Case Report

Integrative Gastroenterology and Hepatology

Loperamide-Induced Pancreatitis: Report of Three Cases

Fantin A*, Peserico G and Barbuscio I

Department of Surgery, Oncology and Gastroenterology, University Hospital of Padova, Italy

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***Correspondence:** Alberto Fantin, Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, University Hospital of Padova, Padova, Italy, E-mail: alberto.fantin@aopd.veneto.it

Abstract

Background: Only 0.1-2% of acute pancreatitis seems to be drug-induced, being this etiology probably underestimated and often classified as idiopathic. Loperamide is an opiate with peripheral action, used in the treatment of diarrhea. Since 2012 it belongs to the FDA list of drugs potentially able to cause acute pancreatitis, because of its capacity of modulating the secretion from the exocrine pancreas and of causing sphincter of Oddi dysfunction.

Case presentation: We report the cases of three women, admitted to our hospital for acute pancreatitis. In their medical history two of them referred remote cholecystectomy. They all reported recent loperamide intake, given to acute diarrhea, denying alcohol consumption, smoking or family history for pancreatic disease. During the hospitalization laboratory tests showed increase of pancreatic enzyme and liver function alteration, with a rapid clinical improvement after loperamide suspension. Pancreatic Magnetic Resonance Imaging (MRI), including MR-cholangiopancreatography, was performed in all the cases, showing a well-defined pancreatic gland without any sign of acute inflammation and excluding common bile duct lithiasis. Given the absence of common risk factors and the temporal correlation between drug intake and occurrence of symptoms, we considered loperamide responsible of these three cases of acute pancreatitis.

Conclusion: In patients with acute pancreatitis, referring recent loperamide intake, in the absence of any other causes, iatrogenic damage must be considered as a possible etiologic factor.

Introduction

Drug-induced acute pancreatitis is responsible only for 0.1-2% of cases, but this pathology seems to be underestimated [1]. Most of them are classified as of "idiopathic etiology". Loperamide is an opiate with peripheral action, used in the treatment of diarrhea. In 2012 the FDA puts loperamide on watch list medicine to monitor after having identified potential signs of serious risk for acute pancreatitis. In this article we present three cases of acute pancreatitis probably caused by loperamide.

Case 1

A 77 years old woman with a remote cholecystectomy

and a strong history of ischemic cardiomyopathy presented herself to our emergency room for abdominal pain, diarrhea and fever. She referred the appearance of diarrhea the day before and for which she had taken loperamide. After she had taken the medicine, she developed fever, stomach ache and nausea. She denied any alcohol consumption, smoking or family history for pancreatic disease. Lab tests revealed elevated serum amylase 184 U/L and liver function tests altered: aspartate transaminase 671 U/L, alanine transaminase 557 U/L with normal levels of serum bilirubin. White cell counts, C-reactive protein were high: 13.3×10^9 and 28 mg/L. An abdominal ultrasound confirmed status post-cholecystectomy with choledochus 1 cm wide, no intra-hepatic bile duct dilation and no other relevant lesion.

Since loperamide was discontinued, patient condition improved and she was released 5 days after admission. A pancreatic Magnetic Resonance Imaging (MRI) including MR-cholangiopancreatography was performed during the hospitalization, showing a well-defined pancreatic gland without any sign of acute inflammation. The principal pancreatic duct was essentially regular. The MRI confidently excluded common bile duct lithiasis.

Case 2

A 46 years old woman with a history of laparoscopic cholecystectomy in 2005 and hereditary thrombophilia presented herself to emergency room for abdominal pain (overall in right-hypochondrium and mesogastrium) and nausea. No associated fever. She referred diarrhea the week before and she taken loperamide for that the day before the hospitalization. She denied any alcohol consumption or smoking. Lab tests revealed elevated liver function tests: aspartate transaminase 406 U/L, alanine transaminase 381 U/L with medium-high levels of serum bilirubin: 21, 8 mmol/L. White cell count, C-reactive protein and amylase were normal. She performed an abdominal ultrasound confirmed status post-cholecystectomy in a steatotic liver and no other relevant lesion. A pancreatic magnetic resonance imaging (MRI) including MR-cholangiopancreatography was performed after the hospitalization, showing no acute inflammation of pancreas. The main pancreatic duct seems to continue preferentially in the duct of Santorini, cause of an angled origin of Wirsung. The MRI confidently excluded common bile duct lithiasis or bile duct dilatation.

Case 3

A 23 years old woman with previous parathyroid adenomas presented herself to emergency room for epigastric pain and nausea. The days before she referred are gastroenteritis with fever, vomiting and diarrhea for which she had taken loperamide and acetaminophen. She referred occasional alcohol consumption and denied smoking. Lab test revealed elevated CRP 79 mg/L and amylase 262 U/L, mild elevated serum bilirubin 39, 1 umol/L and aspartate Transaminase 36 U/L. She performed an abdominal ultrasound in which found only gallbladder sludge. A pancreatic magnetic resonance imaging (MRI) including MR-cholangiopancreatography was performed after the hospitalization, showing no common bile duct lithiasis or bile duct dilatation.

Conclusions

Reviewing the histories, the intake of loperamide was the most relevant element that coincided with the onset

of both episodes. The mechanism of pancreatic injury is not so clear; probably it is caused by two different mechanisms [2]:

- Loperamide, likemorphine, inhibit the release of pancreatic polypeptide which suppress the secretion from the exocrine pancreas. Without this regular suppression, there is most likely an increase of exocrine pancreas secretion [3-5].
- A recent study demonstrated that opiate intake is a frequent cause of suspicion of sphincter of Oddi dysfunction [6] after cholecystectomy, especially in young patients with a narrow common bile duct [7].

In literature there are only other five articles [2][8-11] of acute pancreatitis induced by loperamide, but this relationship doesn't seem so uncommon such as we demonstrated in these cases

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