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Case report

Pancreatic pseudocyst, a delayed complication of organophosphorus poisoning

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Abstract

Acute pancreatitis is a rare, but life-threatening complication of organophosphorus (OP) compounds, and generally shows a subclinical course. In this case, acute pancreatitis and the pseudocysts were diagnosed nearly two weeks post OP ingestion. Possible etiological factors for acute pancreatitis (alcohol, biliary disease, medication, and others) were excluded. Since the patient had a history of OP ingestion, we diagnosed Organophosphorus-induced acute pancreatitis. The CT images showed clearly defined pseudocysts on the pancreas. Supportive medical care and total parenteral nutrition are frequently employed treatment modalities for pancreatic pseudocysts, and we followed the same. Patient was discharged after he showed symptomatic improvement and was lost to follow up since. This case appears to be a rare incident in literature, of a patient developing acute pancreatitis with a pancreatic pseudocyst as a delayed complication of OP (dichlorvos) poisoning.

Key words: Organophosphorus poisoning, pancreatitis, toxicity

Key Messages:

1) Hyperamylasemia is common with acute OP poisoning. At admission, a baseline serum amylase and lipase should be done and the serial levels should be monitored.
2) Recurrent abdominal pain and discomfort should be evaluated for pancreatic damage.
3) Urgent imaging should be performed for any suspected case of pancreatitis.

Introduction

Any exposure to organophosphorus (OP) compounds (accidental, occupational, or voluntary) can cause acetylcholinesterase (AChE) inhibition, thereby showing features of toxicity (such as nausea, hypersalivation, blurring of vision, diaphoresis, headache, bronchorrhoea, and diarrhoea, amongst others). Following OP ingestion, the symptoms developed by a patient can vary; with SLUDGE (Salivation, Lacrimation, Urination, Defecation, Gastric cramps, Emesis) symptoms occurring within minutes to hours (acute manifestations).[1] Most commonly, OP poisoning manifests as cardiovascular, neurological, and/or respiratory symptoms; pancreatitis has been documented in 12.8% cases post OP poisoning and is not uncommon.[1] Some patients may develop delayed (24h to two weeks) or late (beyond two weeks) complications from OP poisoning.

A pancreatic pseudocyst can be defined as an encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas

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with minimal or no necrosis.[2] It has a fibrous wall and contains pancreatic enzymes, amylase, blood and debris in the fluids. It has a considerably low incidence, 0.5-1 per 1,00,000 adults per year and develops as a complication in 7-10% cases of acute pancreatitis of any cause.[3] If untreated, the complications can include rupture, haemorrhage, infections, portal hypertension, splenic complications, and biliary complications.[3] Pancreatic pseudocysts are more common in cases of chronic pancreatitis, as compared to acute pancreatitis; and, exposure to organophosphorus compounds is not a commonly considered aetiology of pancreatic pseudocysts.[4] We present a case wherein the patient developed acute pancreatitis with pancreatic pseudocyst as a delayed complication of OP poisoning.

Case Report

History and physical examination

A 29-year-old male restaurant waiter presented about 24h after an alleged history of consumption of an organophosphorus compound – dichlorvos. He was treated in the past for ileocaecal tuberculosis and received eight months of anti-tubercular drugs, about two years earlier. On presentation, he was restless and drowsy, and complained of blurred vision, abdominal pain, nausea and excessive salivation. On physical examination, he was conscious with a GCS of 10, he did not respond to verbal commands, and his vital parameters were - pulse rate: 70/min regular, blood pressure: 120/80 mmHg, respiratory rate 22/min, temperature: 38.5°C, and oxygen saturation (SpO_2) was 60% on room air indicating severe hypoxia. He had bilateral pinpoint pupils and hypersalivation. Respiratory system examination revealed bilateral coarse crackles. Other physical examination findings were normal. The patient was admitted to the intensive care unit (ICU) and initiated on mechanical ventilation.

Diagnostic Tests

On admission, there were no electrocardiographic abnormalities and his chest X-ray and ultrasonography of the abdomen and pelvis were normal. The patient's haematological and biochemical findings are summarised in Table 1.

Table 1: Table showing salient haematological and biochemical findings of the patient

Parameter	Measured value		
	Day 0	Day 11	Day 18
Haemoglobin	14.6 g/dL	9.6 g/dL	8.4 g/dL
Haematocrit	45.1%	30.2%	26.2%
White blood cell count (WBC)	16000 cells/mm^3	23100 cells/mm^3	23100 cells/mm^3
Platelet count (PLT)	378000 / mm^3	549000/ mm^3	650000/ mm^3
Prothrombin time (PT)	16.6 sec	-	-
Erythrocyte sedimentation rate (ESR)	6 mm/hr	-	142 mm/ hr
Fasting blood glucose	130 mg/dL	151 mg/dL	-
Blood urea nitrogen	15 mg/dL	24 mg/dL	-
Serum creatinine	0.8 mg/dL	0.7 g/dL	0.6 g/dL
Serum sodium	133 mmol/L	142 mmol/L	-
Serum potassium	3.4 mmol/L	4.1 mmol/L	-
Total bilirubin	0.4 mg/dL	3.8 mg/dL	2 mg/dL
Direct bilirubin	0.2 mg/dL	2 mg/dL	1.4 mg/dL
AST	43 IU/L	44 IU/L	41 IU/L
ALT	66 IU/L	69 IU/L	33 IU/L
ALP	129 IU/L	249 IU/L	206 IU/L
LDH	-	100 U/L	-
Total protein	8.8 g/dL	-	6.3 g/dL
Serum albumin	3.8 g/dL	-	2.7 g/dL
Serum globulin	4.8 g/dL	-	3.6 g/dL
Serum calcium	8 mg/dL	-	-

The patient's serum pseudo-cholinesterase (PChE) levels were tracked (Table 2), since it is one of the main prognostic indicators of severity in cases of OP poisoning.[5] PChE < 1000 U/L necessitates prolonged mechanical ventilation and vasopressor support and lengthens the ICU stay.[5] On the sixth day of admission, patient's PChE levels went above 1000 U/L, and he was weaned off ventilator support on the seventh day.

Table 2: Table showing pseudo-cholinesterase levels of patient

Day	Result (Normal range: 5300-12000 U/L)
Day 0/admission	549 U/L
Day 2	224 U/L
Day 4	716 U/L
Day 6	1456 U/L

On the 10th day of illness, after showing signs of recovery from OP poisoning, the patient complained of severe pain abdomen and was noted to have developed icterus. A repeat ultrasonography showed multiple hepatic cystic focal lesions, splenomegaly and mild ascites.

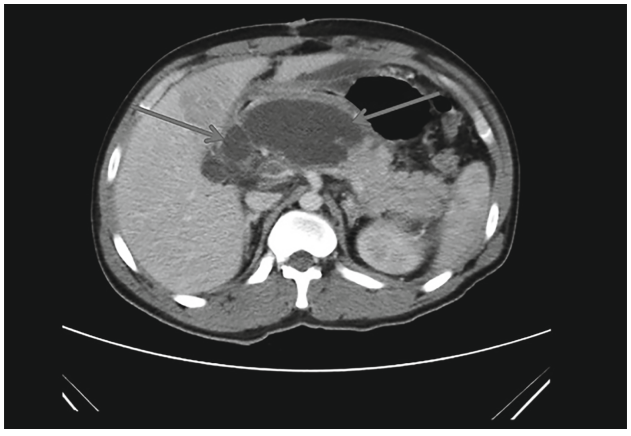

Figure 1: CT image showing large lobulated pancreatic pseudocyst

A contrast-enhanced abdominal tomography (CECT) was done, as well. The CT (Figure 1) showed the following:

- Head and body of the pancreas were replaced by a large lobulated pseudocyst with thin septations and enhancing walls which extended to the porta, gastrohepatic ligament and into the lesser sac.
- Another large pseudocyst in the left subphrenic and subhepatic regions causing scalloping of the superior surface of the left lobe of the liver.
- Thrombosis of the main portal vein and its right branch.
- Mild ascites.
- Left gross effusion with collapse consolidation of the lower lobe.
- Hepatomegaly with central intrahepatic biliary radicle dilatation (IHBRD).

His repeat blood investigations were suggestive of leucocytosis (Table 1) and serial elevation of serum amylase and lipase (Table 3, Figure 2).

Table 3: Table showing serum amylase and lipase levels of patient

Day	Serum Amylase (U/L) Normal Range: 29 -100 U/L	Serum Lipase (U/L) Normal Range: 8 - 80 U/L
0 (admission)	65	45
10 (severe pain abdomen)	310	390
19	527	722
22	624	834
24	1108	1769

Fig 2: Serum amylase and lipase levels of patient

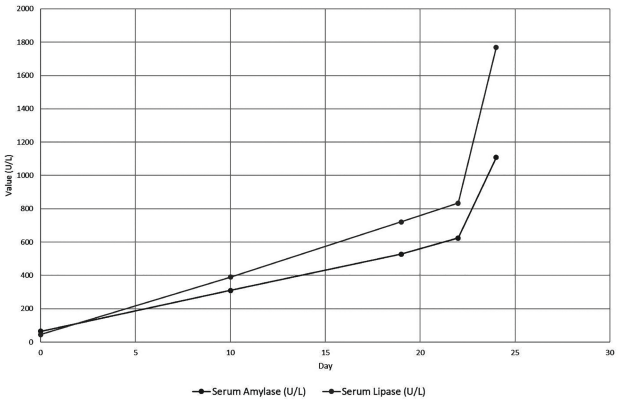

Figure 2: Serum amylase and lipase levels of patient

Diagnosis

Since the patient was known to have OP poisoning, pancreatitis was suspected; and, as a differential diagnosis, stress gastric ulcer and possible perforation of the same was also considered. Based on typical pain abdomen, grossly raised serum amylase and lipase levels, and CECT findings, the final diagnosis was acute pancreatitis, with a pancreatic pseudocyst. Our diagnosis aligns with the Atlanta Classification and Definitions[2] for pancreatitis as in table 4. Ranson's criteria at the time of diagnosis of acute pancreatitis was 1, indicating a low-risk (1%) of mortality due to pancreatitis.

Table 4: Diagnostic criteria for acute pancreatitis and pancreatic pseudocyst[2]

Acute Pancreatitis (requires two of the following three features)	(1) Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); (2) Serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and (3) Characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography.
CECT criteria for pancreatic pseudocyst	(1) Well circumscribed, usually round or oval (2) Homogeneous fluid density, (3) No non-liquid component, (4) Well defined wall; that is, completely encapsulated, (5) Maturation usually requires >4 weeks after onset of acute pancreatitis; occurs after interstitial oedematous pancreatitis

Management and Prognosis

On admission with OP poisoning, activated charcoal was administered, followed by intravenous atropine sulphate initiation, with dose incrementation till he was completely atropinised. We did not use pralidoxime as he presented 24h after alleged ingestion. He was also started on intravenous antibiotics (piperacillin & tazobactum 4.5gm Q8H and metronidazole 500 mg Q8H). The patient was provided mechanical ventilation (for 7 days), and during the course of the illness, he developed ventilator-associated pneumonia too. Furthermore, endotracheal aspirate culture showed growth of *Acinetobacter* (>10^5 CFU/ml) and *Pseudomonas aeruginosa* (2x10^4 CFU/ml), and intravenous amikacin was also added to his drug regime. On day 9, patient was shifted out of the ICU, once he recovered from the effects of OP poisoning, and prognosis appeared good.

Acute pancreatitis with pancreatic pseudocyst was diagnosed 10 days after poisoning, as described above, perhaps as a delayed complication of the poisoning. Patient was put on total parenteral nutrition along with supportive treatment (proton pump inhibitors, analgesics, fluids). His antibiotics were continued. A gastroenterology opinion was also taken. They concurred with the diagnosis and advised conservative management. A gradual reduction in thesize of pseudocyst over a period of weeks to months was expected. Surgical intervention

Table 5: Comparison of cases of acute pancreatitis with a pancreatic pseudocyst, following OP poisoning

	Present case	**Kawabe et al[10]**	**Harputluoglu et al[12]**	**Dressel et al[11]**
Age (Gender)	29 (M)	73 (M)	17 (F)	19(F)
OP compound	Dichlorvos	Unknown	DDVP EC 550, Dichlorvos	O-ethyl-S-phenylethylphospheno dithioate
Initial symptoms	Blurred vision, abdominal pain, nausea and excessive salivation	Respiratory arrest,sweating, hypersalivation,and a foulsmell onhisbreath	Blurred vision, abdominal pain, nausea and hyper-sialorrhea.	Nausea, vomiting, salivation and sweating
Amylase level on presentation	65 U/L	2000 U/L	1466 U/L	>3000 U/L
History of diabetes	No	No	No	No
History of pancreatitis (acute/ chronic/ medication induced)	No	No	No	No
History of alcohol abuse	No	No	No	No

	Present case	**Kawabe et al[10]**	**Harputluoglu et al[12]**	**Dressel et al[11]**
Treatment	Atropine sulphate; injectable antibiotics (piperacillin & tazobactum and metronidazole)	Atropine and pralidoxime	Activated charcoal treatment and 8 mg of atropine sulphate; intravenous 2 mg/day ceftriaxone	Gentamycin and penicillin
Pancreatitis	10 days after OP ingestion	Immediately after OP ingestion	Immediately after OP ingestion	Not defined
Treatment for Pnacreatitis	Proton pump inhibitors, analgesics, fluids and total parenteral nutrition	Not defined	Proton pump inhibitors, analgesic, fluids and total parenteral nutrition	Supportive treatment
Pancreatic pseudocyst	10 days after OP ingestion	4 months after OP ingestion	6 weeks after OP ingestion	9 days after OP ingestion
Treatment for pancreatic pseudocyst	Conservative management	Intravenous hyperalimentation and protease inhibitors; with 200 µg/day octreotidefor one month; Surgical cystogastrostomy after a failed endoscopic ultrasound guided pseudocyst drainage.	No invasive treatment; progress followed for 8 weeks (until when it regressed)	Drained externally

was planned, in case the pseudocyst did not resolve with conservative management.

Case Progression and Outcome

The patient showed improvement in his symptoms during the course of hospital stay and was discharged after he showed symptomatic relief and signs of recovery. He was advised follow-up, wherein repeat testing of serum amylase and lipase, and abdominal imaging was planned. However, patient was lost to follow up.

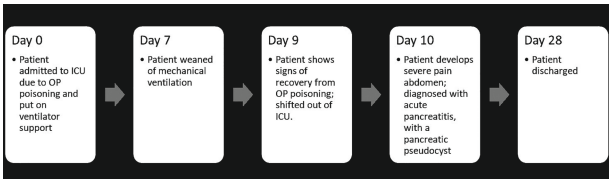

Figure 3: Timeline of events

Discussion

Development of acute pancreatitis after insecticide ingestion is an uncommon, but well-documented severe complication.[6–13] This is relatively more common with dichlorvos than other insecticides[8]. Pancreatitis in OP poisoning is a considered to be a transient manifestation since it usually follows a sub-clinical and mild course.[9,10]

While gastrointestinal symptoms generally occur early on and reverse rapidly with atropine[1], one study demonstrated the presence of OP in the gut 10 days post-ingestion.[14] Hence, we used activated charcoal to reduce any further absorption of the OP from the intestines, but avoided using pralidoxime in view of late presentation.

While pancreatic pseudocysts may resolve with supportive care and no specific treatment over a period of 4 to 6 weeks in cases of acute pancreatitis, they rarely resolve spontaneously in chronic pancreatitis, as cyst wall maturation is complete by then.[4]

Table 5 compares features of our case with other reported cases of acute pancreatitis with a pancreatic pseudocyst following OP ingestion.

The distinguishing features of this case are:

i) Development of acute pancreatitis 10 days after OP poisoning. The effect of OP on the pancreas is usually immediate and disappears in around 72 hours, even complicated cases of the same improve in 3 to 5 days.[15]
ii) Pancreatic pseudocyst was noticed at the same time as pancreatitis. After the onset of pancreatitis, it usually takes more than 4 weeks for the oedematous pancreatitis to mature and subsequent occurrence of pancreatic pseudocysts.[2] Even in pancreatic pseudocysts reported after OP poisoning, most are diagnosed

many weeks later. However, as mentioned in table 5, it has been reported to occur as early as 9 days in one of the cases.[11]

It is unlikely that our patient had a pre-existing pseudocyst, as he never had acute pancreatitis in the past, and was non-alcoholic too. Moreover, the initial ultrasound of the abdomen, on admission, was normal too. Most available medical literature describes pseudocysts in non OP poisoning situations. As the diagnosis of pancreatic pseudocysts is primarily based on CT scan of the abdomen, the presence of the pseudocyst itself is unquestionable and OP poisoning may be a special situation where pseudocysts may mature earlier than the usual 4 weeks described with other causes.

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