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Case Report

Cannabinoid Induced Pancreatitis: A Case Report and Literature Review

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Abstract

Cannabis (cannabinoid) induced pancreatitis is a rare finding. Nevertheless, with the universally increasing consumption of cannabis, the incidence of cannabinoid induced acute pancreatitis is projected to increase in the future. Thus, as patients present with symptoms of acute pancreatitis, including history of illicit drug use becomes essential in proper determination of underlying etiology. While the clinical features, workup, and management remains similar in majority of acute pancreatitis cases, identifying accurate underlying etiology provides more reliable prognosis and allows prevention of future recurrences. As marijuana remains one of the most commonly abused illicit drug globally, the goal of this article is to increase awareness on an unusual but possible side effect, namely, acute pancreatitis. In this case study, we describe a case of marijuana induced acute pancreatitis and its lack of recurrence upon cessation of its use.

Introduction

Marijuana has been advocated for its medical benefits in management of chronic and neuropathic pain, epilepsy, diarrhea associated with Crohn's disease, irritable bowel disease, chemotherapy induced emesis, anorexia associated with AIDS, post-traumatic disorder, multiple sclerosis, and rheumatoid arthritis, among others [1,2]. Thus, various FDA- approved agents (e.g. dronabinol, nabilone) manufactured from synthetic cannabinoid components (tetrahydrocannabinol THC) have entered the market for similar indications. Despite the potential for THC utilization for medical indications, it has been associated with numerous short and long term adverse effects. As marijuana is a heavily controlled substance in schedule I category, federally, it is deemed inappropriate for any medical use. Therefore, studies focusing on its use are very limited in numbers and inconclusive in findings. Some of the speculated but inadequately supported adverse reactions include short and long term memory loss, psychosis, schizophrenia, bipolar disorder, depression, addiction, cancers, reddening of eyes, and respiratory diseases [1,2].

Approximately 2% of acute pancreatitis is medication induced [3]. Most commonly implicated drug agents are metronidazole, tetracycline, azathioprine, furosemide, thiazide diuretics, angiotensin converting enzyme inhibitors, didanosine, aspirin, valproic acid and codeine [3]. A subset of these cases are caused by illicit drugs; likewise, even fewer cases can be confirmed as cannabinoid induced. Thus, very little is known about cannabis induced pancreatitis and its underlying mechanism.

A comprehensive search was conducted to develop understanding of current available literature addressing association of cannabinoids with pancreatitis. The search included articles from any time frame on PubMed and Google Scholar databases with the terms "cannabis [marijuana or cannabinoid] induced pancreatitis", "health effects of cannabis [marijuana or cannabinoid]", "drug induced pancreatitis", and "management of drug induced pancreatitis".

Case Summary

DM, a 24 year-old caucasian female, presents to the emergency department with the chief complaint of 10 out of 10 burning epigastric and periumbilical pain radiating dorsally. She reports associated nausea and vomiting, but denies fever, cough, diarrhea, abdominal distension or history of abdominal trauma. Her past medical history is significant for hypertension, hyperlipidemia, recurrent pancreatitis

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(requiring emergency visits twice monthly), and stage III chronic kidney disease confirmed on biopsy to be focal segmental glomerulosclerosis. No pertinent surgical history exists. Outpatient, she is medically managed solely with amlodipine. She reports a six year history of illicit marijuana smoking in the form of "joint" twice daily (estimated 0.5 to 1 grams of marijuana daily). She denies tobacco, alcohol and any other illicit drug utilization. Patient has incomplete high school education, is unemployed, and resides alone in her apartment.

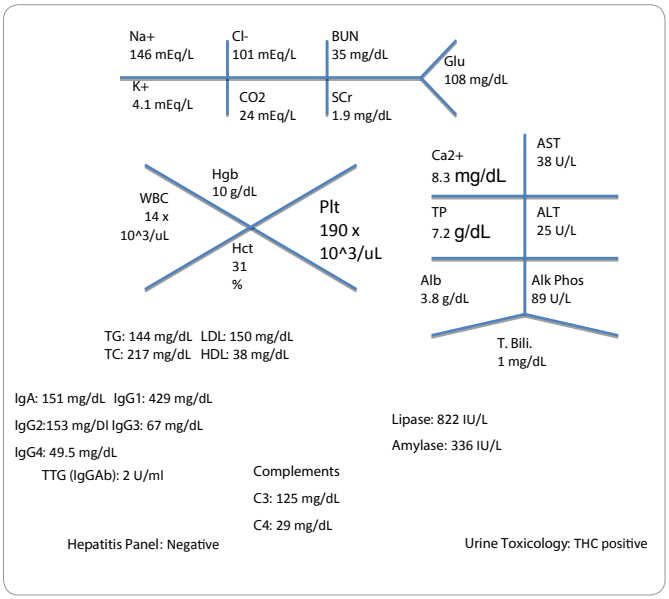
Presenting Vitals

T Max	BP	RR	Pulse	O2 Sat	Weight	Height	BMI
36.7 °C	142/90 mmHg	13/ min	78/ min	97% RA	190 lbs	64 in	32.6 kg/m^2

Physical Exam:

She had epigastric and periumbilical pain without guarding or rigidity; remaining of the exam was unremarkable.

Overview of labs



Overview of a Few Select Imaging Over Multiple Hospitalizations

CT Abdomen	**Dec 2013**: 3.9 cm adnexal cyst or haemorrhagic ovarian cyst. Moderate sized hiatal hernia. No radiologic evidence of pancreatic necrosis. **Feb 2014**: Mild left hydronephrosis noted. No perinephric fat strandings. No renal, ureteral, or bladder calculi present
MRI Abdomen	**Feb 2014**: Radiologic evidence of pancreatitis. Pancreatic tail enlarged. No cholelithiasis or intra- or extrahepatic biliary dilation. Common bile duct 4mm. No ascites or retroperitoneal lymphadenopathy.
US Abdomen	**Jan 2014**: No evidence of gallstones. Echogenic pyramids bilaterally consistent with medullary nephron calcinosis. **Feb 2014**: Liver normal. Gall bladder filled with fluids but no stones or inflammatory wall thickening. No pericholecystic fluids seen. Common bile duct 4.5 mm. Pancreas homogeneous in echotexture. No focal or diffuse pancreatic enlargement.
US Pelvis	Adnexal cyst resolved in comparison to previous imaging. Two small cysts in left ovary with average diameter of 2.6cm, likely ovulatory follicles.
US Endoscopic	**Apr 2014**: No evidence of pancreatic microliths.
Doppler Renal	No evidence of renal artery stenosis

Severe pain, nausea and vomiting, marijuana abuse, leukocytosis, hyperbilirubinemia (baseline 30-40), elevated serum creatinine (baseline 1.6-2.0), elevated amylase, elevated lipase, BMI in obese category, MRI indicative of pancreatitis, and positive THC screen were noted as pertinent findings. Thus, clinical diagnosis of acute pancreatitis was made. Patient was maintained on aggressive intravenous crystalloids fluids and pain control while nil per os. Patient's status subsequently improved by day 3 of admission.

Prior to above mentioned encounter, due to patient's recurrent history of pancreatitis, during each subsequent visit, more extensive studies were conducted in order to determine underlying etiology of her manifestations. Normal hepatobiliary structure and function were confirmed through various laboratories (liver function tests, hepatitis panel, and complete blood count) and imaging studies as mentioned above. As reported through various laboratory findings (immunoglobulins, and complements), immunologic etiology was deemed an unlikely cause. Ultimately, her clinical diagnosis was confirmed as acute pancreatitis secondary to chronic cannabinoid abuse.

Subsequently, patient was vehemently urged to pursue cannabinoid utilization cessation. With patient's adherence to the recommendation, no emergency room visits have occurred in the previous year.

Discussion

Acute pancreatitis is an inflammatory condition of the pancreas, which is associated with sudden and severe onset of abdominal pain. A clinical diagnosis is generally established when two or more of the following criteria are applicable.

1. Abdominal pain: acute, severe, and persistent epigastric or periumbilical pain usually with radiation to back.
2. Elevated serum amylase and/or lipase activity: at least three times greater than the upper limit of normal.
3. Evidence of acute pancreatitis on imaging, usually contrast enhanced CT of abdomen. Other imaging modalities can be MRI abdomen or trans abdominal ultrasonography.

If the patient meets the first criteria, and serum amylase and lipase are moderately elevated, radiologic studies may be performed to aid in confirming diagnosis.

While gallstones and alcohol abuse remain the most common causes of acute pancreatitis, remaining of the causes of acute pancreatitis are summarized in the table below:

Etiologies of acute pancreatitis: [4-6]
1. Mechanical/structural: Gallstones, Endoscopic retrograde cholangiopancreatography, trauma, pancreatic or periampullary cancer, pancreas divisum
2. Toxins: alcohol, methanol, scorpion venom, organophosphate poisoning
3. Drugs: Angiotensin converting enzyme inhibitors, Azathioprine, hydrochlorothiazide, furosemide, didanosine, sulfa drugs, valproate, metronidazole
4. Metabolic; hypercalcemia, hypertriglyceridemia
5. Infections: Coxsackie B virus, cytomegalovirus, mumps
6. Inherited: multiple gene mutations like CFTR (cystic fibrosis transmembrane conductance regulator)
7. Other: pregnancy, postrenal transplant, ischemia due to hypotension and atheroembolism, tropical pancreatitis

Table 1. Etiologies of acute pancreatitis.

The prevalence of marijuana use has exceeded twice-fold (4.1% to 9.5%) in 2012-2013 compared to 2001-2002 [1]. This increase in utilization has been associated with increased risk of multiple medical and psychiatric phenomenon, including acute psychosis, depression, poor quality of life, alternative drug abuse, motor vehicle crashes, erectile dysfunction and emergency room visits [1]. Although approximately 2% of acute pancreatitis is drug induced, exact incidence of cannabinoid caused pancreatitis has not been well established. Nonetheless, a handful of related case reports have surfaced over the last few years [7] and increase in marijuana utilization is likely to escalate marijuana induced pancreatitis.

The inquiries of likely pathophysiologic mechanisms also remain unresolved; although, the phenomenon is more closely associated with chronic marijuana utilization. Cannabinoid receptors, CB1 and CB2, have been identified in the pancreas. Acute pancreatitis is predicted to occur due to chronic marijuana exposure to CB1 receptors [8]. In an experimental study involving rats, higher levels of endogenous cannabinoids was detected in subjects with severe pancreatitis versus ones with mild pancreatitis [9]. When rats with severe pancreatitis were injected with CB1 receptor antagonists, their survival significantly improved [8]. While this finding suggests a correlation between marijuana exposure to CB1 and pancreatitis, further research is warranted for more robust and clinically relevant conclusions.

While cessation of marijuana utilization is an effective preventative mechanism specific to marijuana induced pancreatitis, It shares common clinical presentation with alternative acute pancreatitis etiologies. Due to limited evidence, other causes of acute pancreatitis should be sought and explored prior to interpreting marijuana as the possible culprit for acute pancreatitis. Likewise, diagnostic exams for suspected cannabinoid induced acute pancreatitis should be similar [10].

Acute Pancreatitis Investigation [4,11]
1. Routine Labs: Complete blood count, comprehensive metabolic panel, serum amylase and lipase, serum lipid profile, C-reactive protein
2. Additional Labs: IgG4, ABG if patient is dyspneic, trypsin and trypsinogen 2
3. Routine Imaging: X-ray Kidney, Ureter, Bladder (KUB) in erect position, CT abdomen, Abdominal ultrasonography
4. Additional Labs: Magnetic Resonance Cholangiopancreatography, Endoscopic retrograde cholangiopancreatography, endoscopic ultrasonography
5. Image guided aspiration and drainage, if necrosis or cyst or pseudocyst suspected
6. Ranson's criteria for survival: LDH

Table 2. Acute Pancreatitis Investigation.

Diagnostic evaluations should be individualized for each patient based on pertinent medical history; most of the evaluations must be conducted to, primarily, exclude other possible and more likely pathophysiologic causes. Once diagnosis of marijuana induced pancreatitis is determined through exclusion or other potentials, treatment strategy is relatively conventional. Cessation of marijuana utilization is an essential step to reduce subsequent recurrences. Aggressive fluid and electrolyte management and pain control while NPO is essential, unless contraindicated. Nasogastric tube decompression is not recommended and enteral feeding should be initiated at the earliest possible.

Due to the lack of clinical studies and rarity of the phenomenon, prognosis of cannabinoid induced acute pancreatitis also remains undetermined. Potential for further clinical research includes identifying the risk factors for cannabinoid induced acute pancreatitis, preventive measures, short term and long term complications and underlying pathophysiology. As acute pancreatitis carries significant morbidity and mortality and cannabis utilization is ever increasing, any preventive measures in future could reduce mortality and financial burden of cannabinoid induced acute pancreatitis [12-15].

Conclusion

Cannabinoid induced acute pancreatitis is increasingly becoming more common, however, further clinical research is indicated for enhanced comprehension of the disease. The goal of this article is to increase awareness among health-care providers regarding cannabinoid induced pancreatitis. A comprehensive review should include history of drug abuse; and management should involve thorough counselling on avoiding marijuana and potential adverse effects, including acute pancreatitis.

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