

Case report

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## Acute pancreatitis following medical abortion: Case report

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### Abstract

**Background:** Acute pancreatitis rarely complicates pregnancy. Although most pregnant women with acute pancreatitis have associated gallstones, less common causes such as drugs have been reported.

**Case presentation:** We report the case of a 34-year-old woman who underwent medical abortion with mifepristone and gemeprost and received codeine as pain-relief during the induction of abortion. She developed a severe acute necrotizing pancreatitis which required 14 days of intensive care. Other possible etiological factors, i.e. gallstone, alcohol intake and hyperlipidemia, were excluded.

**Conclusions:** The reported case of acute pancreatitis was most likely drug-induced.

### Background

Acute pancreatitis rarely complicates pregnancy. Acute pancreatitis complicated 1 in 3300 pregnancies at a large public hospital in Dallas, Texas [1], whereas in southern California 1 in 1500 women were affected [2]. Other published reports cite incidences ranging widely from 1 in 1000 to 1 in 12,000 live births [3,4]. Although most pregnant women with acute pancreatitis have associated gallstones, less common causes such as trauma, drugs, and ethanol ingestion have also been reported [5,6]. We report the case of a woman who developed severe acute necrotizing pancreatitis that required 14 days of intensive care following medical abortion.

### Case presentation

The patient was a pregnant gravida IV, para I, 34-year-old woman who due to severe malformation of the fetus underwent medical abortion. She was healthy, was not on any medication and had no known allergies. There was no history of alcohol or any other substance abuse. Previous

interrupted pregnancies had been due to miscarriages in the first trimester and on one occasion medical abortion due to a diagnosed Turner's syndrome of the fetus.

A chorion villi sample during the present pregnancy had shown a normal female chromosomal constitution. However, repeated ultrasound examinations revealed poor fetal growth and a complete lack of amniotic fluid. There was no sign of fluid leakage. Ultrasound examination at week 17 showed a cystic formation in the fetal abdomen, most likely representing a serious renal malformation not compatible with life. The patient decided to terminate pregnancy and was admitted to Uppsala University Hospital for a medical abortion. Treatment was initiated at week 18 of pregnancy with 600 mg mifepristone given orally after which the patient experienced mild gastric pain, which is commonly seen after mifepristone administration [7].

**Table 1: Blood monitoring during the 14 days of hospitalization.**

	Day 1 (day)	Day 1 (evening)	Day 2	Day 3	Day 4 (morning)	Day 4 (evening)	Day 5	Day 6	Day 8	Day 10	Day 14
B-leukocyte count (10 <sup>9</sup> /L)	21.0	16.3	18.7	19.5	17.0	17.6	14.9	13.6	-	12.3	7.4
B-hemoglobin (g/L)	115	100	86	81	80	84	82	112	115	110	125
B-platelet count (10 <sup>9</sup> /L)	269	217	208	200	226	216	249	-	-	373	-
P-CRP (mg/L)	126	147	199	329	290	210	190	173	122	75	<5
P-sodium (mmol/L)	137	-	-	-	-	-	-	136	140	141	-
P-potassium (mmol/L)	3.4	-	-	-	-	-	-	3.6	4.0	4.3	-
P-creatinine (μmol/L)	80	64	62	78	66	62	67	75	74	81	-
P-glucose (mmol/L)	-	-	-	-	-	8.3	-	-	-	-	-
P-urea (mmol/L)	-	1.6	1.8	2.1	-	-	1.4	-	-	-	-
P-cytatin C (mg/L)	-	-	-	0.80	-	-	-	-	-	-	-
GFR. calculated (ml/min)	-	-	-	100	-	-	-	-	-	-	-
P-bilirubin (μmol/L)	11	12	10	5	8	-	-	-	-	-	-
P-albumin (g/L)	-	26	21	22	22	-	-	-	29	28	-
P-triglycerides. fasting (mmol/L)	-	-	-	-	-	-	-	-	-	2.33	-
P-calcium (mmol/L)	-	-	-	-	1.75	-	-	-	-	-	-
P-LD (μkat/L)	6.5	4.7	4.3	5.5	5.7	-	-	-	-	-	-
P-ALP (μkat/L)	2.8	2.1	2.1	3.1	3.5	-	-	-	-	-	-
P-amylase (μkat/L)	23	16	11	4.1	2.4	-	2.3	3.0	-	-	-
P-ASAT (μkat/L)	0.46	0.32	0.37	0.30	0.26	-	-	-	-	-	-
P-ALAT (μkat/L)	-	-	0.12	0.25	0.11	-	-	-	-	-	-
INR	-	1.2	1.2	1.2	1.1	1.1	1.1	-	1.0	-	-
P-antithrombin (%)	-	75	64	-	65	-	30	-	-	-	-
P-APT time (s)	-	28	28	30	31	29	-	-	-	-	-
P-fibrinogen (g/L)	-	3.7	3.7	-	4.2	-	-	-	-	-	-
P-fibrin d-dimer (mg/L)	-	0.5	0.5	-	0.8	-	-	-	-	-	-

The next day, four vaginal pessaries of 1 mg gemeprost were administered every third hour. At the same time as treatment with gemeprost was initiated, she also received oral doses of a codeine 30 mg/paracetamol 500 mg combination due to her above mentioned mild gastric pain. Abortion was induced the same day and the patient underwent exeresis. The fetus exhibited skeletal malformations. However, six hours after administration of the first doses of gemeprost and of codeine/paracetamol, the patient developed severe epigastric pain. She had at this point received a total of 2 mg of gemeprost, 60 mg of codeine, and 1 g of paracetamol, apart from the 600 mg of mifepristone given the day before. Her pain was at first judged as gastritis, but omeprazole had little effect. Visual analogue scale (VAS) score was at this stage between 8 and 9 out of 10, where 10 indicates maximum subjective pain. Repeated doses of 2 mg morphine i.v., and at one occasion 5 mg ketobemidon i.m., were necessary to relieve the pain. An acute CT of the abdomen revealed a swollen pancreas as seen with pancreatitis, and plasma amylase levels were elevated (up to 23 μkat/L, reference interval 0.2–0.8 μkat/L). Although a CT scan is not optimal for imaging gallstones, there were no signs of cholelithiasis or dilated biliary ducts. The patient's pancreatitis was classified as severe acute necrotizing pancreatitis, a condition with a

high mortality rate [8,9]. When the diagnosis was made, she was immediately transferred to the intensive care unit. Her pain was later controlled through epidural anaesthetics. Results from repeated blood samples are shown in table 1. The patient was febrile and had an increased leukocyte blood count and plasma CRP as well as decreased levels of antithrombin and elevated levels of fibrinogen and fibrin d-dimer, indicating activation of the coagulation system. Apart from a decreased plasma albumin level, all liver parameters were normal. The values slowly returned towards normal during the following 14 days of intensive care. During this time, antibiotic treatment with cefuroxime and metronidazole was given. At follow up 1 month later, her plasma amylase level had not yet returned to normal (2.0 μkat/L) and was still elevated after 2 months (1.1 μkat/L).

Examination of the fetus revealed a likely Potter's syndrome with malformations of the hands and feet, poor development of the skeleton in the lower extremities, 13 ribs and a fused lumbar vertebrae. The kidneys were absent, there was a cloacal malformation, and only two vessels were seen in the umbilical cord.

Drug-induced pancreatitis is considered to be rare [10]. However, the exclusion of other possible etiological factors combined with the coincidence in time with the intake of both codeine/paracetamol and mifepristone and gemeprost make these drugs suspect as causative agents. On her previous medical abortion she received only two vaginal pessaries of 1 mg gemeprost, and no mifepristone, without complications. On this occasion, she also received a combination of codeine 30 mg/paracetamol 500 mg. These facts would point out mifepristone or possibly gemeprost as the likely causative agents. However, there have been a handful of published cases of pancreatitis complicating treatment with codeine [10-12]. A common feature of these reported cases are previous cholecystectomies [11,12]. The patient reported here had not been cholecystectomized. Also, three cases of possible codeine-precipitated pancreatitis have been reported since 1965 to the Swedish Drug Information System (SWEDIS) handling reports on suspected adverse reactions to drugs used in Sweden [13]. Codeine is known to cause rapid but transient spasm of the sphincter of Oddi [11]. Laboratory studies have shown that codeine may cause a mild, transient hyperamylasemia [11]. Pancreatitis following paracetamol overdose have been previously reported [11], but the doses taken in the present case are unlikely to have been causative. Gemeprost is a synthetic prostaglandin E1 (PGE1) analogue. Studies indicate that PGE1 is a modulator of pancreatic blood flow and protein production. For instance, PGE1 stimulated the production and secretion of alpha-amylase from minces of porcine pancreas *in vitro* [14], and enzyme output in dogs *in vivo* [15]. PGE1 further increases mesenteric and pancreatic blood flow [15]. Thus, PGE1 is not devoid of actions on the pancreas. Progesterone has also been shown to exert modulating action on the pancreas. In rats, progesterone stimulated pancreatic cell proliferation *in vivo* [16]. Progesterone receptors have also been shown to be present in human pancreatic tissue [17]. However, the effect of a progesterone receptor antagonist such as mifepristone on the pancreas has not been studied. Evidence thus exists that both PGE1 and progesterone exert modulatory action on the pancreas, but to our knowledge, no reports on pancreatitis following treatment with gemeprost or mifepristone have been published.

It is worth noting that a small number of pregnant women with acute pancreatitis have an associated hyperlipidemia, usually hypertriglyceridemia. In the reported case, the p-triglyceride level 10 days after diagnosis was elevated to 2.33 mmol/L (about 75 mg/dl). However, mild to moderate hyperlipidemia may be secondary to acute pancreatitis [18], and it is generally believed that a triglyceride level of >1,000 mg/dl is needed to precipitate an episode of acute pancreatitis [19]. Furthermore, a follow-up measurement of p-triglycerides six months later was 1.22 mmol/L.

## Conclusions

In conclusion, due to the coincidence in time and exclusion of other possible etiological factors such as cholelithiasis, alcohol and hyperlipidemia, the reported case of severe acute necrotizing pancreatitis was most likely drug-induced. Since codeine, although uncommonly, has previously been reported to precipitate pancreatitis, this drug must be the first to suspect. However, we cannot exclude gemeprost or mifepristone as the causative agents.

## Competing interests

None declared.

## Authors' contributions

PH coordinated the collection of information on the patient and wrote the manuscript. HA was the patient's treating physician and provided all of the information on the patient, as well as reported the case to the local pharmacovigilance agency. EH first received the report, made a preliminary summary of the case, and searched SWEDIS for previous reports on drug-induced pancreatitis. All authors participated in the final adjustments of the manuscript.

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