Pancreatitis induced by nitrofurantoin

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Abstract

The case of a woman is described who suffered from acute pancreatitis related to the ingestion of low dose nitrofurantoin, as shown by involuntary rechallenge. Because this is only the second case reported in published works, this side effect must be rare and is probably dependent on individual susceptibility.

(Gut 1994; 35: 712-713)

Many drugs have been reported to cause acute pancreatitis.¹ Among them, nitrofurantoin has been reported only once,² although it is widely used. We report here another case where pancreatitis was clearly related to the ingestion of nitrofurantoin.

Case report

A 26 year old woman presented for the first time to the casualty department in February 1991, complaining of abdominal pain. Her past history was unremarkable. She was a medical doctor. She had taken oral contraceptives for five years and there was an unclear history of hypercholesterolaemia in her family. She drank alcohol rarely and denied any recent alcohol consumption.

Three days before admission she experienced urinary frequency and dysuria. She took macrocrystalline nitrofurantoin 100 mg four times daily for three days. She had not taken this drug before. A few hours after the first tablet she suffered from epigastric pain and vomited once. She came to casualty when the pain and anorexia persisted. Physical examination was normal except for tenderness on palpation in the epigastrium and the left hypochondrium. Laboratory examination (normal values in parentheses) showed: erythrocyte sedimentation rate 35 mm in first hour (<10); C reactive protein 6.2 mg/dl (<0.5 mg/dl); serum amylase 480 U/l (<200); lipase 1198 U/l (<170). Liver enzymes, full blood count, serum creatinine, urea, and electrolyte tests were normal. It was concluded that the patient had 'a gastritis syndrome associated with mild pancreatitis' and she was discharged with metoclopropamide, antacids, paracetamol, and ofloxacin. The symptoms resolved in a few days and the patient had no symptoms for several months. She continued to take oral contraception.

In late October 1991 she again had urinary frequency and dysuria. Over a period of 10 hours she took a 100 mg macrocrystalline nitrofurantoin four times. Three hours later she experienced epigastric pain radiating to the left hypochondrium. She also complained of arthralgia, myalgia, and of generally feeling 'unwell'. She had not drunk alcohol in the preceding hours. Physical examination showed

only epigastric tenderness and mild, tender cervical lymphadenopathy, which had been present, according to the patient, for about one week. Her temperature was 37.2°C. Laboratory data of note were: serum amylase 287 U/l; lipase 406 U/l; white blood cell count 14 330/mm³ (neutrophils 83%, lymphocytes 10%, eosinophils 1%). C reactive protein was normal on admission but had risen to 6.5 mg/dl by the next day. Liver enzymes, bilirubin, calcium, urea, and creatinine were in the normal range. Serum cholesterol was high (9.9 mmol/ml) but serum triglyceride was only 1.5 mmol/ml. Serological examination for mumps, adenovirus, Coxsackie and Epstein-Barr viruses showed no evidence of recent infection. The antibody titre against *Mycoplasma pneumoniae*, however, was 1/32 on admission and rose to 1/64 16 days later. Viral culture of the faeces was negative. Urine examination showed no significant leucocyturia or haematuria and culture remained sterile. Ultrasound examination showed an enlarged and heterogenous pancreatic head with normal pancreatic and biliary ducts. No gall stones were seen. Two days later, gastroduodenoscopy and computed tomography of the abdomen were normal.

Serum amylase and lipase peaked at 321 and 1070 U/l, respectively, 30 hours after the onset of symptoms and then rapidly returned to normal. The patient quickly improved and was discharged two days later. Withdrawal from nitrofurantoin treatment was recommended.

An endoscopic retrograde cholangiopancreatography performed one week later was normal. Twenty months later she had not experienced any symptoms suggestive of pancreatitis.

Discussion

Our patient experienced two episodes of mild, acute pancreatitis separated by an eight month interval. On each occasion she had ingested moderate doses of macrocrystalline nitrofurantoin a few hours before the onset of symptoms. She had not taken nitrofurantoin and had not had an attack of pancreatitis at any other time. Serological tests may have suggested a recent infection by *Mycoplasma pneumoniae* before the second episode, but this seems difficult to integrate into a history of recurrent pancreatitis. Other causes of pancreatitis were excluded and we therefore believe that the drug was responsible for the episodes of pancreatitis.

There is only one previously reported case of nitrofurantoin induced pancreatitis.² The disease was more severe, with cholestatic jaundice attributed to narrowing of the common bile duct by swelling of the pancreatic head. The role of nitrofurantoin was confirmed by rechallenge. Systemic manifestations were also more promi-

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nent than in our case, with a temperature of 38.9°C, although our patient experienced myalgia and arthralgia. The authors thought that fever and the rapid reappearance of signs of pancreatitis after ingestion of a low dose nitrofurantoin were more suggestive of an allergic than a toxic reaction.

In their review of drug induced pancreatitis published in 1988, Malloary and Kern¹ commented on the first published case 'although this single case history clearly suggests a causal relationship, more cases are needed for confir-

mation'. Our case reasserts the existence of nitrofurantoin induced pancreatitis. The pathophysiology remains unclear but probably results from individual susceptibility factors. Although this side effect of a widely used drug seems rare, it is important to be aware of it, as avoiding giving the drug in an affected patient will prevent recurrence of the condition.

1 Mallory A, Kern F. Drug-induced pancreatitis. *Baillieres Clin Gastroenterol* 1988; 2: 293-7.

2 Nelis GF. Nitrofurantoin-induced pancreatitis: report of a case. *Gastroenterology* 1983; 84: 1032-4.