# Acute Pancreatitis Secondary to Marijuana Consumption

## Laura Nunez Herrero, Benjamin Chaucer, Shiwani Singh, Vrushak Deshpande, Sunil H Patel

Richmond University Medical Center, Department of Internal Medicine, Staten Island, NY 10310, United States

#### ABSTRACT

Acute pancreatitis is a common disease with many well-known etiologies. Rare causes of pancreatitis are still being discovered. We present the 13th reported case of marijuana induced acute pancreatitis. The role of marijuana in pancreatitis is not clearly defined. Studies have begun to clarify the role that cannabinoids may play in this disease process. This case demonstrates the need for further research.

#### **INTRODUCTION**

Acute pancreatitis is a serious disease with a mortality rate as high as 20%. Common causes of acute pancreatitis include, alcohol, obstruction and drug side effect. Marijuana has been documented as a rare cause of acute pancreatitis. While the pathophysiology of this disease process is not yet proven reports of its occurrence have increased in the last decade. This increase in reported cases of acute pancreatitis in conjunction with local legalization of medical and recreational marijuana use make this case of particular importance. We report the 13<sup>th</sup> case of cannabis induced acute pancreatitis worldwide and the 4<sup>th</sup> in the United States.

## **CASE REPORT**

A thirty-year-old male presented to the emergency department with a chief complaint of severe abdominal pain. He described the pain as stabbing, non radiating pain that he rated as 10/10. The pain had occurred for a 1 day duration and was associated with nausea and vomiting. Physical examination was positive for tenderness in the abdomen to light palpation. Laboratory evaluation was positive for an elevated lipase of 4218 U/L. Ultrasound was performed to rule out obstruction. Computed tomography (CT) subsequently performed showed no anatomical abnormalities. Alcohol, biliary, medication and infectious causes were excluded. A urine toxicology screen was done revealing a urinary drug screen positive for tetrahydrocannabinol (THC). After further questioning, he admitted to consistent user of copious amounts of

Received December 30th, 2015-Accepted February 03rd, 2016 Keywords Pancreas; Pancreatitis Correspondence Benjamin Chaucer Department of Internal Medicine 400 Forest Avenue Apt 2r Staten Island, New York 10301 United States Phone +1 473-444-4175 E-mail benchaucer@gmail.com marijuana. The patient was made NPO and IV fluids were started with a peripheral line. Clinical improvement was achieved with supportive treatment. After resolution of symptoms the patient was counseled on the dangers of illicit drug use and discharged home.

#### DISCUSSION

Marijuana has been used for centuries in native medicine for the treatment of several health problems [1]. Adverse effects associated with the chronic use of cannabis include infertility, erectile dysfunction, visual disorders and schizophrenia [2]. Pancreatitis is one of the least reported complications, with only 12 reported cases of cannabis-induced pancreatitis [2-11]. Well know causes of acute pancreatitis include obstruction, alcohol consumption and drug use. Of these, obstruction and alcohol represent 70-80% of cases. The reporting of drug induced acute pancreatitis is challenging. Data about this pathology is dependent on physician reporting. This diagnosis is further compounded by the frequent use of polypharmacy making the specific offending agent difficult to pinpoint. The true incidence of cannabis-induced pancreatitis may therefore be underestimated. The financial and public health importance of acute pancreatitis is evident with 25% of acute pancreatitis cases resulting in an Intensive Care Unit stay [12].

Cannabis induced acute pancreatitis has only been reported 12 times in current literature. Of these, 2 resulted in chronic pancreatitis. The first documented case occurred as recently as 2004 [3]. In order to diagnosis cannabis induced pancreatitis, all other causes must be excluded. Interestingly in all documented cases chronic consumption was reported by each patient.

Reasons for the increase in reported cases are multifaceted. Marijuana is the most widely used illicit drug worldwide. Marijuana use has increase from 5.8% of people in the US above 12 years of age using marijuana in 2007 to 7.5% of the US population in 2013 [13]. This increase in the use of marijuana may in part explain the increased incidence of cannabis-induced pancreatitis. Cannabis

was not previously thought to play a role in the etiology of acute pancreatitis. As more cases come to light we may see an increase in this diagnosis. Marijuana induced pancreatitis may represent a percentage of acute pancreatitis previously diagnosed as idiopathic. The difficulty of this diagnosis is further compounded by the legal status of this substance. Patients may feel resistant to divulge illegal drug use, making urine toxicology screening essential in its diagnosis.

The pathophysiology of marijuana-induced pancreatitis is not understood. Studies aimed at understanding this mechanism have begun to explain the role of cannabanoids in acute pancreatitis. The active component in marijuana is tetrahydrocannabinol (THC), which acts on cannabinoid receptors CB1 and CB2. Several compounds target these receptors know as cannabinoids. The CB1 receptor is found in the smooth muscle of blood vessels, endothelial cells and nervous system and is responsible for many of the symptoms associated with marijuana intoxication [14]. CB2 receptors are found on blood and immune cells [15]. Both CB1 and CB2 are present in the islet of Langerhans cells of the human pancreas [16]. In the pancreas, effect of cannabinoid on the course of pancreatitis is not clarified [1]. Ananadamide (arachidonylethanolamide) is produced my macrophages and is an endocanabanoid [17]. This works as an endogenous ligand of the CB1 receptor. A recent study showed that endocannabonoids may play a role in septic shock and that therapy targeted at removal of these compounds may improve outcomes [18]. In one study by Kazuhisa et al. levels of plasma anandamide was significantly elevated after induction of sever acute pancreatitis in a rat experimental model [19]. Another study done in 2008, showed that the effect of cannabinoids on pancreatitis may depend on the time of administration [1]. Treatment with anandamine prior to induction of pancreatitis aggravated pancreatic damage, while its administration after induction of pancreatitis reduced the severity of the disease. It is important to note that in all reported cases of cannabis induced acute pancreatitis excessive cannabis use was reported [2-12].

Data is lacking regarding the pathophysiology and role of cannabis in acute pancreatitis. While the role of marijuana in acute pancreatitis is not yet defined it remains an important differential in cases without a clear etiology. As such urine toxicology screen should be part of the laboratory work up for all idiopathic cases of acute pancreatitis.

## Acknowledgement

We would like to thank and acknowledge Dr. Dennis Bloomfield for his help and support.

## **Conflict of interest**

The authors declare that there are no conflicts of interest.

## References

1. Dembiński A, Warzecha Z, Ceranowicz P, Warzecha AM, Pawlik WW, Dembiński M, Rembiasz K, et al. Dual, time-dependent deleterious and protective effect of anandamide on the course of cerulein-induced acute pancreatitis. Role of sensory nerves. Eur Journal Pharmacol 2008; 591:284–292. [PMID: 18593574]

2. Wargo KA, Geveden BN, McConnell VJ. Cannabinoid-induced pancreatitis: a case series. JOP. J Pancreas (Online) 2007; 8:579-583. [PMID: 17873462]

3. Grant P, Gandhi P. A case of cannabis-induced pancreatitis. JOP. J Pancreas (Online) 2004; 5:41-43. [PMID: 14730121]

4. Fatma H, Mouna B, Leila M, Radhouane D, Taoufik N. Cannabis: A rare cause of acute pancreatitis. Clin Res Hepatol Gastroenterol 2013; 37:e24-5. [PMID: 22749694]

5. Belze O Jr, Legras A, Ehrmann S, Garot D, Perrotin D. Cannabisinduced acute pancreatitis. Am J Emerg Med 2011; 29:131.e3-4. [PMID: 20825867]

6. Akkucuk MH, Erbayrak M. A rare and unexpected side-effect of cannabis use: abdominal pain due to acute pancreatitis. Case Rep Emerg Med 2015; 2015:463836. [PMID: 25759763]

7. Nayak SK, Preethi M, Zanwar S, Palaniswamy KR. Cannabis induced recurrent acute pancreatitis. Trop Doct 2015. pii: 0049475515613238. [Epub ahead of print][PMID: 26519137]

8. Espino García A, Jorge Tufet C, Lafarga Giribets MA, Justribó Sánchez ME, Carré Gaya G. Cannabis-induced pancreatitis. Semergen 2015; pii: S1138-3593(15)00066-0. [Epub ahead of print]. [PMID: 25817851]

9. Lorvellec A, Thiriet L, Andrianjafy C, Gervaise A, Seigne AL, Rey P. Recurrent cannabis-induced acute pancreatitis. Presse Med 2015; 44(4 Pt 1):468-71. [PMID: 25650297]

10. Mikolašević I, Milić S, Mijandrušić-Sinčić B, Licul V, Štimac D. Cannabis-induced acute pancreatitis. Med Glas (Zenica) 2013; 10:405-7. [PMID:23892868]

11. Howaizi M, Chahine M, Haydar F, Jemaa Y, Lapoile E. Cannabisinduced recurrent acute pancreatitis. Acta Gastroenterol Belg 2012; 75:446-7. [PMID: 23402090]

12. Neoptolemos JP, Raraty M, Finch M, Sutton R. Acute pancreatitis: the substantial human and financial costs. Gut 1998; 42:886–891. [PMID: 9691932]

13. Drugabuse.gov. Nationwide Trends 2015.

14. Arguello PA, Jentsch JD. Cannabinoid cb1 receptor-mediated impairment of visuospatial attention in the rat. Psychopharmacology 2004; 177:141-150. [PMID: 15290005]

15. Facci L1, Dal Toso R, Romanello S, Buriani A, Skaper SD, Leon A. Mast cells express a peripheral cannabinoid receptor with differential sensitivity to anandamide and palmitoylethanolamide. Proc Natl Acad Sci USA 1995; 92:3376-3380. [PMID: 7724569]

16. Bermúdez-Silva FJ, Suárez J, Baixeras E, Cobo N, Bautista D, Cuesta-Muñoz AL, Fuentes E, et al. Presence of functional cannabinoid receptors in human endocrine pancreas. Diabetologia 2007; 51:476-487. [PMID: 18092149]

17. Mechoulam R, Ben-Shabat S, Hanus L, Ligumsky M, Kaminski NE, Schatz AR, Gopher A, et al. Identification of an endogenous 2-monoglyceride, present in canine gut that binds to cannabinoid receptors. Biochem Pharmocol 50:83-90. [PMID: 7605349]

18. Wang Y, Liu Y, Ito Y, Hashiguchi T, Kitajima I, Yamakuchi M, Shimizu H, et al. Simultaneous measurement of anadamide and 2-arachidonoylglycerol by polymxin B-selective absorption and subsequent high performance liquid chromatography analysis: increase in endogenous cannabinoids in the sera of patients with endotoxic shock. Anal Biochem 2001; 249:73-82. [PMID: 11412008]

19. Matsuda K, Mikami Y, Takeda K, Fukuyama S, Egawa S, Sunamura M, Maruyama I, et al. The cannabinoid 1 receptor antagonist, am251, prolongs the survival of rats with severe acute pancreatitis. Tohoku J Exp Med 2005; 207:99-107. [PMID: 16141678]