

# Rolling up Trouble: Adult Intussusception Possibly Sparked by Cannabis Use or Pheochromocytoma

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## Abstract

Intussusception is a rare phenomenon in adults which is typically associated with neoplasms, post-operative adhesions, strictures, inflammatory bowel diseases, and endometriosis. With the rise of legalization and widespread use, a growing body of evidence has emerged suggesting a possible association between cannabis use and intussusception in adults. We describe a case of a middle-aged male with a history of uncontrolled hypertension and regular marijuana use who presented with intussusception and was incidentally found to have an adrenal nodule with laboratory evidence strongly suggestive of pheochromocytoma. Through our investigation, the culprit cause of the intussusception could not be fully elucidated due to the patient eloping. The link between cannabis and intussusception lies in the hypothesis that activation of cannabinoid receptors in the enteric system results in inhibition of acetylcholine release in presynaptic neurons leading to slowed contractile activity and peristalsis, establishing a point for invagination leading to intussusception. Meanwhile, the incidental adrenal nodule could have possibly contributed to the intussusception in two different ways. The mass effect of an adrenal nodule or its nearby metastasis could have served as a classic lead point. The other means revolve around the suspected pheochromocytoma producing excess catecholamines, which, like cannabinoids, also slow contractile activity and peristalsis. This case demonstrates how a more thorough diagnostic evaluation may be warranted in cases of intussusceptions in adults and highlights how cannabis use and pheochromocytoma may have been two potential predisposing risk factors.

## Keywords

Adult Intussusception, Pheochromocytoma, Cannabinoids, Catecholamines, Gut Motility

## 1. Introduction

Intussusception refers to the invagination of a proximal portion of bowel into an adjacent segment. It is exceedingly rare in adults and usually presents in the context of underlying pathologies such as neoplasms, post-operative adhesions, strictures, inflammatory bowel diseases, and endometriosis [1]. However, growing evidence suggests a possible association between adult intussusception (AI) and cannabinoid use, hypothesized to exist due to its anti-peristaltic effects [2]. Derived from the *cannabis sativa* marijuana plant,  $\Delta^9$ -tetrahydrocannabinol ( $\Delta^9$ -THC), the main psychoactive compound in cannabis, has been cultivated by humans for medicinal and other purposes for thousands of years (Table 1) [3]. Cognizance of the anti-peristaltic properties of cannabinoids has predominantly arisen from randomized placebo-controlled trials on human subjects using the synthetic form of  $\Delta^9$ -THC, dronabinol, an appetite stimulant that is FDA approved for certain patient populations [4].

**Table 1.** Overview of most common commercially available THC compounds depending on state law.

THC Compound	Brief Description
Delta-9-THC ( $\Delta^9$ -THC)	The primary psychoactive compound in cannabis, responsible for the “high” effect.
Delta-8-THC ( $\Delta^8$ -THC)	A milder, less potent psychoactive version of Delta-9-THC, often derived from hemp.
Delta-10-THC ( $\Delta^{10}$ -THC)	Similar to Delta-8 but with slightly different effects, sometimes described as more uplifting.
THC-A (Tetrahydrocannabinolic Acid)	The raw, non-psychoactive precursor to Delta-9-THC, which converts when heated (decarboxylation).
THC-V (Tetrahydrocannabivarin)	A variant of THC that may have appetite-suppressing and energizing effects, often found in small amounts.
THC-P (Tetrahydrocannabiphorol)	A more potent analog of THC, estimated to be several times stronger than Delta-9 in binding to cannabinoid receptors.
THC-O (THC-O-acetate)	A synthetic cannabinoid that is reported to be significantly more psychoactive than Delta-9-THC.
HHC (Hexahydrocannabinol)	A hydrogenated form of THC with slightly different psychoactive effects, potentially offering a longer shelf life.

While previous case reports have suggested an association between catecholamine-secreting tumors and intestinal pseudo-obstruction [5], this case study also explores how pheochromocytoma may possibly be associated with AI. While the more commonly known gastrointestinal (GI) manifestations of pheochromocytomas are nausea, vomiting, and abdominal pain [6], less is known on what specific GI complications it may predispose afflicted patients to. Two potential mechanisms by which pheochromocytomas may increase the risk of AI include (a) their mass effect acting as a lead point for AI development and (b) the catecholamines they secrete inhibiting peristalsis [7] [8], thereby serving as a lead point.

While marijuana and catecholamine-secreting tumors are generally not considered to increase the risk of AI, this case demonstrates how a more comprehensive diagnostic work-up may be warranted in adult patients who present with intussusception and in whom typical risk factors for AI are absent. We present a case of a 50-year-old man with a history of uncontrolled hypertension, hyperlipidemia, and heavy cannabis use who presented with intussusception, and in whom an incidental adrenal nodule was found that was highly suspicious for pheochromocytoma given his clinical picture.

## 2. Case Presentation

A 50-year-old male with a past medical history significant for uncontrolled hypertension and hyperlipidemia not on medications and a prior appendectomy presented to the emergency department with three days of nausea, vomiting, abdominal pain, and loss of appetite. He had no bowel movement for two days, yet reported he was still passing gas. He denied fever, chills, headache, dizziness, chest pain, SOB, upper respiratory tract infection symptoms, abdominal pain, diarrhea, recent weight loss, family history of cancer, and UTI symptoms. He denied any previous episodes with similar presenting symptoms. The patient denied alcohol or cigarette use yet did endorse daily marijuana use, sometimes multiple times a day exclusively through smoking dried marijuana flower obtained from a local dispensary.

He had been at a different emergency room two days prior for the same complaints, at which time a computed tomography (CT) scan of the abdomen was unremarkable for acute findings. On arrival, his initial vital signs were notable for hypertension (159/109) and tachycardia (104 BPM). Physical examination was notable for moderate tenderness to palpation in the epigastric region without rebound tenderness. His labs were remarkable for hypokalemia, a modest leukocytosis, proteinuria, microscopic hematuria, pyuria without bacteria, and a urine toxicology positive for cannabinoids. His liver function labs including lipase were normal (**Table 2**). Inflammatory markers (ESR, CRP) were within normal limits. Polymerase chain reaction stool studies for common bacteria, viruses, and parasites were negative.

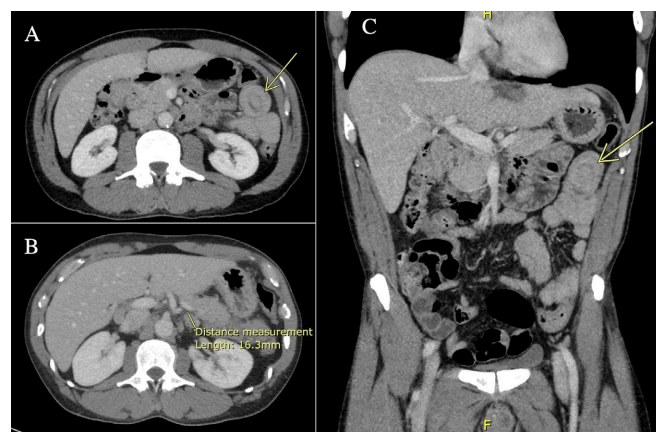
Given the unclear clinical picture, the patient was sent for repeat CT imaging of the abdomen, which demonstrated short segment proximal jejunal intussusception within the left abdomen measuring 3.6 cm in length and mildly irregular wall thickening of a short segment of proximal jejunum immediately upstream to the intussusception, which was suggestive of an underlying mass, and incidentally, a 1.6 cm left adrenal nodule (**Figure 1**). He was treated conservatively with fluids, placement of a nasogastric tube with low intermittent suctioning for gastric decompression, and intravenous proton pump inhibitors and antiemetics for two days.

The patient subsequently had oral contrast administered through the nasogastric tube and a subsequent CT enterography study revealed interval resolution of

the small bowel intussusception in the left hemiabdomen with a normal mucosal pattern noted in the small intestines where a previous description of a suggestive underlying mass was previously described. There were no findings on repeat CT which suggested ileus, mechanical causes, or inflammatory stranding or changes to suggest a nidus for the intussusception. The patient was subsequently advanced to a regular diet and soon became entirely asymptomatic and eager for discharge.

**Table 2.** Initial laboratory values on presentation.

Laboratory Study	Component	Result
Comprehensive Metabolic Panel (CMP)	Sodium (135 - 145 mmol/L)	136
	Potassium (3.5 - 5.0 mmol/L)	3.2
	Chloride (98 - 110 mmol/L)	99
	Carbon Dioxide (24 - 32 mmol/L)	25
	BUN (5.0 - 25 mg/dL)	12
	Creatinine (0.60 - 1.20 mg/dL)	0.87
	Glucose (70 - 100 mg/dL)	132
	AST (5 - 46 U/L)	23
	ALT (4 - 51 U/L)	12
	Alk Phos (40 - 129 U/L)	96
	Total Bilirubin (0.10 - 1.50 mg/dL)	0.7
	Lipase (10 - 60 U/L)	29
Complete Blood Count (CBC)	WBC (4.40 - 10.5 10 <sup>3</sup> /uL)	12
	Hemoglobin (12.6 - 16.7 g/dL)	16.7
	Platelets (139 - 361 10 <sup>3</sup> /uL)	316
Urinalysis	Protein (Negative)	3+
	RBC ( $\leq$ 4/HPF)	1+
Urine, Microscopic	RBC ( $\leq$ 4/HPF)	9
	WBC ( $\leq$ 4/HPF)	15



**Figure 1.** (A) Transverse abdominal computed tomography study demonstrating “target sign” telescoping small bowel (yellow arrow); (B) Same computed tomography scan as A. but showing a 1.6 cm incidental adrenal mass; (C) Coronal abdominal computed tomography study again demonstrating the classic “target sign.”

Given the incidental adrenal adenoma, hypokalemia, and persistently elevated blood pressures and heart rate, we ordered urine metanephrines and a plasma-to-aldosterone ratio be collected before discharge, with a strong recommendation that he needed to follow up on these results. It was only the patient's urine normetanephrine that was elevated at 1.56 nmol/L (reference range: 0.00 - 0.89 nmol/L). Unfortunately, the patient was lost to follow-up despite multiple attempts to be reached.

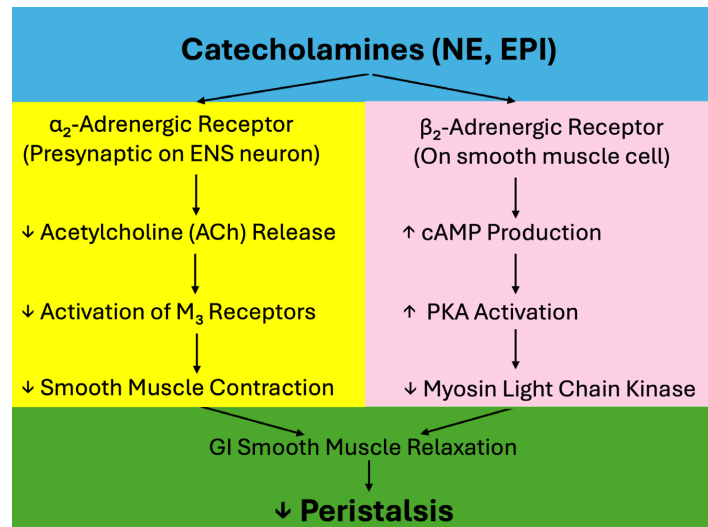
### 3. Discussion

Intussusception remains an exceptionally rare condition in adults, most commonly affecting pediatric populations. While the underlying cause in pediatric cases is often idiopathic, a distinct lead point is typically identified in the majority of the cases affecting adults. AI is classically encountered in the context of intra-abdominal neoplasms, post-operative adhesions, strictures, and endometriosis [9]. While this patient did not carry the typical risk factors, we hypothesize that his marijuana use and/or possibly the existence of a pheochromocytoma may have predisposed him to develop an intussusception. This case raises important points regarding considering intussusception earlier on in the differential diagnosis and highlights potential risk factors to consider such a diagnosis.

One possible explanation for his presentation was his recreational use of cannabis, which he admitted to using multiple times daily. A 2022 case report of four patients [10], two recent case series of [11] [12], and three individual case reports [13]-[15] have suggested an association between AI and cannabis use. It is suggested that the activation of cannabinoid receptors in the enteric system results in inhibition of acetylcholine release in presynaptic neurons leading to slowed contractile activity and peristalsis [16]. A classic manifestation of this phenomenon is cannabinoid hyperemesis syndrome, which is characterized by cyclic vomiting and attributed to gastroparesis and peristalsis inhibition. The subsequent decrease in intestinal transit times and an overall inhibitory effect on peristalsis is hypothesized to inhibit peristalsis and invertedly manifests a lead point for invagination leading to intussusception.

The other possibility is that the patient had a pheochromocytoma with or without an extra-adrenomedullary lesion that served as the lead point for his intussusception. Unfortunately, the patient was lost to follow-up and this diagnosis could not be explored further. Nevertheless, his clinical course of having persistent hypertension and tachycardia, even after the resolution of the intussusception, an incidental adrenal adenoma on imaging, and elevated normetanephrine levels were highly indicative of pheochromocytoma. Elevated normetanephrines have been found to be more sensitive than elevated metanephrines for pheochromocytoma [17]. While there have been some case reports of pheochromocytomas being associated with intestinal pseudo-obstruction [18] [19], none exist to date that suggest an association with intussusception, with gastrointestinal stromal tumors being the more common neoplastic culprits [20]. While a direct mass effect may

have contributed to a lead point, the effects of catecholamine excess on gut motility cannot be ignored. Catecholamines are well known to cause slowed and disordered peristalsis (**Figure 2**) [21], which could have in theory contributed to the formation of a lead point.



**Figure 2.** Molecular mechanisms by which catecholamines inhibit GI peristalsis. Legend: Norepinephrine (NE), Epinephrine (EPI), Muscarinic (M), Cyclic Adenosine Monophosphate (cAMP), Protein Kinase A (PKA).

Identification of a lead point generally takes precedence as lead points can be intervened on conservatively (*i.e.*, enema) or surgically resected if an underlying mass is suspected. In this case, the elevations of serum normetanephrines were suspicious for a neoplastic focus. Had the patient remained hospitalized or followed up in the outpatient setting, he could have undergone further diagnostic studies for malignancy (*i.e.*, EGD, colonoscopy), pheochromocytoma (*i.e.*, 24 urinary fractionated metanephrines, abdominal MRI), and genetic predispositions to pheochromocytoma if confirmed (*i.e.* RET, VHL, SDHB mutations) [22]. If pheochromocytoma was confirmed on follow-up, the patient could have potentially undergone surgical resection and cured his hypertension and possibly reduced his risk of future AI recurrence.

While the management of pediatric intussusception classically includes air or contrast enemas, management of intussusception in adults are less defined. While surgical resection was once universally considered the standard of care for AI, more recent evidence is emerging that suggests conservative approaches involving serial abdominal exams, bowel rest, and intravenous fluids may not have inferior outcomes than surgical approaches [23]. While this case of AI was treated conservatively like many cases of AI, one unique aspect in regards to management, was the use of CT enterography with oral contrast and its possible therapeutic effect on the resolution of his intussusception. Garnering further data on the possible advantages and disadvantages of CT enterography with oral contrast in the man-

agement of AI may supply healthcare providers with an additional diagnostic and potentially therapeutic tool at their disposal.

#### 4. Conclusion

In conclusion, the diagnosis of intussusception in adults should precipitate inquiry into possible underlying pathologies that may be afflicting the patient insidiously. Cannabinoids and pheochromocytomas have not been extensively described as well-known causes of AI. However, in this case, no other risk factors were determined to be associated with the development of the intussusception. It remains prudent to continue gathering data on these risk factors, especially with the rising use of cannabis and its growing cultural normalization and legalization. The limitations of this case report include the lack of follow-up and further investigations to diagnostically confirm the presence of a pheochromocytoma. Nonetheless, this case demonstrates how a more thorough diagnostic evaluation may be warranted in cases of adult intussusception and suggests that cannabis use and pheochromocytoma may be two potential predisposing risk factors.

#### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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