

# Cannabis-induced acute pancreatitis

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## TRANSPARENCY DECLARATION

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## Defekt dijafragme ili sekvestracija pluća u petogodišnjeg dečaka

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## SAŽETAK

Cilj ovoga prikaza slučaja dijafragmalnog defekta s kasnim kliničkim ispoljavanjem, u petogodišnjeg dečaka, jeste još jedan doprinos boljoj dijagnostici u pedijatrijskoj populaciji. Radiologu i pedijatrija rendgenološki i CT nalaz grudnog koša imponovao je kao sekvestracija pluća, dečjim hirurzima kao benigni teratom, a u toku operacije utvrđen

je mišićni hemidijafragmalni defekt desne strane. Ovaj slučaj naglašava sledeće: retkost ispoljavanja dijafragmalne kile u dece starijeg uzrasta, značaj "naglašene" kliničke sumnje na osnovu održavanja znakova blage respiratorne insuficijencije, potrebu za dopunskim radiološkim ispitivanjima i operacijom u cilju dijagnoze ove abnormalnosti i "uspešnost" prenatalne ultrazvučne dijagnostike.

**Cljučne reči:** dijafragmalne kile, oštećenje pluća, starija deca, prenatalni ultrazvuk

## CASE REPORT

### Cannabis-induced acute pancreatitis

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## ABSTRACT

Acute pancreatitis is a common disease. Despite the frequent use of cannabis worldwide, only six reports have described cases of acute pancreatitis secondary to the use of tetrahydrocannabinoid (THC). Here we describe two cases of THC-induced pancreatitis. The first case occurred in a 38-year-old man with multiple admissions for THC-induced pancreatitis; the second case involved a 22-year-old man with no previous medical history. In both cases, other possible causes of acute pancreatitis were ruled out.

**Key words:** common disease, tetrahydrocannabinoid, etiology

## INTRODUCTION

Acute pancreatitis (AP) is an inflammatory disorder of the pancreas (1). In different parts of Europe, the annual AP incidence is 20 to 30 new cases per 100 000 population (1). Acute pancreatitis has many known causes, including gallstones, alcohol abuse, hypertriglyceridaemia, trauma, pancreatic malformations, infection, and drug use

(1). Drug-induced AP is relatively rare. A German study reported a 1.4% incidence of drug-induced AP (1). Drugs that cause AP include antibiotics (metronidazole), immunosuppressants (azathioprin), antihypertensives (angiotensin converting enzyme inhibitors, furosemide, or thiazide diuretics), aspirin, and valproic acid (1-3). Cannabis use can also cause AP, but only six patients have been described in the literature (4-7). Here we report two patients with cannabis-induced AP.

**CASE REPORT**

**Case 1**

In December 2010, a 38-year-old man was admitted to the Department of Gastroenterology, who complained of upper abdominal pain, nausea, and vomiting over the past 36 hours. The pain was described as constant, sharp, aggravated by movement, propagated to the back, and between the scapulae. The patient history included multiple episodes of pancreatitis. He claimed that he did not drink alcohol, smoke, or take any chronic medications. He initially denied illicit drug use. Family history was insignificant (Table 1). The abdominal ultrasound was normal; however, follow-up high resolution multi-slice tomography (MSCT) scans revealed mild pancreatitis with no biliary disorders. After a diagnosis of tetrahydrocannabinol (THC)-induced pancreatitis was suspected, the patient admitted smoking THC for the previous three years. The patient records showed that, since 2008, the patient had been admitted to our department eight times, with similar symptoms, laboratory results, and imaging findings. However, no urine drug screen had been performed previously. He was advised to avoid THC, and he has not been admitted since.

**Case 2**

In April 2008, a 22-year-old man was admitted to our department with a one-day history of sudden onset, severe abdominal pain, radiating to the back, with nausea, but no vomiting. He had no previous medical history. He did not smoke, drink alcohol, or take any chronic medications. There was no family history of similar abdominal problems. He initially denied illicit drug use (Table 1). An ultrasound examination of the abdomen showed no abnormalities. Abdominal computed tomography (CT) scan revealed a mild pancreatic swelling, but no

**Table 1. Clinical characteristics of two patients with acute pancreatitis**

Clinical measures	Case 1	Case 2	Reference range
Heart rate (beats/min)	100	106	M
Blood pressure (systolic/diastolic; mmHg)	150/80	140/75	M
Respiratory rate (breaths/min)	20	20	M
Body temperature (°C)	normal	37	M
Epigastric examination	mild tenderness	mild tenderness	
Bowel movement	decreased	decreased	
White blood cell count (×10 <sup>9</sup> /L)	13.4	9.2	3.4-9.7
Lipase (U/L)	150	220	13-60
Amylase (U/L)	400	800	23-91
Triglycerides (mmol/L)	1.3	1.12	<1.7
Serum calcium (mmol/L)	2.31	2.33	2.14-2.53
Infectious agents*	negative	negative	
Alcohol	negative	negative	
Urine tetrahydrocannabinol (THC)	positive	positive	

\*serum was tested for mumps virus, herpes simplex viruses 1 and 2, varicella zoster virus, cytomegalovirus, Epstein-Barr virus, HIV 1 and 2, hepatitis A, B and C viruses, coxsackie virus, and echoviruses evidence of gallstones or biliary tree dilatation/obstruction. A magnetic resonance cholangiopancreatography (MRCP) confirmed the absence of biliary tree pathology and structural abnormalities in the pancreas. Initially, we treated the patient supportively, and his recovery began well. Seven days after the admission, the patient had a second episode of severe, worsening pain. He required sedation and epidural analgesia. Elevations were noted in serum amylase at 2277 U/L, lipase at 2574 U/L, and CRP at 52 mg/L (reference value 0 – 5.0 mg/L). When questioned, the patient denied intake of prohibited food or drugs, other than those prescribed.

At 15 days after admission, he experienced a third attack of acute pain. Again, amylase and lipase levels were elevated, and CRP was 200 mg/L. A second CT scan revealed initial signs of pancreatic necrosis. After finding a positive THC urine drug screen, the patient finally admitted to smoking marijuana during hospitalization and the day before admission. He was strongly advised to avoid THC. He recovered well, and he was discharged from the hospital. For this patient, regular use of cannabis resulted in several hospitalizations with acute pancreatitis relapses. Finally, he developed chronic pancreatitis with pseudocyst formation.

Because marijuana use is illegal, it is difficult to raise public awareness of its systemic effects (4,5). Thus, little clinical evidence is available showing a link between THC and systemic disorders (5-8).

The exact mechanism by which THC causes AP remains unclear (4-7). Humans express two types

of cannabinoid receptors, known as CBI and CBII. Both receptors are expressed throughout the body; CBI is mostly expressed in the central and peripheral nervous systems, endothelial cells, and vascular smooth muscle cells; CBII is expressed in macrophages; and both CBI and CBII are expressed in the pancreas (8). In the digestive system, cannabinoids have both beneficial and harmful effects (8,9). They inhibit gastric acid secretion, inhibit small intestinal secretions, and delay gastric emptying (7-10). Dembinski et al (8), showed that these protective effects were achieved by activating CBI receptors in the stomach; there, CBI-receptor signalling maintains gastric mucosal blood flow, promotes gastric mucosal DNA synthesis, and inhibits the release of interleukin-1 $\beta$ , an acute inflammatory mediator (8). However, in the pancreas, cannabinoids may have a harmful effect; mice with cerulein-induced pancreatitis showed increased severity when they received, anandamide, an endogenous cannabinoid receptor agonist. The exact mechanism for this effect remains unknown (6-11).

In our cases the AP was the most probably caused by THC. The first patient was advised to elude THC and has not been admitted since, while in the second case, the regular use of cannabis in our patient resulted in several hospitalizations for this patient because of acute pancreatitis relapses, which at last led to the development of chronic pancreatitis with pseudocyst formation. Also, it is important to emphasize that in almost 30% of cases, the etiology of AP is unknown, especially due to the unavailability of some methods, such as manometry of Odd's sphincter and tests for IgG4 evaluation (1-6).

Acute pancreatitis is a common disorder associated with the use of marijuana. However, the exact mechanisms remain unknown and require further investigation. Because marijuana use has spread throughout the world, all patients with AP of unknown etiology should be carefully investigated for drugs that might contribute to the disease. This may be difficult, because patients are reluctant to admit using cannabis, due to its illegal status in most countries.

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#### TRANSPARENCY DECLARATIONS

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#### Kanabis kao etiološki čimbenik akutnog pankreatitisa – prikaz slučaja

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#### SAŽETAK

Akutni pankreatitis (AP) je česta bolest. Unatoč raširenoj primjeni kanabisa diljem svijeta, prema dostupnoj literaturi do sada je prijavljeno samo šest slučajeva kanabisom izazvanog AP-a. U ovom radu prikazali smo dva slučaja akutnog pankreatitisa izazvanog tetrahidrokanabinolom (THC). Prvi slučaj zabilježen je kod 38-godišnjeg bolesnika s višestrukim hospitalizacijama zbog akutnog pankreatitisa izazvanog THC-om, a u drugom slučaju radilo se o 22-godišnjaku bez prethodne povijesti