ACUTE PANCREATITIS AND ORGANOPHOSPHATE POISONING – A CASE REPORT AND REVIEW

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ABSTRACT

The association between acute pancreatitis and organophosphate (OP) poisoning may still not be widely recognised. A case of organophosphate (diazinon) poisoning presenting as acute pancreatitis is described. The diagnosis of OP was not made during admission to hospital as the history of exposure to OP was not obtained then. Obtaining the history of OP exposure is most important. Recognising that OP poisoning can present as acute pancreatitis may be life-saving in a critically ill patient.

Keywords: hyperamylasemia, diazinon, acute pancreatitis, organophosphate poisoning, pesticide poisoning

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INTRODUCTION

There have been a number of case reports of acute pancreatitis associated with acute organophosphate (OP) poisoning (1-4). A cause and effect relationship has been demonstrated in animal studies (5). However, this association may still not be widely recognised. Commonly used medical textbooks do not describe acute pancreatitis as one of the presenting features of OP poisoning. Nor is OP poisoning listed as one of the causes of acute pancreatitis.

OP poisoning is not uncommon given the widespread availability and use of OP insecticides. Poisoning can be occupational, accidental or suicidal. Occasionally, the history of exposure to OP compounds is not obtained. The clinical picture then can be rather confounding as illustrated in this case report. In such cases, it is important to recognise the association between acute pancreatitis and OP poisoning.

CASE REPORT

On 26 July 1983 at 7.15am in a horticultural nursery in Singapore, two Malay female gardeners were in a small store room. While changing into their work clothes, one of them (Mdm A) accidently knocked over an open bottle of diazinon (an OP). Liquid diazinon was splashed onto the clothes of the other woman (Mdm B) and the floor. Mdm A then mopped the floor with rags while Mdm B changed her clothes. Without washing themselves, they proceeded to work in the nursery.

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Mdm A who was 56 years old felt giddy and had one bout of watery stools at 10.00am while at work. On her way home she vomited twice. She was brought to Hospital 1 at noon. On arrival, she was drowsy, tachypnoeic, frothing from the mouth and cyanosed. The pulse rate was 110 per minute and the blood pressure was 140/90 mm Hg. Heart sounds were dual and regular. Coarse bilateral crepitations were detected in both lungs. Her pupils were small and reactive. She was treated for acute pulmonary oedema with intravenous lasix, aminophylline and morphine. She was intubated, put on a respirator, given 60% oxygen and transferred to the intensive care ward.

The daughter gave the history that the patient worked as a gardener but did not mention about the accidental spillage of OP. There was no past history of hypertension, diabetes mellitus or heart disease.

The Chest X-Ray was normal. The electrocardiogram recorded sinus tachycardia with no evidence of infarction. All three "cardiac enzymes" were raised. The serum glutamate oxalate transaminase (SGOT) was 45 U/L (Normal range: 15-33 U/L), serum total lactate dehydrogenase (LDH) was 616 U/L (Normal range: 180 -380 U/L) and serum creatine phosphokinase (CPK) was 187 U/L (Normal range: 35-164 U/L). A repeat was done the next day. SGOT was 81 U/L, LDH was 729 U/L and CPK was 1575 U/L.

Hyperglycaemia, hypokalaemia and leucocytosis were present on admission. The blood glucose was 240 mg/dl (13.4 mmol/L). On 29 July it was 104 mg/dl (5.8 mmol/L) and on 1 August it was 76 mg/dl (4.3 mmol/L). A glucose tolerance test done on 4 August confirmed that she was not suffering from diabetes mellitus. The serum potassium was 2.9 mmol/L (Normal range: 3.5-5.0 mmol/L). On 1 August it was 3.7 mmol/L. The white cell count was 31100 cells per uL. (Neutrophils were 81%). The next day it was 11600 cells per uL. Serum area, sodium, chloride, calcium, phosphate, haemoglobin concentration and platelet count were normal.

Meanwhile her condition had improved and she was taken off the respirator. At 6.00pm she was fully

conscious and her lungs were clear. The blood pressure and pulse rate were still raised at 150/108 mm Hg and 127 per minute respectively.

At 6.45 pm she complained of vomiting and epigastric pain. Acute pancreatitis was suspected. The serum amylase was markedly raised at 3067 U/L (Normal range: 58-328 U/L). It decreased to 1380 U/L on the next day (27 July) and to 335 U/L on 28 July. The urinary diastase was raised at 2385 U/L (Normal range: 169 – 2200 U/L). The next day (27 July) the levels increased to 12595 U/L and then decreased to 941 U/L on 28 July. She was treated as for acute pancreatitis.

On 27 July her blood pressure was 100/75 mm Hg and the pulse rate was 88 per minute. The diagnosis on discharge was acute left ventricular failure and acute pancreatitis. The history of exposure to OP compounds was not obtained. No cholinesterase (ChE) levels were done and no specific treatment for OP poisoning given.

Mdm B who was 48 years old developed nausea, vomiting, abdominal colic, diarrhoea and giddiness at about 2.00 pm. She was admitted to Hospital 2 at 6.30 pm. She gave a history of insecticide spilling onto her back that morning. She had no past history of diabetes mellitus. She was conscious and not in respiratory distress. Pulse rate was 100 per minute. Blood pressure was 130/80 mmHg. Her lungs were clear. The family brought along a label showing that the insecticide involved was diazinon. The diagnosis of OP poisoning was made and she was started on atropine treatment.

The serum ChE level was depressed. On admission it was 25 U (Normal range: 97-177U). The serum ChE levels increased gradually over the next few days: 33U (27 July), 54U (28 July), 64U (29 July) and 74U (1 Aug).

Hyperglycaemia, hypokalaemia and leucocytosis were also present on admission. Blood glucose was 339 mg/dl (19.0 mmol/L). Serum potassium was 3.1 mmol/L. The white cell count was 14200 cells/UL (Neutrophils were 76%). Two days later, the serum potassium was normal. Fasting blood glucose levels (7.00 am) done were above 140 mg/dl (7.8 mmol/L) on at least 3 occasions : 223 mg/dl (1 Aug), 178 mg/dl (2 Aug) and 187 mg/dl (4 Aug). On 1 Aug the white cell count was 8300 cells/UL. She was discharged with a diagnosis of OP poisoning and diabetes mellitus.

DISCUSSION

The diagnosis of OP poisioning

Both cases had OP poisoning. In Mdm A's case, the diagnosis was made retrospectively. Both had significant exposure to diazinon, a potent ChE inhibitor. Absorption through the intact skin is an important route of entry for such compounds (6). Both the spillage of diazinon and the attempts to mop it probably resulted in considerable skin contact and absorption. Furthermore, the workers did not take the appropriate measures to deal with the spillage, thus further enhancing absorption.

The presenting symptoms were consistent with those commonly reported for OP poisoning i.e. nausea, vomiting, diarrhoea, abdominal colic and giddiness occurring within a few hours after exposure to OP. The occurrence of frothy sputum and basal pulmonary rales in OP poisoning may lead to an erroneous diagnosis of pulmonary oedema (7). This was seen in Mdm A's case where the Chest X-Ray on admission was normal. The respiratory difficulty seen in cases of OP poisoning can be contributed by weakness of the respiratory muscles, paralysis of the respiratory centre, bronchospasm and increased bronchial secretion. Generally, the blood pressure and pulse rate are increased in the acute stage in severe poisoning (7). This was also seen in Mdm B's case.

Mdm A also presented with a clinical and biochemical picture of acute pancreatitis. It was the symptoms of abdominal pain, nausea and vomiting which led to the suspicion of the diagnosis. The markedly raised serum amylase and urinary diastase confirmed this. Other biochemical and hematological features of acute pancreatitis were also present; hyperglycaemia, leucocytosis and a raised LDH and SGOT. As mentioned earlier, acute pancreatitis can be associated with OP poisoning.

The diagnosis of OP poisoning in Mdm B's case was confirmed by significantly reduced serum ChE levels. The diagnosis in Mdm A's case was based on circumstantial evidence from its association with Mdm B's case, the history of exposure to OP and the clinical presentation.

The association of acute pancreatitis with OP poisoning

In 1979, Dressel (1) described the first case report of pancreatitis in a patient with OP poisoning. The patient, a previously healthy young woman presented with signs and symptoms of OP poisoning. She was in coma 4 on admission. However, as in Mdm A's case, the diagnosis of OP poisoning was only made later. This was because of the delay in obtaining the history that she had accidentally ingested O-ethyl-S-phenylethylphospheno dithioate. On the day of admission she had a serum amylase which was raised 20 times above the upper limit of normal. The serum amylase returned to normal levels by the 4th day.

In 1981, Moore and James (2) described another case of OP poisoning with acute pancreatitis. A 32-year old male was admitted in coma 4 and with signs and symptoms of OP poisoning. Because of the past psychiatric history, self administered OP poisoning was suspected. This was confirmed by the low serum ChE levels and the finding of an empty bottle of coumaphos in the patient's locker at his workplace. It was not clear why serum amylase estimation was carried out in this case. On admission, the serum amylase was 4 times the upper limit of normal. Twenty hours later it decreased to normal levels. Transient hyperglycaemia was also present.

Also in 1981, Dagli (3) reported a case of diazinon poisoning who developed acute pancreatitis. Following that, Dagli and Shaikh (4) studied 75 cases who were admitted to a General Hospital with a definite history of malathion ingestion. Hyperamylasemia was found in 47 cases (63%). In 10 of these cases (21%) the levels were more than twice the upper limit of normal. The highest level was more than four times the upper limit of normal. In 42 cases (89%) the levels retumed to normal within 48 hours of admission. Mild hyperglycaemia was found in 3 of the 47 cases, a slight elevation of SGOT in 2 cases and mild leucocytosis in 3 cases. CPK and LDH were not done. However, no attempt was made to correlate the severity of the poisoning with the level of serum amylase. The case reports mentioned earlier and Mdm A's case appear to be rather severe cases of OP poisoning. It would be interesting to know whether acute pancreatitis is associated only with the more severe cases of OP poisoning.

Even as early as 1971, a raised serum amylase has been observed in dogs and miniature swine fed with diazinon (8). In addition, a raised LDH, SGOT, OCT (ornethine carbamyl transferase) and alkaline phosphatase were found in some of the dogs. OCT and CPK were raised in all the swine. A raised serum amylase, LDH, CPK and SGOT were found in Mdm A's case.

Hyperamylasemia is generally believed to be caused by pancreatic injury. Takahashi studied 61 traumatic shock patients without pancreatic injury and

found hyperamylasemia in 80% of them (9). Isoenzyme studies in 19 of these patients revealed that 94% had a salivary type of hyperamylasemia. Increased permeability of the cell membrane of the salivary glands was suggested as the mechanism for traumatic hyperamylasemia. Thus hyperamylasemia may not be synonymous with acute pancreatitis.

Is the hyperamylasemia observed in OP poisoning due to a pancreatitis ? No isoenzyme studies or pancreatic biopsies have been done in the cases reported. However, experiments done on dogs (5) showed quite convincingly that pancreatitis could be produced by an intravenous infusion of secretin and diazinon. Significant increases of serum amylase and lipase were found at one, two and three hours. Light microscopy revealed acinar cell vacuolization and progressive interstitial oedema. In a control group of dogs (which received secretin only) and another group (where atropine was given prior to the secretin and diazinon), serum enzyme levels and histologic results were normal.

Pancreatic duct cannulation in another group of dogs to prevent ductal hypertension prevented hyperamylasemia and hyperlipasemia but not the acinar cell vacuolization and interstitial oedema. The authors suggested that the serum enzyme elevations were due primarily to ductal hypertension and the acinar cell pathology due primarily to cholinergic stimulation.

In 1971, long before there was any case report of acute pancreatitis in association with OP poisoning, Namba (10) had already observed transient hyperglycaemia, abnormal liver function tests and leucocytosis in patients with OP poisoning. It is likely that these abnormalities are part of the acute pancreatitis picture associated with OP poisoning.

Mdm A had all these features of acute pancreatitis. Mdm B had leucocytosis and hyperglycaemia. As the liver enzymes and serum amylase were not done, the possibility of acute pancreatitis in Mdm B's case cannot be excluded.

CONCLUSION

Based on the study by Dagli and Shaikh (4), it would appear that acute pancreatitis associated with OP poisoning is not that uncommon. As serum amylase is not routinely done in known cases of OP poisoning, any associated acute pancreatitis is often unrecognised. While it may not significantly influence the treatment or outcome of known cases of OP poisoning, the importance of recognising this association is illustrated by Mdm A's case and the case described by Dressel (1). In both cases the hyperamylasemia was detected on the day of admission but not the diagnosis of OP poisoning. No atropine or pralidoxime was given in either case. Fortunately both cases survived. Obtaining the relevant history of exposure to OP whether occupational, accidental or suicidal is still most important. Nevertheless, recognising that OP poisoning can be important differential diagnosis in a case presenting with acute pancreatitis may be life-saving in a critically ill patient.

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