Systemic Sclerosis Sine Scleroderma as a Rare Presentation of Chronic Intestinal Pseudo-Obstruction

Mitchell V Edwards, MD1, Jennifer M Ray, MD2, Ahmad Al-Taee, MD2, Elizabeth Marsicano, MD3

1Department of Medicine, Queen’s University, Kingston, ON, Canada; 2Department of Gastroenterology and Hepatology, Saint Louis University Hospital, St Louis, MO, USA; 3Mercy Clinic, Washington, MO, USA

Author for correspondence: Mitchell V Edwards: 0mve@queensu.ca

Received: 21 October 2020; Accepted after revision: 25 February 2021; Published: 21 September 2021
DOI https://doi.org/10.22374/cjgim.v16i3.494

Abstract
Chronic intestinal pseudo-obstruction (CIPO) is a disruption of the enteric nervous system characterized by chronic intestinal dysmotility and dilation. It has many underlying causes. We present a 52-year-old woman with 53-kg unintentional weight loss, abdominal pain, and vomiting. She had dilated small bowel loops with air fluid levels and no transition point on Computed Tomography scan. Esophagogastroduodenoscopy revealed aperistalsis and undigested duodenal food. The secondary cause was found to be systemic sclerosis sine scleroderma (ssSSc), a classification of systemic sclerosis without skin involvement. Systemic sclerosis sine scleroderma.

We present an interesting case of CIPO secondary to ssSSc.

Résumé
La pseudo-obstruction intestinale chronique (POIC) est une perturbation du système nerveux entérique caractérisée par un trouble de motilité et une dilatation intestinale chronique. Elle compte de nombreuses causes sous-jacentes. Nous présentons le cas d’une femme de 52 ans manifestant une perte de poids involontaire de 53 kg, des douleurs abdominales et des vomissements. Elle présente des anses dilatées de l’intestin grêle accompagnées de niveaux hydro-aériques et aucun point de transition à la tomodensitométrie. L’œsophagogastroduodenoscopie révèle une absence de péristaltisme et la présence de nourriture non digérée dans le duodénum. Il a été déterminé que la cause secondaire était la sclérose systémique sans sclérodermie (ssSSc), soit une forme de sclérose systémique sans atteinte cutanée. Sclérose systémique sans sclérodermie. Nous présentons un cas intéressant de POIC secondaire à ssSSc.

Introduction
Chronic intestinal pseudo-obstruction (CIPO) is a rare disorder characterized by disruption of intestinal motility causing features mimicking obstruction.1 It could be idiopathic or caused by a variety of infectious, neurologic, endocrine, genetic, autoimmune, or iatrogenic etiologies.1 Systemic sclerosis sine scleroderma (ssSSc) is a classification of systemic sclerosis without skin involvement. We highlight an interesting case of CIPO secondary to ssSSc.

Case Report
The patient is a Caucasian 52-year-old woman referred to the gastroenterology clinic with chronic complaints of unintentional weight loss of 53 kg, abdominal pain, vomiting, and constipation, along with a new cough. She was admitted from clinic to an academic internal medicine service because of hypotension, and gastroenterology was consulted.

She had a medical history of Raynaud’s phenomenon (RP) (with onset reported within the last few years), anxiety,
gastroesophageal reflux disease (GERD), peptic ulcers, chronic common bile duct (CBD) dilation, and chronic constipation. She was a former smoker, grew up on a farm, and had no allergies, but her mother had systemic lupus erythematosus (SLE). Her medications included docusate, diazepam, omeprazole, ondansetron, and magnesium oxide. Review of systems was positive for 10 minutes of daily morning stiffness and arthralgia in the bilateral hands and feet and right shoulder.

For the prior 2 years, she had multiple hospital admissions and clinic visits for these symptoms. On multiple occasions, Computed Tomography (CT) scan with contrast demonstrated dilated small bowel loops with air fluid levels and no transition point and a dilated CBD. Abdominal free air was identified during a visit to an emergency department for abdominal pain. An exploratory laparotomy was conducted and a healed perforation was presumed. On physical examination, she appeared cachectic with a body mass index (BMI) of 15.4 kg/m². She had bilateral coarse expiratory crackles, periumbilical tenderness, hypoactive bowel sounds, bilateral Heberden and Bouchard nodes, and tenderness to palpation of the right shoulder, bilateral proximal interphalangeal joints, and bilateral metatarsophalangeal joints. She had no skin changes or edema.

Initial laboratory investigations revealed hypoalbuminemia of 14 g/L and macrocytic anemia with hemoglobin of 97 g/L and mean corpuscular volume of 101.4 fL. Electrolytes, creatinine, and urinalysis were unremarkable. Liver function tests were notable only for an elevated aspartate transferase of 50 U/L.

During this hospitalization, CT scans again demonstrated dilated small bowel loops with air fluid levels, no transition point, and a dilated CBD (Figure 1). Scans also revealed a dilated fluid-filled esophagus and a cavitary lesion in the left lung apex. Esophagogastroduodenoscopy (EGD) identified aperistalsis, residual duodenal food after an overnight fast, and duodenal wall atrophy, friability, and erythema with acute inflammation on biopsy (Figure 2). CIPO was diagnosed due to the re-demonstrated radiological findings, aperistalsis, undigested duodenal food, and presentation of weight loss with episodic symptoms of obstruction. This prompted work-up to identify the underlying cause of CIPO in this patient, involving consults to infectious diseases, respirology, and rheumatology services.

Bacterial and fungal cultures were negative as were assays for various endemic fungi, mycobacteria, and respiratory viruses. The only exception was positivity for rhinovirus. She had normal measurements of angiotensin-converting enzyme, creatine kinase, C-reactive protein, and erythrocyte sedimentation rate. Bronchoscopy yielded no positive infectious or pathological findings, but led to presumption of necrotizing pneumonia causing the lung lesion. Serum was strongly positive
for antinuclear antibodies (ANA) (1:1280, speckled). The patient had titers above the normal limit for the following antibodies: anti-centromere (>8.0 antibody index [AI]; reference range [ref.]: 0–0.9 AI), anti-mitochondrial (122.6 units [U]; ref.: 0–20 U), anti-histone (2.1 U; ref.: 0–0.9 U), anti-Smith (30.5 U; ref.: 0–19.9 U), and anti-ribonucleoprotein (96 antibody units [AU]/mL; ref.: <90.40 AU/mL). The patient had titers within the normal reference range of the following antibodies: anti-citrilullinated protein, rheumatoid factor, anti-double stranded DNA, anti-Hu, anti-F-actin, anti-Jo-1, anti-Scl-100, anti-Scl-70, anti-Sjögren’s syndrome type A (anti-SSA), anti-Sjögren’s syndrome type B (anti-SSB), and anti-RNA polymerase III antibodies. Despite the elevated levels of anti-mitochondrial antibody level, further work-up of primary biliary cholangitis was not pursued, given the patient’s normal alkaline phosphatase level and lack of other characteristic signs and symptoms. Echocardiogram was normal and showed no evidence of pulmonary hypertension. She did not undergo nailfold capillaroscopy. After receiving antibiotics and medications to manage gastrointestinal symptoms, she tolerated substantial oral nutrition, and was discharged.

After 4 months, the patient lost 5.4 kg and was still symptomatic. Pulmonary function test done as an outpatient was unremarkable. Her most likely diagnosis was ssSSc. She was treated with hydroxychloroquine for her joint pain and with promotility agents for her gastrointestinal symptoms. Although she continued to have RP and constipation even after 8 months of discharge, she regained 1.4 kg, had less significant arthralgia, and her vomiting and abdominal pain were well-controlled.

Discussion
CIPO is a rare disorder characterized by disruption of intestinal motility, causing features mimicking obstruction. According to a Japanese study, it affects 0.9 in 100,000 adults by the mean age of 61 years. Many pathophysiologic mechanisms are responsible for CIPO, which variably affect smooth muscle cells (SMCs), interstitial cells of Cajal, or enteric neurons. While the majority of CIPO patients are idiopathic, many secondary etiologies cause CIPO, including the following: infectious (Chagas), neurologic (stroke, Parkinson’s disease, Hirschsprung’s disease), paraneoplastic (carcinoid tumors, central nervous system [CNS] neoplasms, leiomysarcomas), endocrine (diabetes, hypothyroidism, and hypoparathyroidism), genetic (Duchenne muscular dystrophy, mitochondrial, neurogastrointestinal, encephalomyopathy, and other neuronal or SMC mutations), autoimmune diseases (systemic sclerosis, SLE, and dermatomyositis), or iatrogenic causes (radiation, antidepressants, antiparkinsonian agents, and antineoplastics).

Diagnosis of CIPO is challenging as it inconsistently affects parts of the gastrointestinal tract. Small bowel involvement causes weight loss and vomiting; large bowel involvement causes abdominal pain, distension, and constipation; and esophageal involvement causes dysphagia and gastroesophageal reflux. Biliary dilation can occur, especially in SLE patients. Our patient had many nonspecific gastrointestinal diagnoses such as GERD, “chronic constipation,” and “chronic CBD dilation,” all of which may be explained by CIPO. The clinical course is episodic with exacerbations often caused by bacterial or viral infections, probably both of which occurred in our patient with pneumonia and rhinovirus positivity. Diagnosis is usually confirmed with motility studies, but given the characteristic radiologic and endoscopic findings, clinical presentation, and putative etiology, further confirmation of CIPO was unnecessary.

In secondary CIPO, treatment involves optimizing nutritional and electrolyte balance, managing gastrointestinal symptoms, treating complications such as intestinal failure and small intestinal bacterial overgrowth, and treating the underlying cause. Systemic sclerosis (SSc) is a rare disease that typically causes fibrosis of the skin with classic skin thickening and fibrosis of internal organs such as the gastrointestinal tract, lungs, heart, and kidneys. It has a pooled prevalence of 22 cases per 100,000 population. Among all ethnic groups worldwide, the prevalence of SSc is widespread among the indigenous people of Canada at 47 cases per 100,000 population. SSc is thought to affect the gastrointestinal tract through vasculopathy, which induces ischemia and death of enteric neurons. Denervation of the gastrointestinal tract then leads to muscular atrophy. ssSSc is a subset of SSc that does not affect the skin, but similar to SSc, it still affects the peripheral vascular system. It should be noted that controversy exists in the rheumatologic community on whether ssSSc comprises a unique disease state or is simply a subset of limited cutaneous systemic sclerosis, which has not yet fully manifested. ssSSc is thought to comprise about 10% of patients with SSc. In Poormoghim et al.’s defining case series of ssSSc, including 68 patients with ssSSc, 70% of such patients had gastrointestinal involvement, while 71% had pulmonary involvement, 26% had cardiac involvement, and 4% had renal involvement. Despite the gastrointestinal tract being a very commonly involved internal organ system, in just 10% of instances, patients with SSc only present with a gastrointestinal complaint as their initial symptom. While there exists no single treatment to reverse the pathogenesis of SSc and its subtypes, treatment is directed at individual manifestations of disease on an organ-specific level in addition to periodically monitoring for disease progression to new organ systems. The most likely unifying diagnosis of the patient’s condition is ssSSc with internal organ involvement limited to the gastrointestinal
system. This is supported by the classification criteria intended by Poormohghim et al., who proposed that patients should be considered to have this diagnosis if they possess all of the following features: absence of skin thickening; peripheral vascular involvement (RP, digital pitting ulcers, digital-tip gangrene, or abnormal nailfold capillaries); positive ANA; evidence of internal organ involvement of the gastrointestinal tract (distal esophageal or small bowel hypomotility), pulmonary (interstitial fibrosis or pulmonary hypertension), cardiac, and/or renal systems; and absence of any other defined connective tissue disorder or clear alternative cause for any of the aforementioned manifestations. Presence of anti-centromere antibodies further supports this diagnosis. In our patient, skin thickening was absent, but had a history of RP, a strongly positive ANA titre along with a positive anti-centromere antibody titre, evidence of distal esophageal hypomotility (dilated fluid-filled esophagus on CT) and small bowel hypomotility (aperistalsis on EGD), and lack of any other connective tissue disease or explanation for these manifestations. Despite having auto-antibodies characteristic of SLE and mixed connective tissue disorder, she did not have other convincing features of these conditions.

This patient highlights a unique case of ssSSc presenting initially with gastrointestinal symptoms leading to a diagnosis CIPO. This represents a rare phenotype of patients with SSc, which is itself an already rare condition. We demonstrate that once CIPO is diagnosed clinically, it requires a thorough diagnostic work-up to understand the underling etiology to employ disease-targeted treatment.

Author contributions
M Edwards collected the data, and drafted and edited the manuscript. J Ray and A Al-Taee critically reviewed the manuscript. E Marsicano critically reviewed and oversaw writing of the manuscript.

Disclosure
The authors declare no conflicts of interest. Informed patient consent was obtained for this case report.

References