Necrotizing pancreatitis due to poisoning with organophosphate pesticides

G. Roeyen[1], T. Chapelle[1], P. Jorens[2], B. Op de Beeck[3], D. Ysebaert[1]

Departments of (1) Hepatobiliary, Endocrine and Transplantation Surgery ; (2) Critical Care Medicine ; (3) Radiology, University Hospital Antwerp, Edegem, Belgium.

Abstract

Several complications have been reported in relation to organophosphate poisoning. Pancreatitis due to cholinergic hypersecretion related to this type of poisoning, is however rare and has usually a subclinical course. Necrotizing pancreatitis has only been reported in 3 patients. We present a case of a young man who deliberately ingested the organophosphate dichlorvos and developed a necrotizing pancreatitis. A distal spleen and vessel preserving pancreatectomy was performed already 36 hours after ingestion. We believe that due to this very early surgery, this patient could be discharged as early as 12 days after surgery. (Acta gastroenterol. belg., **2008**, 71, **27-29**).

Key words : organophosphate, intoxication, poisoning, dichlorvos, DDVP, dichlorovinyldimethylphosphate, necrotizing pancreatitis, acute pancreatitis, pesticides, distal pancreatectomy.

Introduction

Organophosphate compounds are pesticides which irriversibly complex with acetylcholinesterase enzymes (1). The accumulation of large amounts of acetylcholine results in excessive cholinergic stimulation of several organ systems.

Cholinergic stimulation can also lead to pancreatic hypersecretion and oedema. Pancreatitis secondary to organophosphate toxicity is however rare (1,2). The course of the pancreatitis is usually subclinical. We report a case of severe necrotizing pancreatitis, in which early surgical intervention has lead to a favourable outcome. We found only 3 other case reports of necrotizing pancreatitis in the literature (1,2).

Case report

A 23-year old man was admitted to the emergency department of a peripheral hospital because of acute ingestion of an unknown amount of dichlorvos, an organophosphate pesticide, as a suicide attempt. The patient received a single dose of 1 milligram of the anticholinergic drug atropine, and was immediately transferred to our university hospital.

Three hours after ingestion, the patient presented with profuse sweating, vomiting and mild epigastric pain. There were no other signs of cholinergic stimulation. No signs of shock were present. Laboratory examination revealed a hematocrit of 48,2% (normal range : 40-50%), a serum amylase of 1100 units per liter (normal range : 24-72 units per liter), lactate dehydrogenase was 912 units per liter (normal range : 313-618 units per liter) and white blood count 25×10^9 per liter (normal range : $4.3\text{-}10 \times 10^9$ per liter). Serum cholinesterase was significantly decreased to 1330 units per liter (normal range : 5900-12220 units per liter). Ranson score was 5, predicting a mortality risk of 40% Pralidoxime, a specific antidote that effectively reverses phosphorylation of the cholinesterase, was given at a dose of 1 gram. This drug noncompetively antagonises both the peripheral muscarinic and central nervous system effects. As no overt signs of cholinergic stimulation were present, no additional doses of either pralidoxime or atropine were administered.

Six hours after ingestion, a CT-scan revealed an acute pancreatitis with patchy necrosis of the pancreatic body and tail. Balthazar computed tomography severety index was 8 (3). Fourteen hours after ingestion, the hematocrit had increased to 50,5% (normal range : 40-50%).

Thirty six hours after ingestion, high fever persisted and C-reactive protein was increased to 23,8 milligram per deciliter (normal range : < 0.5 milligram per deciliter). With exacerbation of other inflammatory signs, the patient developed a state of pancreatitis with signs of shock without evidence of an underlying infection. A control CT-scan revealed a well preserved vascularization of the pancreatic head, whereas the tail became more necrotic (Fig. 2).

The patient underwent a distal spleen and vessel preserving distal pancreatectomy. During surgery, a clear demarcation between the viable pancreatic head and the necrotic tail was seen. The area of transsection of the pancreas was secured with a stapler at the level of the neck of the pancreas.

Early postoperative recovery without any complication was achieved. The patient did not require exogenous insulin to preserve normoglycemia. Inflammatory parameters (white blood cell count and C-reactive proteine) returned to normal.

Pathological examination confirmed the necrotizing pancreatitis. Microbiological examination of peroperatively taken samples confirmed a sterile necrosis.

Correspondence to : Dr. Geert Roeyen, Department of Hepatobiliary, Endocrine and Transplantation Surgery, University Hospital Antwerp, Wilrijkstraat 10, B-2650 Edegem, Belgium. E-mail : geert.roeyen@uza.be

Submission date : 04.12.2006
Revised version : 22.10.2007
Acceptance date : 01.11.2007

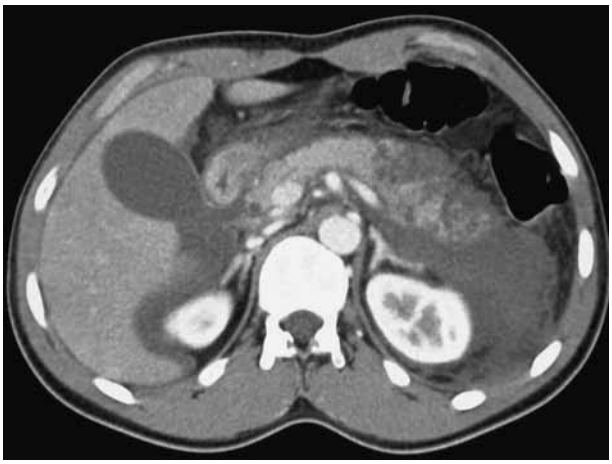

Fig. 1. — Necrotizing pancreatitis in the tail of the pancreas infiltrating the surrounding retroperitoneum.

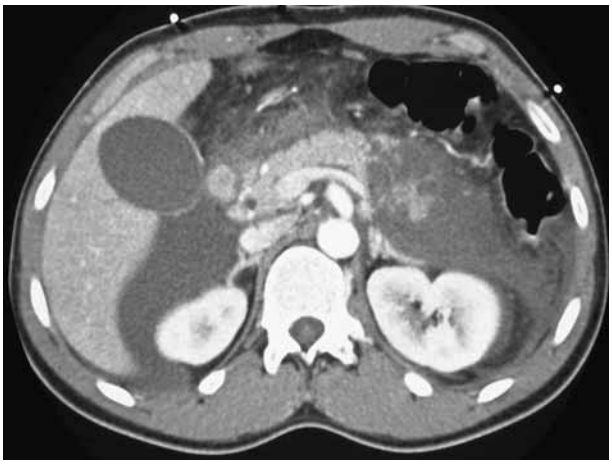

Fig. 2. — IV contrast enhanced CT-scan of the abdomen, 36 hours after ingestion of dichlorvos, showing a well preserved vascularization of the pancreatic head.

The patient could be discharged 12 days after surgery to a psychiatric ward. At follow-up 3 years after surgery, normal exocrine and endocrine pancreatic function was observed.

Discussion

Several complications have been described in the literature after ingestion of or cutaneous exposure to organophosphate pesticides, all related to cholinergic excess. Especially in the southern part of Europe where these pesticides are still currently used by greenhouse-workers, these complications may even be observed without suicide attempt (4,5).

Dichlorvos, as all other organophosphate pesticides, causes an irreversible acetylcholinesterase inhibition leading to cholinergic stimulation of many organs. Most

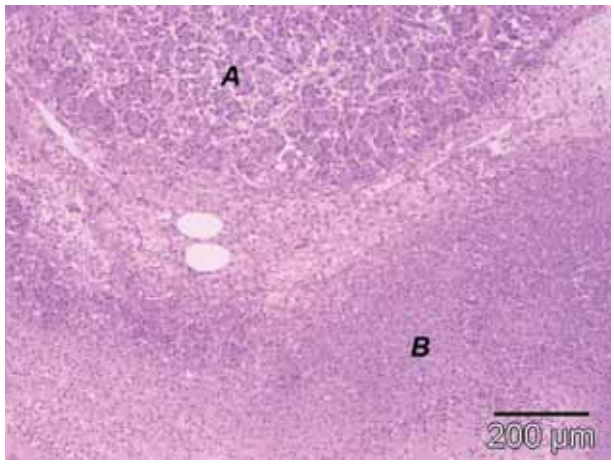

Fig. 3. — Transition zone between preserved tissue near the pancreatic head (A) and the necrotic pancreatic tail (B).

frequently reported clinical manifestations are excessive salivation and bronchial secretions (present in 83% of the patients), miosis (65%), respiratory paralysis (57%), diarrhea (13%) and abdominal pain (9%), vomiting (4%), muscular fasciculations (17%), impaired consciousness (78%) and convulsions (13%), cardiac arrythmia (78%), and fever (78%) (6). Hypertension and cardiac block have been reported. Pancreatitis is also noticed (7,8,9) but has usually a subclinical course and is extremely rarely complicated by necrosis. In the literature, only three case reports of necrotizing pancreatitis due to organophosphate poisoning have been reported (1,2).

As a consequence of this irreversible cholinesterase inhibition, cholinergic stimulation of the pancreas leads to a hypersecretion by the acinar cells and to ductular hypertension (10,11), leading to outflow obstruction and ductular oedema in dogs exposed to organophosphates. This ductal hypertension, as well as the increased pancreatic secretion secondary to cholinergic stimulation seems to be responsible fo the development of pancreatitis after organophosphate poisoning (11). Moreover, some organophosphates, which inhibit the two cholinesterase isoenzymes in the human pancreas, further increase the sensitivity of viable human pancreas fragments to acetylcholine (12).

In general, a surgical intervention is only recommended in patients with necrotizing pancreatitis when infection of the necrosis is well documented (1,2,3,4). This necrosectomy and drainage of the lesser sac, often results in a pancreatico-cutaneous fistula, because the main or secondary pancreatic ducts can not be secured properly. In patients with organophosphate poisoning however, the maximal effect of the irreversible cholinesterase binding is reached in the first 24 hours. As the pancreatic head, as opposed to the tail, remained well vascularized on CT-scan the day after admission, an early intervention with surgical closure of the pancreatic duct was considered as a therapeutic option. By

performing this necrosectomy, we tried to prevent progressive necrosis of the pancreatic head after the maximal toxicological effect, which apparently resulted in preserved exocrine and endocrine function on long term follow-up (3 years).

In the literature, it is obvious that delayed surgery does not imply an uncomplicated postoperative recovery (8). One patient, initially managed conservatively, had finally to be operated on day 44 after admission because of hemorrhagic necrosis of the pancreas and surrouding organs (stomach, duodenum and mesocolon). He died the next day due to ongoing bleeding. In the second patient, a necrosectomy was performed and a irrigation system was installed on day 13. He underwent a second surgical intervention on day 23 and could be discharged after 75 days of hospitalisation. In contrast, the patient in the third case report (9), who underwent partial pancreatectomy on the third day after ingestion, recovered succesfully and could be discharged as early as after two weeks. Although no large series are available, the latter case and our patient suggest that early necrosectomy might be considered in case of necrotizing pancreatitis after organophosphate exposure.

In conclusion, we believe that early surgical removal in our patient has lead to uncomplicated postoperative recovery from pancreatic necrosis due to organophosphate poisoning. In contrast with the common practice to only operate patients with an infected necrosis, our case report suggests that it may be unwise to delay surgical necrosectomy in patients with this very rare complication of organophosphate poisoning.

References

1. PANIERI E., KRIGE J.E., BORNMAN P.C., LINTON D.M. Severe necrotizing pancreatitis caused by organophosphate poisoning. *J. Clin. Gastroenterol.*, 1997, **25** : 463-465.
2. ZAMIR D.L., NOVIS B.N. Organophosphate poisoning and necrotizing pancreatitis. *Israel J. Med. Sci.*, 1994, **30** : 855.
3. BALTHAZAR E.J. Acute pancreatitis : assesment of severity with clinical and CT evaluation. *Radiology*, 2002, **223** : 603-613.
4. SAHIN I., ONBASI K., SAHIN H., KARAKAYA C., USTUN Y., NOYAN T. The prevalence of pancreatitis in organophosphate poisonings. *Hum. Exp. Toxicol.*, 2002, **21** : 175-177.
5. MARTIN RUBI J.C., YELAMOS RODRIGUEZ F., LAYNEZ BRETONES F., CORDOBA ESCAMEZ J., DIEZ GARCIA F., LARDELLI CLARET A., BLANCO CORONADO J.L., VINCENTE RULL J.R. Poisoning caused by organophosphate insecticides. Study of 506 cases. *Rev. Clin. Esp.*, 1996, **196** : 145-149.
6. LEE P., TAI D.Y.H. Clinical features of patients with acute organophosphate poisoning requiring intensive care. *Intensiv Care Med.*, 2001, **27** : 694-699.
7. MARSH W.H., VUKOV G.A., CONRADI E.C. Acute pancreatitis after cutaneous exposure to an organophosphate insecticide. *Am. J. Gastroenterol.*, 1998, **83** (10) : 1158-1160.
8. MOORE P.G., JAMES O.F. Acute pancreatitis induced by acute organophosphate poisoning ? *Postgrad. Med. J.*, 1981, **57** : 660-662.
9. LANKISCH P.G., MÜLLER C.H., NIEDERSTADT H., BRAND A. Painless acute pancreatitis subsequent to anticholinesterase insecticide (parathion) intoxication. *Am. J. Gastroenterol.*, 1990, **85** (7) : 872-875.
10. DRESSEL T.D., GOODALE R.L., ARNESON M.A., BORNER J.W. Pancreatitis as a complication of anticholinesterase insectide intoxication. *Ann. Surg.*, 1979, **189** : 199-204.
11. KANDALAFT K., LIU S., MANIVEL J.C., BORNER J.W., DRESSEL T.D., SUTHERLAND D.E., GOODALE R.L. Organphasphate increases the sensitivity of human exocrine pancreas to acetylcholine. *Pancreas*, 1991, **6** : 398-403.
12. GOODALE R.L., MANIVEL J.C., BORNER J.W., LIU S., JUDGE J., LI C., TANAKA T. Oraganophosphate sensitizes the human pancreas to acinar cell injury, an ultrastructural study. *Pancreas*, 1993, **8** : 171-175.
13. BUCHLER M.W., GLOOR B., MULLER C.A., FRIESS H., SEILER C.A., UHL W. Acute necrotizing pancreatitis : treatment strategy according to the status of infection. *Ann. Surg.*, 2000, **232** : 627-629.
14. BRADLEY E.L. Indications for Surgery in necrotizing pancreatitis – A millennial review . *J. Pancreas (Online)*, 2000, **1** : 1-3.