



Early Onset of Ventricular Tachyarrhythmias in Organophosphate Intoxication

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Millions of organophosphate poisonings are reported annually worldwide, most of them due to insecticide exposure. In addition, the potential exposure to organophosphate as a warfare agent (“nerve gas”) is a well-recognized threat in our society. Cardiac complications of organophosphate poisoning are potentially fatal, but preventable if recognized early and treated adequately. We describe a woman who sustained domestic organophosphate intoxication and was admitted with a typical clinical presentation. Yet, her electrocardiogram showed ventricular bigeminy and a normal QT interval. She was treated with atropine and obidoxime hydrochloride with marked clinical and laboratory improvement. Long QT interval and ventricular arrhythmias, which usually appear rather late in this intoxication syndrome, developed within a few hours in our patient. The rhythm disturbances were treated successfully with magnesium sulfate.

Patient Description

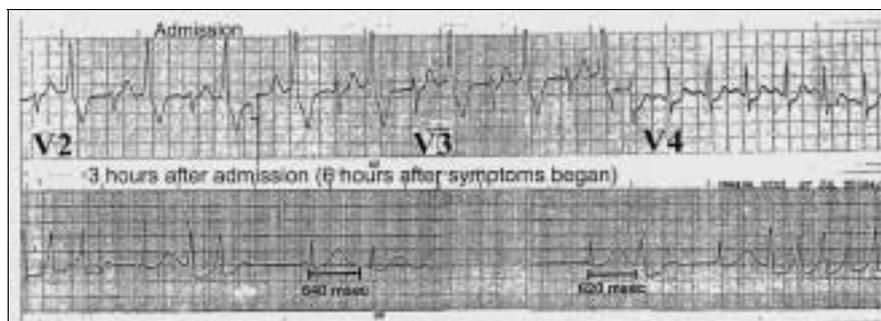
A 46 year old woman was brought to the emergency room due to altered mental

status. Three hours earlier she began to feel weak and experienced one episode of diarrhea. Her past medical history was unremarkable, and family members denied any drug use or abuse. On admission the patient was semicomatose; she was sweating profusely with marked salivation. Her clothes were wet and covered with urine and soft stools. Body temperature was 37°C and blood pressure 139/96 mmHg with a heart rate of 110 beats per minute. Pinpoint pupils were noted. Respiration was shallow with widespread crepitations heard over both lung fields. The rest of the physical examination was unrevealing.

Complete blood count showed leukocytosis (white blood cell count 17,100 cells/ μ l) with neutrophilia (12,500 cells/ μ l), blood chemistry (potassium 4.1 mEq/L, magnesium 1.8 mg/dL, phosphorus 2.5 mg/dL); urinalysis was normal. Arterial blood gas values (while breathing room air) were PO₂ 65.6 mmHg, PCO₂ 35 mmHg, HCO₃ 20.4 mEq/L, pH 7.38, saturation 92%. The electrocardiogram on admission revealed sinus rhythm, ventricular bige-

minism and normal QT interval (QTc 340 msec) [Figure, top panel].

Organophosphate intoxication was suspected. To confirm the suspicion butyryl-choline-esterase level was tested and was found to be 2.1 units/L (normal reference values 3.4–7). The patient was treated with an intravenous bolus of atropine 2 mg and a slow infusion of obidoxime hydrochloride 250 mg. The clinical response was very good and rapid. Throughout the following 13 hours the patient was treated with a total dose of 500 mg obidoxime and 10 mg atropine. Three hours after admission (6 hours after her symptoms began), and while the electrolyte levels were very similar to the admission levels and within the normal range, the following ECG changes occurred: Prolonged QT interval was detected (QTc 694 msec/QTm 640 msec), and the ECG revealed sinus rhythm with repeated episodes of non-sustained ventricular tachycardia [Figure, lower panel] with infrequent short runs of polymorphic VT. The sole manifestation of the arrhythmias was palpitation. The rhythm was converted to normal sinus rhythm with a single intravenous bolus of magnesium sulfate (2.5 g). An IV infusion of magnesium sulfate 0.25 g/hour was continued throughout the following 24 hours. Within 14 hours the BChE level recovered to a supranormal value of 14.3 units/L.



ECG = electrocardiogram
VT = ventricular tachycardia
BChE = butyryl-choline-esterase

The patient retained full consciousness and suffered only mild abdominal cramps. Her husband disclosed the fact that their next door neighbors had been using a large amount of pesticide liquid in the preceding days. Unfortunately we failed to recover the specific pesticide. The QT interval normalized on the second day of admission and the patient was discharged after 1 week of observation.

Comment

The clinical presentation of organophosphate poisoning is due to intoxication of the cholinergic system. Muscarinic effects include sweating, salivation, lacrimation, urination, diarrhea, gastrointestinal discomfort, emesis ("SLUDGE" syndrome), rhinorrhea, increased bronchial secretion, bronchoconstriction and dyspnea. Myosis is a common sign, usually accompanied by blurred vision. Nicotinic signs include muscle twitching, fasciculations, weakness, and in severe cases also paralysis. Central nervous system effects may include restlessness, tremor, confusion, convulsions, respiratory depression and coma [1].

The cardiac manifestations of organophosphate intoxication may be described in three phases: The first is a brief period (lasting only a few minutes) of hypertension and sinus tachycardia, which is considered a nicotinic effect. This is followed by a prolonged second phase, which usually begins within minutes after intoxication and may last a few hours, which is characterized by sinus bradycardia and hypotension due

to extreme parasympathetic overflow. This is usually accompanied by ST-T segment changes, atriovenous conduction disturbances of varying degrees, and bradycardia-dependent rhythm disturbances that can deteriorate to malignant ventricular arrhythmia. In the third phase one may observe QT prolongation, polymorphic VT ("torsade de pointes"), and sudden cardiac death. Although this third phase may appear shortly after the intoxication (as was the case in our patient in whom it developed 6 hours after symptoms appeared), it usually occurs 1 to 15 days following exposure to organophosphate, when the signs of clinical intoxication have already subsided [2,3]. It is possible that if the organophosphate is a chemical warfare agent, that vulnerable period may last longer. Late arrhythmias may occur even if the treatment in the acute phase was efficient. According to Ludmirsky et al. [2], a QTc of more than 580 msec (in the presence of organophosphate intoxication) denotes a high risk for sudden cardiac death.

Ventricular tachyarrhythmias are not a frequent manifestation of early organophosphate intoxication [4]. However, our patient's clinical course was unusual, as she presented (after 3 hours of symptoms) with ventricular bigeminy and a normal QT interval. To the best of our knowledge, this rhythm has not yet been reported in organophosphate intoxication. After an additional 3 hours (6 hours after the exposure) the rhythm deteriorated into ventricular tachycardia with a long QT interval. Ventricular

bigeminy creates a typical "long-short" sequence that might trigger "torsade de pointes." Emergence of ventricular bigeminy in the presence of a long QT interval is an arrhythmogenic phenomenon and should thus be diagnosed as "impending torsade" and treated accordingly (e.g., with magnesium) [5].

This case emphasizes the risk of early ventricular tachyarrhythmias even in the absence of marked cholinesterase inhibition, and the effectivity of magnesium sulfate as a useful drug in organophosphate-associated long QT syndromes.

References

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