Cannabis-induced recurrent acute pancreatitis

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Abstract

Acute pancreatitis has a large number of causes. Major causes are alcohol and gallstones. Toxic causes, mainly represented by medication-induced pancreatitis account for less than 2% of the cases. Cannabis is an anecdotally reported cause of acute pancreatitis. Six cases have previously been reported. Herein we report a new case of cannabis-induced recurrent acute pancreatitis. (Acta gastroenterol. belg., **2012**, 75, **446-447**).

Key words : acute pancreatitis, cannabinoids.

Case report

A 30 year-old woman was admitted to our unit for severe upper abdominal pain radiating to the back. She described permanent nausea without vomiting. She was afebrile. There was no change in bowel movement or other symptoms. Her past medical history was mainly remarkable for one episode of acute pancreatitis in 2009 requiring admission to our own unit. She denied alcohol use or medication intake and admitted smoking irregularly cannabis since the age of 17. Her cannabis consumption dramatically rose two weeks prior to the present episode. During this period she used to smoke 4 to 6 "cannabis cigarettes" per day. On physical examination, the patient's abdomen was distended and diffusely tender. Blood tests revealed a lipase level of 956 IU/L(reference values : 60 IU/L), normal white cell count, platelet, hemoglobin and a moderately elevated C-reactive protein level of 15 mg/L (reference values : 5 mg/L). Serum values of urea, creatinine, AST, ALT, alkaline phosphatase, triglycerides, cholesterol, calcium and bilirubin were within reference limits. Immunoglobulin level was normal. The IgG level and IgG subtype 4 were within normal ranges. Antinuclear, anti DNA and ANCA auto antibodies were negative. Urine detection of Tetrahydrocannabinol (THC) was positive 5 days after the admission.

Parathormone serum level was normal. Genetic mutation research of CFTR&CTRC, PRSS1, SPINK1 were negative. Abdominal ultrasound and CT scan revealed normal findings of pancreas parenchyma and the Wirsung duct. No gallstones or biliary abnormalities were found. MRCP was performed and ruled out pancreas divisum or abnormal findings of the Wirsung duct. Pancreatic endoscopic ultrasonography failed to find abnormal findings. Wirsung diameter was estimated at 3 mm.

The patient was treated with analgesics, rehydration and transient fasting. Four days later she was asymptomatic. The lipase level dropped gradually to normal ranges during the same time. Review of our medical records demonstrated that she had been admitted in 2009 to our unit for a similar setting of acute pancreatitis with a mild regressive course after one week. No etiology was found and "idiopathic" pancreatitis was established as the diagnosis at that time. She also revealed a transient period of overconsumption of cannabis prior to the episode of pancreatitis in 2009 followed by a long period of withdrawal.

The final diagnosis was recurrent cannabis-induced pancreatitis after all the usual causes of acute pancreatitis had been ruled out.

Discussion

Acute pancreatitis is known to be related to multiple causes. Major causes are gallstones and alcohol, representing 85% of cases in contrast with rare or anecdotic causes such as hypertriglyceridemia, medication induced pancreatitis or hereditary pancreatitis. Some causes are controversial such as pancreas divisum. The list of less common causes is long. Cannabis-induced acute pancreatitis has been first reported in 2004 (1). Since the first report, one series of 3 cases and 2 anecdotic case reports have been published (2-4).

All these cases share the same setting ; a young regular user of cannabis (16-29 year-old) whose drug consumption had been rising few days or weeks prior to the episode of acute pancreatitis. Furthermore, among theses cases two were experiencing recurrent pancreatitis. In general, the course of the attack was benign and no complication was observed.

The main active constituent of cannabis is d-9 tetrahydrocannabinol (THC). Other important natural cannabinoids present in cannabis are d-8 THC, cannabinol and cannabidiol (5). Exogenous and endogenous cannabinoids produce their biological effects by specific

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cannabinoid 1 (CB1) and cannabinoid 2 (CB2) receptors. CB1 receptors are widely distributed throughout the central peripheral and enteric nervous system. CB2 receptors are located peripherally and are closely linked with in the immune tissue, predominantly the spleen and macrophages. Both receptors have been found in acinar and endocrine pancreatic cells. Cannabinoids CB1- and CB2 receptors are involved in the modulation of exocrine and endocrine pancreatic secretion (5).

However the exact effect of cannabinoids on the pancreas is still unclear. Data are contradictory. In an experimental study in rats, acute pancreatitis was induced by cerulein. Anandamide, an endogenous cannabinoid, was administered before and after cerulein administration. Stimulation of sensory nerves was performed by capsaicin. The effect of anandamide on the severity of acute pancreatitis depended on the phase of disease. Administration of anandamide, before induction of the pancreatitis, aggravated pancreatic damage ; whereas anandamide administered after induction of the pancreatitis, reduced the severity of acute pancreatitis. Sensory nerves seemed to be involved in the mechanism of this biphasic effect of anandamide (6).

Michalscki *et al.*, showed in a study on acute pancreatitis an up-regulation of cannabinoid receptors and elevated levels of endocannabinoids in the pancreas. Administration of a synthetic agonist of CB1 and CB2 abolished abdominal pain associated with pancreatitis and also reduced inflammation and decreased tissue pathology in mice without producing central, adverse effects. Antagonists of CB1- and CB2-receptors were effective in reversing agonist CB1 and CB2 induced antinociception, whereas a combination of CB1- and CB2-antagonists was required to block the anti-inflammatory effects of agonist in pancreatitis (7).

Establishment of firm and conclusive data on the mechanism of cannabinoids on pancreas needs further studies.

Cannabis is by far the most widely abused illicit drug. About 147 million people, 2.5% of the world population, consume cannabis (annual prevalence) (8). Although cannabis remains a very rare reported cause of acute pancreatitis, its thorough prevalence is probably underestimated. Individual susceptibility to develop dose dependent pancreatic toxicity to THC may play a role as cofactor. However as an illicit drug, cannabis may also include variable unknown and toxic ingredients that could be responsible for acute pancreatitis per se. In this case report, the setting of the acute pancreatitis is quite similar to those reported in the literature : a young patient, regular user of cannabis whose consumption had dramatically risen before the onset of acute pancreatitis. Moreover, our patient had experienced a similar attack 2 years before in the same condition of transient heavy usage of cannabis. Other etiologies of acute or chronic pancreatitis were carefully ruled out before we consider a potential link between cannabis and acute pancreatitis. Estimation of Naranjo adverse drug reaction probability scale was in favour of a probable link (9).

In conclusion, we report a new case of cannabis induced acute pancreatitis. The mechanism of toxicity is unclear but similar to the other reported cases a dose dependant relationship is highly probable.

This etiology must be known in order to avoid costly and unnecessarily investigations in this setting. In general the course of cannabis related acute pancreatitis is uneventful.

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