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Acute Colonic Pseudo-Obstruction Caused by Dexmedetomidine: A Case Report and Literature Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 50
Final Diagnosis: Acute colonic pseudo-obstruction
Symptoms: Abdominal pain • cough • fever
Medication: —
Clinical Procedure: Colonoscopy decompression and colectomy
Specialty: Critical Care Medicine

Objective: Rare co-existance of disease or pathology

Background: Acute colonic pseudo-obstruction (ACPO) is an infrequent entity characterized by non-toxic, non-mechanical, abrupt, functional dilation of the colon. Clinically patients present with abdominal distention, anxiety, severe abdominal pain, nausea, and vomiting. This rare entity can lead to a fatal outcome if not recognized early. A high level of suspicions is paramount for early diagnosis and prompt intervention.

Case Report: A 50-year-old male was admitted to the intensive unit care due to acute hypoxic respiratory failure, pneumonia, and septic shock requiring mechanical ventilation and intravenous vasopressors. Two weeks after admission, his clinical course deteriorated and was complicated with acute abdominal distension, pain, and ileus. Imaging confirmed acute onset of ileus and after ruling out metabolic and infectious causes, the diagnosis of ACPO was made. Aggressive medical and surgical management resulted in a favorable outcome.

Conclusions: Critically ill patients on ventilator are commonly sedated; therefore, usual symptoms of ACPO can be missed or misinterpreted leading to late diagnosis with increased morbidity and mortality. Clinicians must be aware of potential harm and side effects from common sedatives used in the intensive care unit and should be current on medical literature. Alpha-2 agonists, i.e., dexmedetomidine, is increasingly been used in critical care setting and there are few reports of a possible association with ACPO. We present here a case of a patient with dexmedetomidine-induced ACPO, and we provide a review of the existing literature and pathophysiology of the condition.

MeSH Keywords: Abdomen, Acute • Colectomy • Colonic Pseudo-Obstruction • Colonoscopy • Dexmedetomidine • Decompression, Surgical • Adrenergic alpha-2 Receptor Agonists • Intestinal Pseudo-Obstruction • Ileus

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/913645

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Background

Acute colonic pseudo-obstruction (ACPO) it is an infrequent entity characterized by massive colon dilation without apparent mechanical obstruction [1]. The incidence of ACPO is approximately 100 cases per 100 000 inpatient admissions [2,3]. Vanek and colleagues reported 400 patients diagnosed with ACPO and found that 94.5% of patients had an underlying medical or surgical condition [4]. ACPO is more frequently seen in males with an average age of 60 years of age and an underlying chronic disease [3,4]. ACPO has also been reported as a complication of surgery, between 0.06–5% in post cardiac surgery, 0.29% in burn patients, and between 0.7–1.3% in orthopedic surgery [2,3].

Case Report

A 50-year-old Vietnamese male was admitted to the intensive care unit with diffuse abdominal pain, vomiting, and watery diarrhea associated with fever, productive cough, and bilateral pleuritic chest pain for 1-week prior to admission. Medical history was remarkable for intermittent asthma and seizure disorder. He denied sick contact or recent traveling. He was a heavy alcohol drinker, but no other toxic habits.

Initial examination revealed a patient on severe respiratory distress, tachycardic, afebrile, hypoxic, and borderline hypotension with a blood pressure of 90/60 mm Hg. Diffuse rhonchi were noted on lung examination, and the rest of examination was unremarkable. He required intubation and mechanical ventilation. Pertinent laboratories on admission showed leucopenia, thrombocytopenia, lactic acidosis, and severe transaminitis. Chest x-ray showed bilateral infiltrates.

He was started on intravenous fluids and broad-spectrum antibiotics with vancomycin, piperacillin tazobactam, oseltamivir, and azithromycin for septic shock due to pneumonia. Subsequently, he developed acute respiratory distress syndrome. Piperacillin, tazobactam, and azithromycin were changed to meropenem and levofloxacin for suspected leptospirosis. Fiberoptic bronchoscopy with bronchoalveolar lavage was positive for *Klebsiella pneumoniae* and parainfluenza, and antibiotics were de-escalated. Blood, urine and spinal fluid cultures as well as hepatitis profile were all negative. Head computed tomography (CT), and transthoracic echocardiography was normal.

The patient was initially sedated with propofol, fentanyl, and lorazepam. The patient's condition started improving by day 4, and weaning attempts were started. Due to severe agitation, dexmedetomidine was started on day 4 from admission while other sedatives were tapered off. On day 9 from admission, he developed acute abdominal distension and ileus associated with abdominal pain and non-bloody diarrhea. Abdominal x-ray showed a dilated cecum measuring over 15 cm of diameter, and abdominal CT without contrast revealed dilatation of the colon with internal diameter measuring up to 10.1 cm without evidence for bowel perforation highly suspicious for ileus with toxic megacolon versus volvulus (Figure 1). Medical management with nasogastric and rectal tube for decompression and aggressive replacement of electrolytes and fluid failed. Serial imagining showed persistent abdominal distention. Strong consideration of an infectious etiology prompted the start of antibiotics to cover infectious colitis including *Clostridium difficile* infection; other differential diagnosis included metabolic and electrolyte derangement leading to ileus (see Table 1) which where aggressively corrected during his intensive care unit admission. *C. difficile* toxin A and B and GDH antigen were negative in 2 stool samples taken 1 day apart, stool for ova, parasite, and culture were negative as well. Several blood cultures remained negative. On day 11 of hospitalization, several attempts of endoscopic decompressions of colon were unsuccessful. Table 1 shows pertinent laboratory and medications trend.

In consideration of the patient's clinical deterioration, elevated intrabdominal pressure, and findings suggestive of toxic megacolon, the patient underwent surgery which revealed cecal perforation with serosal tear. A side-to-side ileocolic anastomosis along with diversion loop ileostomy was performed. Pathology findings described patchy transmural suppurative acute and chronic inflammation with ulceration, mucosal necrosis, and serositis (clinically perforation). Special stain PAS (Periodic acid-Schiff) showed focal superficial ulcer with fungal hyphae which were considered colonization.

Final impression diagnosis from clinical and pathological data was ischemic colitis and perforation due to ACPO, the pseudo-obstruction having occurred in a setting of dexmedetomidine exposure. At this point patient, the was weaned off of other sedative medication, metabolic causes of ileus were addressed early, and infectious causes proven to be non-existing in the gut.

The patient had a prolonged hospital course; he was liberated from mechanical ventilation and discharged to a skilled nursing facility with jejunostomy tube feeding and tracheostomy.

Discussion

The incidence of ACPO is low but occurs usually in patients with underlying conditions and carries significant morbidity and mortality.

The cecum is located in the right iliac fossa; in comparison with the descending colon, sigmoid colon, and rectum, the cecum and ascending colon are saccular, larger in diameter, and

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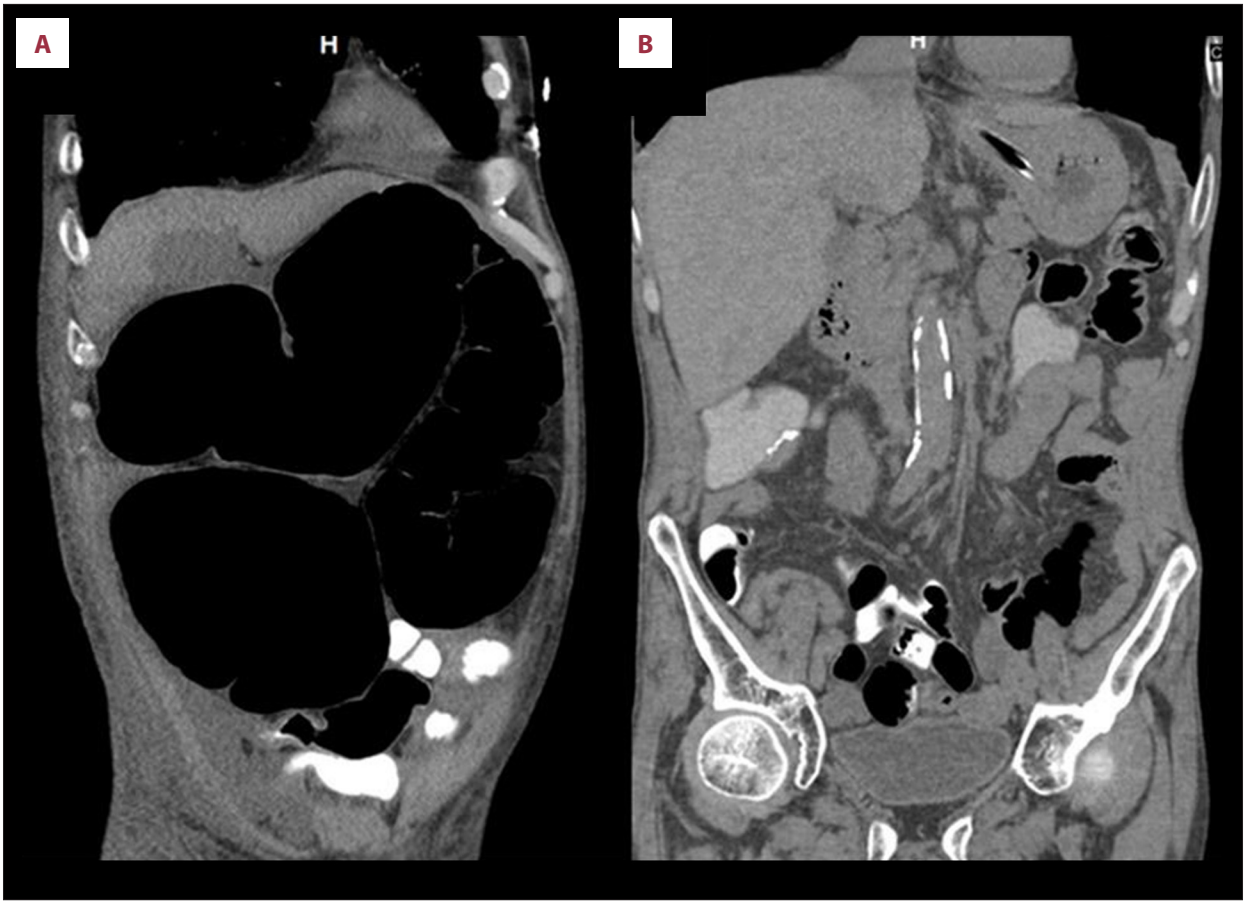

Figure 1. Shows abdominal computed tomography scan at (**A**): time of diagnosis of acute colonic pseudo-obstruction with very dilated colonic loops and (**B**): a week later after surgical intervention.

have thinner walls. The largest bowel dilatation in patients with ACPO usually develops in the cecum. As the wall tension of the colon increases, ischemia with longitudinal splitting of the serosa, herniation of the mucosa, and perforation (including iatrogenic perforation during open or laparoscopic procedures) can occur.

The pathophysiology of ACPO remains poorly understood with several risk factors been proposed [1,3,4]. This condition is presumed to be a functional type of obstruction due to a dysfunction of the normal colonic motor activity. The gut motor activity is controlled at several levels which include colonic smooth muscle, interstitial cell of Cajal, intrinsic enteric nervous system, prevertebral and spinal reflex arcs, and modulation from autonomic nervous system along with hormonal system [3].

The vagus nerve supplies the parasympathetic tone from the upper gastrointestinal tract to the splenic flexure, and the sacral parasympathetic nerves (S2 to S5) supply the left colon, sigmoid, and rectum. Sympathetic stimuli result in the inhibition of bowel motility and the contraction of sphincters. The lower 6 thoracic segments supply the sympathetic tone to the right colon, whereas lumbar segments 1–3 supply the left colon. Ogilvie first proposed an autonomic imbalance with sympathetic deprivation of the colon as an explanation for bowel dilation [1]. Newer theories favor an excess of the sympathetic over the parasympathetic tone secondary to a reduced parasympathetic innervation to distal colon, leading to a non-functional or atonic segment which therefore results in functional obstruction [3–5]. Additionally, critically ill patient tends to have higher levels of sympathetic activity which adds on autonomic disbalance. Because sympathetic and parasympathetic anatomic innervation has overlap on colon at level of splenic flexure this might explain colonic distention at this level [3]. Figure 1 show pathophysiological factors implicated in ACPO.

Proposed risk factors associated with ACPO and comparison with our patient can be seen in Table 2. In addition of the use of narcotics, an interesting association of ACPO with dexmedetomidine has been proposed. Alpha-2 agonist receptors (i.e., clonidine and dexmedetomidine) produce reduction in peristalsis by activating such receptors in the enteric neurons; this effect has been studied in humans showing delay in gastric emptying and gastric transit, effects that are known to be

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Table 1. Pertinent laboratory and medications.

Laboratory	Day 1 admission	Pre ACPO		ACPO				Day 42 discharge
		Day 4	Day 8	Day 9	Day 10	Day 11	Day 11 surgery	
pH	7.30	7.43	7.49	7.46	7.46	7.48	7.49	7.40
PCO_2 mmHg	37.4	35.2	38.8	42	39	35.4	36.1	29
PaO_2 mmHg	N/A	110	74.3	155	135	87.3	95	119
Sodium mEq/L	140	146	149	142	144	142	140	139
Potassium mEq/L	5.4	4.2	2.9	3.9	3.9	3.5	3.8	3.7
Glucose mg/dL	47	142	100	150	130	122	140	94
BUN mg/dL	11	18	10	14	14	12	13	14
Creatinine mg/dL	1.4	0.6	0.4	0.5	0.5	0.3	0.4	0.4
Magnesium mg/dL	2.1	1.9	1.9	2.5	2.2	2.1	1.9	2.0
Phosphorus mg/dL	3.3	1.4	2.2	2.8	2.9	2.4	3.0	4.5
Calcium mmoles/L	8.7	7.8	7.5	7.9	7.7	7.5	7.1	9.6
Bicarbonate serum mmoles/L	15	23	28	26	30	28	24	23
Hemoglobin g/dl	15.7	10.9	10.5	9.3	8.2	8.1	9.7	10.2
Alanine aminotransferase unit/L	1,823	322	141	N.a.	56	45	50	13
Aspartate transaminase unit/L	11,128	249	90	N.a.	37	33	58	66
Total bilirubin mg/dL	2.6	6.6	4.8	N.a.	4.4	3.2	4.0	0.2
Fentanyl	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Midazolam	Yes	No	No	No	Yes	Yes	Yes	No
Dexmedetomidine	No	Yes	Yes	Yes	No	No	No	No
Intermittent morphine	No	No	Yes	Yes	Yes	Yes	No	No

ACPO – acute colonic pseudo-obstruction; BUN – blood urea nitrogen.

dose dependent. There are several reports in humans and animal studies showing an association between use of clonidine and increase risk for ACPO [6–10]. Figure 2 shows a summary of physiopathology of ACPO.

The clinical presentation of patients with ACPO is similar to small bowel obstruction with abdominal distention, fever, nausea, and emesis (60% of patients), and abdominal pain (80% of patients). Other symptoms like constipation (50%), paradoxical diarrhea (40%), and rarely dyspnea, have been reported. Symptoms can be acute or subacute, ranging from few days to 1–2 weeks duration.

Diagnosis remains a challenge, and the focus is differentiating small bowel obstruction from ACPO. Abdominal x-ray will usually show distended bowel loops with air-fluid levels. Abdominal CT with oral and ideally intravenous contrast is advisable to rule out mechanical bowel obstruction and evaluate for ischemia. Evaluation of electrolytes, acid base status, thyroid function test, and basic metabolic panel is required as they lead or worsen any colonic dysmotility. Lastly, other diagnostic tool would be water contrast enema which in some cases could have therapeutic effect by inducing osmotic bowel movements potentially decompressing colon, however, the small risk of perforation needs to be considered [11–14]. The severity of ACPO ranges from mild distention to obstruction, followed by ischemia of the bowel and perforation [11].

Management of ACPO depends on the severity of the condition; it is mainly supportive with a focus on correction of predisposing factors and discontinuing factors that prolong its course or predispose it [11]. In patients with intestinal lumen of <12 cm, conservative measures should be attempted first with correction of electrolyte imbalance and avoidance

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Table 2. Known risk factors associated with ACPO [5].

Severe infection or disease process
Cardiac disease: myocardial infarction; congestive heart failure
Surgical Intervention (intra-abdominal, urologic, gynecologic, orthopedic, cardiac, obstetrics, spinal surgery)
Advance age
Neurologic disorder: Guillain-Barré syndrome
Metabolic disorder: hypothyroidism; diabetes; liver failure
Electrolyte imbalances (hyponatremia, hypokalemia, hypocalcemia, hypercalcemia, hypomagnesemia)
Respiratory disorders: chronic obstructive pulmonary disease
Renal insufficiency
Medications including but limited to: opiates, tricyclic antidepressants, phenothiazines, anti-Parkinson drugs, anesthetic agents, clonidine, anticholinergic
Toxic insults: alcohol abuse
Gastrointestinal carcinoma
Intestinal hypoperistalsis syndrome
Plasma cell dyscrasias: multiple myeloma; amyloidosis
Systemic lupus erythematosus and systemic sclerosis (rare)
Miscellaneous: trauma; spinal cord injury, severe constipation, burns
Our patient's risk factors
Severe infection
Electrolyte imbalance: hypokalemia and hypophosphatemia
Respiratory disorders: Respiratory Failure
Medication: narcotics and alfa-2 agonist (dexmedetomidine)
Alcohol abuse

of opioids, anticholinergic medications, and calcium channel blockers. Adequate fluids resuscitation, early ambulation, and knee to chest or prone positioning to promote flatus have been recommended [15].

If initial supportive management fails, a trial of neostigmine or colonic decompression could be attempted. Neostigmine is recommended in patients with uncomplicated ACPO; main contraindications include presence of colonic ischemia or perforation, pregnancy, severe cardiac arrhythmias or active bronchospasm [11]. Neostigmine transiently increases acetylcholine levels in muscarinic receptors from parasympathetic nervous system, promoting contractility, and accelerating colon transit. Neostigmine has also been shown to trigger colonic high amplitude propagating sequences providing decompressive mechanism [3]. In patients with non-complicated ACPO, the success rate of neostigmine ranges from 60–90% [11,16] with a recurrence rate of 0–31% with good long-term response [11]. Those patients with partial response could benefit from a second dose [11,17]. Clinical response is assessed by the decrease in abdominal distention, passage of flatus, and decrease in cecal diameter on serial imaging. Adverse effects of neostigmine include abdominal pain (50–73%), sialorrhea (23–38%), vomiting (10–20%), and bradycardia (5–9%).

Colonic decompression should be considered in non-responsive patients or in those who are not candidate for neostigmine [11]. Colonic decompression has a reported success rate of 60–90% with some patients requiring repeated procedures [4,11,18]. Rate of perforation associated with colon decompression is low, with a reported rate of 1–3% [4,11].

Surgical intervention either tube ostomies or resection is reserved for patients failing medical management or patients with ACPO associated perforation or necrosis of the bowel [11]. Perforation associated with ACPO is generally low, seen in

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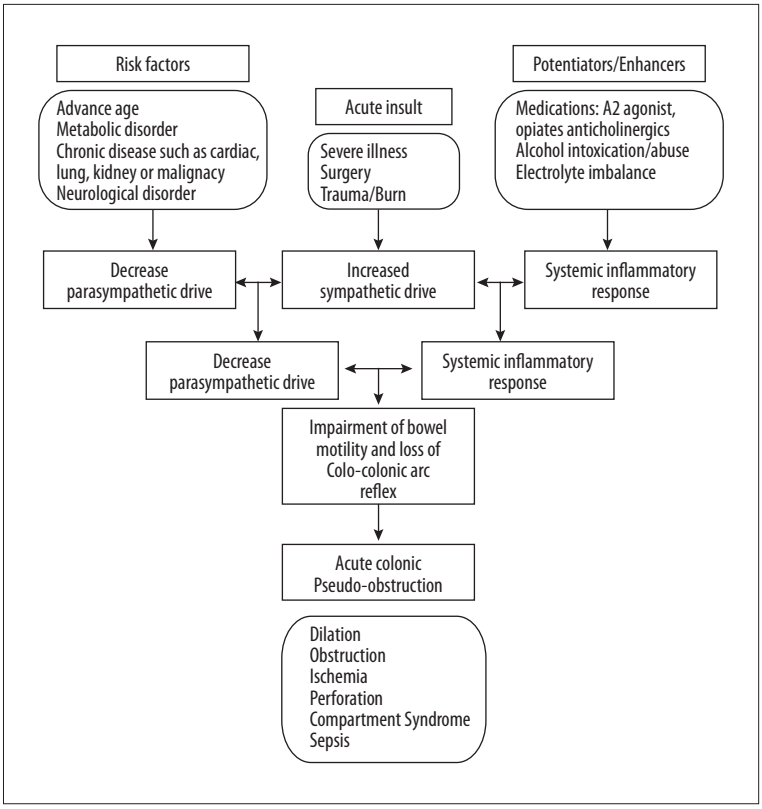

Figure 2. Pathophysiology of acute colonic pseudo-obstruction.

around 3–10% of patients. A major risk factor for perforation is a cecal diameter >12 cm lasting for >6 days [4,11].

Prognosis of patients with this condition depends on the severity of comorbidities and clinical status and predisposing factors. The diameter of the colon is important, larger diameters poses more risk for perforation [4,11,15]. Recently, Zhao and colleges demonstrated the relation between colonic wall thickness and poor outcomes; in general, nonsurgical treatment in ACPO with no wall edema had higher successful rate of cure compared with patients with wall edema. Additionally, they found worse prognosis and a higher rate of complications like intra-abdominal hypertension, acute compartment syndrome, sepsis, gastrointestinal hemorrhage, necrosis, and perforation among patients with colon wall edema compared to those without it. Overall mortality ranges from 14–40%, with higher mortality seen in those patients with cecal perforation [3,4,15,17,19–22].

The clinical pathway in our patient was remarkable as all metabolic causes and electrolytes imbalance that potentially could create ileus were corrected in a timely manner. Primary infectious diseases of the gut, such as colitis and commonly *Clostridium difficile*, were treated empirically until their exclusion by toxin PCR; additionally, medication induced ileus was considered and opioids were discontinued except dexmedetomidine. Development of ACPO was timely related to the introduction of dexmedetomidine, so it is reasonable to deduct that it was the cause of the gastrointestinal syndrome.

Conclusions

ACPO is a potential life-threatening condition that can affect critically ill patients. Many of the common medications used in the critically ill can add to the predisposing risk factors of the patient. Earlier recognition, aggressive correction of potential factors like electrolyte and fluid imbalance and discontinuation of medications which worsen ileus is highly recommended. A low index of suspicion and serial examination is paramount for early recognition. A multidisciplinary approach to management with the intensivist, gastroenterologist and surgery is of outmost importance in order to decrease morbidity and mortality associated with this condition.

Use of dexmedetomidine has been increasing in the care of the critically ill patient due to his favorable profile and low association with complications like prolonged sedation or delirium. Our patient represents a rare case of a drug related complication. The use of α-$_2$-adrenorecptors agonist, such as dexmedetomidine, in the critically ill could either directly be related to development of ACPO or potentiate other risk factors associated with it. This association has not yet fully been explored and still remains underdiagnosed and therefore under-report event.

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Conflict of interest

None.

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