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Coronary Artery Bypass Grafting in a Patient with Organophosphate Poisoning

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ABSTRACT

A 43-year-old male, with no previous history of mental illness, was diagnosed with coronary heart disease, after which he became acutely depressed and attempted suicide by ingesting an organophosphate pesticide. He was admitted to an intensive care unit and treated with pralidoxime, atropine, and oxygen. His coronary occlusion pattern required early coronary artery bypass grafting (CABG) surgery. His family, apprehensive of a repeat suicidal attempt, requested surgery be performed as soon as possible. He recovered well from the OP poisoning and was mentally fit to express informed consent 2 weeks after admission. Seventeen days after poisoning, he underwent coronary artery bypass grafting and recovered uneventfully. Six years later, he remains in excellent health. We report this case because to the best of our knowledge there is no literature regarding CABG performed soon after organophosphate poisoning.

INTRODUCTION

It is estimated that there are as many as one million serious unintentional poisonings worldwide each year, and an additional 2 million people hospitalized per year due to suicide attempts with pesticides. Organophosphate (OP) compounds, popular as pesticides, are readily available in agricultural countries, and ingestion of OP compounds is a popular method of suicide in such regions [Jeyaratnam 1990]. The compounds were also developed as weapons of chemical warfare.

Patients who present for CABG have multiple comorbidities. Many of them are complex and little is known about some. Literature on CABG in a patient after OP poisoning has not been published in a PubMed-indexed journal.

Intoxication with OP compounds cause nicotinic, muscarinic, and central nervous system effects. With some OPs, a delayed neurotoxicity is observed. Their mechanism of action is inhibition of acetyl cholinesterase (AChE) and butyryl cholinesterase (BuChE) enzymes, resulting in an accumulation of the neurotransmitter acetylcholine (ACh). This causes continued stimulation of ACh receptors. Overstimulation of the neuromuscular junction of motor nerves results in muscle weakness, fatigue, muscle cramps, fasciculation, and paralysis. Overstimulation of ganglionic adrenergic neurons causes tachycardia. Mediated via nicotinic receptors in the central nervous system, the patients have anxiety, headache, ataxia, tremor, convulsions, respiratory depression, haemodynamic instability, general weakness, and coma. Acting on muscarinic receptors, symptoms of visual disturbances, wheezing, increased bronchial secretions, sweating, increased salivation, lacrimation, peristalsis, and urinary incontinence may occur [Jeyaratnam 1990; Karalliedde 1999].

Patients with OP poisoning should be urgently treated with resuscitation, circulatory and ventilator support as indicated, and in addition the standard specific treatment, which consists of administering an oxime antidote (for reactivation of the inhibited AChE) and atropine (for reversal of the AChE). Patients who receive timely aggressive treatment usually recover from the acute toxicity but may suffer later from the intermediate syndrome or delayed neurological sequelae [Jeyaratnam 1990].

OP poisoning causes numerous challenges to general anaesthesia, major surgery, and post-operative care [Karalliedde 1999]. AChE inhibition can cause increased sensitivity to drugs hydrolysed by this enzyme, such as suxamethonium and mivacurium. It also causes dysfunction at the neuromuscular junction, which can produce altered responses to nondepolarizing neuromuscular blockers [Karalliedde 1999]. Changes in the neuromuscular junction can alter the response to both depolarising and non-depolarising neuromuscular blockers [Karalliedde 1999]. Drugs such as local anaesthetics and esmolol, which are hydrolysed by ChE, can have their activity prolonged [Karalliedde 1999]. Disturbed electrolyte balance (e.g., hypokalaemia), altered endocrine function (eg reduced adrenocorticotrophic hormone levels and hyperglycaemia), and disturbances in temperature regulation, immune responses, and life-threatening arrhythmias may cause major problems in managing patients postoperatively [Karalliedde 1999]. In addition, such patients may also develop pancreatitis and extrapyramidal disorders [Karalliedde 1999]. They may also exhibit changes in mental acuity, and memory and bilateral vocal cord paralysis has been reported [Karalliedde 1999]. Thus, any surgery under general anaesthesia in a patient who had OP poisoning presents unique challenges that should be considered thoroughly.

CASE REPORT

A 43-year-old known hypertensive male was investigated for exercise-induced chest pain of 3 months duration. His coronary angiogram revealed advanced triple vessel

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disease. The left anterior descending artery (LAD) was 100% occluded. The large caliber first obtuse marginal artery was 40% occluded and the terminal left circumflex artery (LCx) was 85% occluded. The right coronary artery (RCA) was 100% occluded.

When the patient was advised to have CABG surgery, he became initially depressed, later agitated, and attempted suicide by ingesting an OP pesticide. He did not have any previously known psychiatric illness and was living an active, normal life.

He was brought to a tertiary care private hospital a few hours later. He was conscious but irritable, sweaty, and had a regular pulse rate of 96/minute, blood pressure of 160/100 mmHg and a respiratory rate of 22/minute. His pupils were normal and reactive. His random blood sugar was 95 mg/dL. He was treated with atropine first as a bolus of 2.4 mg, followed by an infusion titrated to maintain the pulse rate between 80-100 beats/minute, oxygen inhalation by mask, and pralidoxime 1 g 6 hourly by slow IV bolus over 10-20 minutes. He was already on atenolol 50 mg once daily, amlodipine 5 mg once daily, and losartan 25 mg once daily. Losartan was increased to 50 mg. Ischemic heart disease was treated with aspirin, clopidogrel, and subcutaneous heparin. He also received Nicorandil 20 mg twice daily, isosorbide mononitrate 90 mg daily, and nitroglycerin 2.6 mg twice daily. He was also given alprazolam 0.5 mg bd. He was monitored in the ICU with ECG, noninvasive blood pressure, pulse rate, oxygen saturation, serial blood glucose levels, and daily AChE.

His serial AChE levels (in IU/L) were 117 on day one and three, 124 on day five and seven, 130 on day 10, and 244 on day 14 and 16.

The family strongly requested CABG during the same admission, fearing a repeat attempt at suicide. Psychiatric evaluation confirmed that the suicide bid was in response to an acute depressive state. On admission, he exhibited anxiety. At 2 weeks post admission, the patient was fully conscious, rational, and oriented with excellent cognitive function. Furthermore, after meeting patients who themselves have had CABG, the patient was more positive regarding the procedure. At an interdisciplinary meeting, it was decided to proceed with CABG, although the AChE levels had not returned to normal. After informed consent from the patient and family, CABG was performed 17 days after his suicide attempt.

The patient had off-pump coronary artery bypass (OPCAB). The left internal mammary artery was grafted to the LAD. Endarterectomy was performed on the diffusely diseased posterior descending artery (PDA). The radial artery was sequenced to the PDA and terminal circumflex artery and the proximal end was anastomosed to the ascending aorta.

Postoperatively, the patient was cared for in semi-isolation. He had an isoelectric electrocardiogram with good hemodynamics on 0.02 mcg/kg/min of noradrenaline and 0.5 mcg/kg/min of diltiazem.

The first 3 hours of drainage from his chest tubes was in excess of 100 cc/hour. The coagulation parameters were normal. Bleeding settled as the patient was warmed to 37°C.

Postoperative serial AChE levels (in IU/L) were 426 (day 19), 1046 (day 22), and 1562 (day 24).

The patient recovered well and was discharged on the 10th post-operative day, 27 days after poisoning. Two-dimensional echocardiogram showed no regional wall motion abnormality with a normal ejection fraction. His discharge medication included aspirin, low-dose warfarin, diltiazem, losartan, and atorvastatin.

Six years after CABG, the patient is free of angina, has a good exercise tolerance, is not using nitrates or antidepressants, and leads an active life with his family.

DISCUSSION

The initial cholinergic phase in OP poisoning is a medical emergency and should always be treated in an intensive care unit. OP poisoning in this patient was diagnosed on history and clinical presentation, which is usually sufficient in most cases [Aardema 2008]. He did not require ventilator or cardiovascular support and received standard treatment for OP poisoning with atropine infusion and pralidoxime. In the setting of severe ischemic heart disease, arrhythmia, tachycardia/bradycardia, and hemodynamic instability should be treated aggressively. In the presence of respiratory problems, myocardial ischemia will be aggravated and should be addressed urgently. This patient only had tachycardia and high blood pressure. He had escalation of his anti-hypertensive medication and maximum medical management of his angina. He did not exhibit chest pain, ECG changes, or elevation of cardiac biomarkers.

Although atropine is the fundamental drug in treating OP poisoning, many protocols vary regarding the starting dose, dose escalation, and duration of therapy [Aardema 2008; Good 2007]. The atropine was administered according to the standard protocol used in Sri Lankan hospitals [Fernando 2011]. This regimen, as well as WHO, recommends pralidoxime to be given by a continuous infusion of 8-10 mg/kg per hour until clinical recovery [Aardema 2008; Fernando 2011]. In less severe toxicity, it recommends 1 gram 6 hourly by slow IV bolus over 10-20 minutes [Fernando 2011]. This patient had the latter dosing.

Although still frequently used, gastric lavage and administration of activated charcoal have no proven beneficial effect [Eddleston 2004]. Neither procedure was performed on this patient.

Selective serotonin reuptake inhibitors are considered frontline drugs for depression. However, cardiac side effects seen in most of these drugs prohibited their use. Instead, alprazolam was used, as it was felt most important to relieve anxiety in this patient.

Even in healthy subjects 20-40% individual variation is seen in serum AChE levels [Karalliedde 2002]. There are numerous reasons apart from OP poisoning that may result in low AChE levels [Karalliedde 2002]. AChE estimation is a readily available, simple test and its principle role is diagnosis and screening of OP exposure [Karalliedde 2002; Worek 2005]. It has not been shown to be reliable in estimating severity or prognosis and recovery and lacks sensitivity and specificity [Karalliedde 2002; Worek 2005]. Thus CABG was performed after adequate clinical recovery without waiting for AChE levels to return to normal.

The patient was also in good mental health with comprehension of the surgical procedure, its benefits, and its complications at the time of surgery.

Although this patient did not have unstable angina, his occlusion pattern required early revascularization. Due to chronic total occlusions of two major coronary arteries, percutaneous intervention was not an option.

His good health status before, young age, speedy clinical recovery from OP poisoning, lack of other risk factors except hypertension, preserved left ventricular function, and the severe coronary occlusion pattern all favored performing early surgery. Possible complications of surgery and anesthesia after OP poisoning (described in the Introduction) were detrimental to early surgery. Total lack of literature describing similar cases was a concern. The family's demand for early surgery was mainly in fear of a repeat suicide attempt. The patient, too, was agreeable to the family's request and actively participated in all discussions.

Our practice was to perform 85% of CABG cases using the off-pump technique. We favored OPCAB in this patient, due to unknown effects of cardiopulmonary bypass (CPB) in a patient soon after OP poisoning. In the event of a conversion to CPB, we had explained to the patient and family that another unknown variable would be added to his treatment. In young patients, we routinely offer total arterial revascularization, which was performed in this instance. The radial artery was grafted to a 100%-occluded right coronary artery. There is evidence that the radial artery gives excellent results irrespective of the grafted target native vessel [Gaudino 2004; Nezic 2006].

Our experience with OPCAB endarterectomy has given good results. We perform it when we encounter a complex plaque likely to compromise anastamotic integrity. The entire surgery including the endarterectomy progressed uneventfully.

Postoperatively, the patient had increased drainage for a few hours. OPCAB patients have mild to moderate increase in bleeding until the body temperature is brought to 37°C. This patient's body temperature was 35.9°C and was warmed with a warming blanket and the bleeding settled as the patient became normothermic. Coagulation disorders are not commonly described after OP-poisoning [Karalliedde 1999; Aardema 2008]. Few case reports describe varied effects of OP poisoning on coagulation from prolonged prothrombin time to activation of coagulation [Murray 1994; Jastrzebski 1994]. This patient had a normal coagulation profile.

Intermediate syndrome starts 1-4 days after acute poisoning and complete recovery occurs within 4-18 days. Its main feature is muscle weakness including respiratory muscles and cranial nerve palsies [Karalliedde 1999]. This patient did not have any such symptoms. If one could postpone surgery until the end of this period, it may provide a more optimal postoperative respiratory function and easier weaning from mechanical ventilation.

OP causes altered immunity to infection. Depression of IgG and IgM responses, chemotaxis, and impaired natural killer cell and cytotoxic T-cell function have been demonstrated [Karalliedde 1999]. This patient had barrier nursing with semi-isolation and did not develop any postoperative infection.

Some effects of OP poisoning which could influence perioperative management were not present in this patient. These include profuse diarrhea with electrolyte abnormalities, hypokalemia and hypomagnesaemia, hypoxia, metabolic acidosis, myocarditis, hypotension, and impaired thermoregulation.

Six years after the episode, the patient is symptom-free from coronary heart disease, OP poisoning, and depression. He is leading a socially and professionally active life with his family and attending regular follow-up with his cardiologist.

Conclusion

The following statements are our thoughts on managing a patient with OP poisoning and ischemic heart disease. They are not evidenced-based, particularly in regard to CABG after OP poisoning, as this entity has not been reported on in the literature. They are a reflection on the subject after much reading, thought, exposure to this single case, and one author's extensive experience with OP poisoning:

Cardiovascular effects of OP poisoning vary from hypotension/hypertension to arrhythmias/ ECG abnormalities and cardiac arrest [Karalliedde 1999]. Immediate resuscitation in an ICU setting with optimization of heart rate/blood pressure and aggressive ventilatory management, taking into account possibilities of bronchorrhea and bronchoconstriction, is vital for these patients. Bradycardia or other arrhythmias need aggressive management. Cardiovascular and respiratory parameters together with levels of consciousness should be intensively monitored.

Administration of atropine and pralidoxime should be carried out immediately according to locally established guidelines.

Induced vomiting, gastric lavage, and administration of activated charcoal should be avoided as they are of doubtful benefit. Vomiting may lead to aspiration and compromise oxygen delivery further.

Convulsions should be controlled. In treating depression and anxiety, drugs with the best cardiovascular safety profile should be used.

Neuropsychological effects after OP poisoning include impaired memory, reduced information processing and psychomotor speed, memory deficit, linguistic disturbances, depression, anxiety, and irritability. These features may compromise informed consent and postoperative compliance. Education of the family and extreme vigilance for such symptoms are vital for management of these cases.

A decision about definitive management of cardiac ischemia has to be made early; this could be medical management, angioplasty/stenting, or CABG.

Maximal medical management of ischemic heart disease should commence as early as possible while awaiting definitive treatment, or as the sole long-term treatment option.

These patients should be nursed and managed with consideration to their increased susceptibility to bacterial and viral infections.

Coagulation may be rarely effected in these cases and should be monitored perioperatively

Timing of intervention should not be based on serum AChE. Clinical recovery should guide timing of surgery.

One should watch for intermediate syndrome. If possible, intervention should be postponed for approximately 18 days after the acute poisoning by which time effects of intermediate syndrome would have subsided.

We preferred off-pump CABG, as cardiopulmonary bypass would add yet another unknown variable. However, after successfully managing this patient, we feel that cardiopulmonary bypass can be used cautiously in a patient stabilized after the acute phase of the poisoning.

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