortality and morbidity cases in the developing world. The reasons include easy availability, being inexpensive, and lack of regulations regarding their sale and storage. Another factor that has made organophosphate insecticides a major source of suicidal ingestion is the perceived fatality associated with them. Though the muscarinic, nicotinic and central nervous system complications of organophosphate poisoning are well known, the organophosphate toxidrome can sometimes present with unusual presentations and unexpected complications. In the scenario that exists wherein there are substantial number of cases, there arises the possibility that these presentations and complications will only increase in number. In this context it becomes important to know the possible mechanisms that cause unusual presentations and take adequate safeguards. In the case examined herein, a geriatric patient consumed organophosphorus insecticide. Treatment included an initial stomach wash, standard atropine therapy and supportive management. The patient experienced multiple diverse presentations related to the poisoning before eventually succumbing after 1 month. On autopsy the immediate cause of death was found to be pulmonary thromboembolism. The increased susceptibility of thromboembolism could have multiple reasons such as increased immobilization, myopathy resulting in inefficient venous return and deep vein thrombosis, or vessel damage due to inflammatory mediators. This case illustrates the need to consider pulmonary thromboembolism as a potential lethal complication of organophosphorus poisoning.

Keywords*: Organophosphorus poisoning, Pulmonary thromboembolism, heparin prophylaxis, inflammatory response*

Introduction

Among the group of chemicals used as insecticides in agriculture, organophosphates (Ops) are among the most widely used. Easy availability, being inexpensive, and lack of regulations regarding their sale and storage are some of the reasons due to which OPs are regularly used as suicidal poisons in additions to accidental, occupational and bystander exposures. The most common routes of poisoning are ingestion, absorption through the skin or by inhalation. Organophosphate poisoning mostly affects the nervous system. [(1)] Organophosphates bind irreversibly as well as covalently at the activity region of acetylcholinesterase (AChE).[(1)] Hence clinical presentation of acute organophosphorus poisoning includes symptoms of the nicotinic, muscarinic and central nervous systems. To counteract these symptoms, the treatment protocol consists of atropine, oximes (AChE reactivators) and diazepam. It has been stated that prior studies on the poisonous effects of organophosphates in non-target tissues have been limited.[(2)] The studies that were conducted however, indicate that organophosphate poisoning may induce

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oxidative stress, increase lipid peroxidation and reduce glutathione levels.[3] Due to this high oxidative stress, tissues may show a persistent inflammatory response and sustain damage leading to cellular necrosis.[4] This chronic inflammatory response due to OP poisoning can lead to endothelial injury or dysfunction which in turn can cause coagulation abnormalities and an increased risk of pulmonary thromboembolism and deep vein thrombosis.[5] This paper presents a case of pulmonary thrombosis (PT) in a patient of suicidal OP ingestion, and will list out various possible mechanisms for the same.

Case Description

A sixty-two-year-old male geriatric patient had consumed approximately two hundred millilitres of an organophosphate insecticide compound. He was taken to a primary care centre where initial first aid and stomach wash was performed. He was then transferred to a tertiary care centre where atropine infusion was started immediately. The patient then developed breathlessness, muscle weakness and hypotension. He also had an episode of a cardiac arrest but was brought back to sinus rhythm. In addition, the patient started having myoclonic movements and was treated for the same. At this juncture a diagnosis of intermediate syndrome was made as a result of organophosphorus poisoning. The patient initially succumbed one month later. Due to unremittent breathlessness and respiratory failure, the patient had to undergo a tracheostomy procedure. At the time of death, the patient was also diagnosed to have sepsis with septic shock along with broncho-pneumonia as a complication of organophosphorus poisoning. The autopsy showed atypical findings of basal ganglia haemorrhage in the brain. On histopathological examination, both lungs showed findings of pulmonary thromboembolism with the lobar pneumonia. There were however no thromboemboli present in the heart or the veins of the lower limbs. The stomach wash that was collected at the time of primary treatment tested positive for organophosphate insecticide compound whereas the other viscera and blood sent from the autopsy tested negative. The final cause of death was opined as due to pulmonary thromboembolism as a complication of organophosphorus poisoning.

Discussion

To our knowledge, this is the first documented case of pulmonary thromboembolism in a case of organophosphorus poisoning with no associated deep vein thrombosis or heart involvement. The clinical presentations of OP poisoning are classically shown as one of the following three stages: (i) Initial acute cholinergic crisis due to accumulation of acetylcholine at nicotinic and muscarinic sites and accumulation within the central nervous system resulting in altered sensorium and seizures, which present within 24-72 hours; (ii) intermediate syndrome, wherein weakness of ocular, neck, respiratory muscles and proximal limbs is seen after 24-96 hours; and (iii) delayed peripheral neuropathy that is often permanent.(6) As per Virchow's triad, the three major risk factors that primarily contribute to thrombosis are (i) hypercoagubility; (ii) turbulence or stasis (haemodynamic instability); and (iii) dysfunction of the endothelium or its injury.[7] In general, organophosphate poisoning may not be a risk factor for pulmonary thromboembolism or deep vein thrombosis per se, but chronic inflammatory conditions are associated with coagulation abnormalities and increased risk of deep vein thrombi, and pulmonary thromboembolism.[5] A recent study however showed that lipid peroxidation and increased reactive oxygen species (ROS) may be associated with OP poisoning.[8] One of the outcomes of thus high oxidative stress is an intense inflammatory response.[9] This inflammatory response may cause thrombotic tendencies leading to microvascular thrombosis as a result of inhibiting natural anticoagulant pathways and increasing procoagulant factors.[10] The properties of the endothelium may also become affected leading to loss of anticoagulant, vasodilatory and anti-aggregation properties.[10] These mechanisms may explain the causation of pulmonary thromboembolism in our patient. In addition, prolonged immobility due to hospitalization which lasted almost a month may have been an additional factor. However, lack of deep vein thrombosis points to additional factors and mechanisms. We would also like to hypothesise that muscle weakness and myopathy as a result of OP poisoning are additional risk factors for the formation of deep vein thrombi and pulmonary thromboembolism.

A Taiwanese study, which was a population-based longitudinal cohort study done nationwide on the danger of development of deep vein thrombi and pulmonary thromboembolism on patients with organophosphate poisoning, found that these patients had a 1.55-fold increased risk of deep vein thrombi when equated with the general population. A recent report has also been published of pulmonary thrombosis in acute organophosphate poisoning.[11] Another case of OP poisoning presenting with clinical features of coronary thrombosis and pulmonary thromboembolism has been reported that occurred during the delayed phase.[12] A rare case of upper extremity deep vein thrombosis in OP poisoning has also been published.[13]

Conclusion and Implications for Clinical Practice

With more studies now showing a clearer association between a chronic inflammatory state and organophosphorus poisoning, deep vein thrombosis and pulmonary thromboembolism must be considered significant complications that may arise. This is especially true in those cases that require prolonged hospitalization. In view of this, we recommend prophylactic heparin therapy for those patients that progress to the delayed phase of organophosphorus poisoning. We also suggest that in cases of OP poisoning with a presentation or development of breathless and hypoxaemia, pulmonary thromboembolism as a complication of organophosphate poisoning should be considered a differential diagnosis.

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