

## Sporadic Visceral Myopathy: Full Thickness Rectal Biopsy to Clinch the Diagnosis

Swapna B Reddy, Christopher M Hamerski, Sheetal S Gavankar, Zarema J Singson, Suvarna Deshmukh-Rane, Joseph C Carmichael, Mark Li-cheng Wu, George V Lawry, Robert H Lee, Gregory C Albers, Nimisha K Parekh

Swapna B Reddy, Christopher M Hamerski, Sheetal S Gavankar, Zarema J Singson, Suvarna Deshmukh-Rane, Joseph C Carmichael, Mark Li-cheng Wu, George V Lawry, Robert H Lee, Gregory C Albers, Nimisha K Parekh, University of California, Irvine Medical Center, 101 The City Drive, Orange, CA 92868, the United States

Correspondence to: Swapna B Reddy, MD, 2150 South State College Blvd. #3001, Anaheim, CA 92806, the United States. [sbreddy@uci.edu](mailto:sbreddy@uci.edu)

Telephone: + 1-510-754-7685

Received: February 9, 2012

Revised: March 20, 2012

Accepted: March 26, 2012

Published online: September 21, 2012

Rane S, Carmichael JC, Wu ML, Lawry GV, Lee RH, Albers GC, Parekh NK. Sporadic Visceral Myopathy: Full Thickness Rectal Biopsy to Clinch the Diagnosis. *Journal of Gastroenterology and Hepatology Research* 2012; 1(8): 161-164 Available from: URL: <http://www.ghrnet.org/index./joghr/>

### INTRODUCTION

Chronic intestinal pseudo-obstruction (CIPO) results from dysfunctional intestinal nerves or muscles. Clinical manifestations may include nausea, vomiting, diarrhea, constipation and abdominal pain. The majority of adult cases of CIPO are due to secondary causes that include connective tissue disorders, endocrinopathies, infections, neuromuscular disorders, medications, and idiopathic myenteric ganglionitis. Primary causes of CIPO are uncommon and include familial and sporadic visceral neuropathies and myopathies. Visceral myopathy may be characterized by CIPO, ureterohydronephrosis, and hepatobiliary dilation<sup>[1]</sup>. The diagnosis is made by the clinical history and characteristic findings of fibrous replacement of the muscularis propria, vacuolar degeneration, and cytoplasmic inclusions in myocytes on a full thickness specimen of affected viscera. Familial hollow visceral myopathy has been reported in both children and adults. In contrast, few cases of adult sporadic hollow visceral myopathy (SHVM) are described in the literature<sup>[2-5]</sup>. Clinicians may find making the diagnosis difficult early in a patient's clinical course. Furthermore, the management of patients with SHVM is challenging, particularly if the entire gastrointestinal (GI) tract is involved. Here, we present a case of abrupt onset SHVM in an adult involving the entire GI, biliary, and urinary tract.

### CASE REPORT

A 35-year-old Mexican woman with no significant past medical history was admitted to our medical center in October 2010 with intractable nausea, vomiting, abdominal discomfort, and diarrhea for two months. She had lived in the United States for the past 15 years, working as a housekeeper. Her four children were healthy. She did not use tobacco, alcohol or drugs, and had no significant family history of gastrointestinal diseases. Her most recent history included a one-year stay in Acapulco, Mexico, which was uneventful. However upon her return to the U.S. on foot, she was abducted, held,

### ABSTRACT

Chronic intestinal pseudo-obstruction (CIPO) may result from dysfunctional intestinal nerves or muscles. Primary causes are uncommon and include familial and sporadic visceral myopathies. Visceral myopathy may be characterized by CIPO, ureterohydronephrosis, and hepatobiliary dilation. The diagnosis is made by the clinical history and characteristic findings of fibrous replacement of the muscularis externa, vacuolar degeneration, and cytoplasmic inclusions in myocytes on a full thickness specimen of affected viscera. Few case reports highlight sporadic hollow visceral myopathy (SHVM) in an adult involving the entire GI, biliary, and urinary tract. We present a unique case of abrupt onset of CIPO, biliary and urinary tract dilation in a 35-year-old Mexican woman, initially presumed to have lupus enterocolitis, and after failure to respond to immune modulating therapy, diagnosed by full thickness rectal biopsy with SHVM. Early full thickness biopsy of affected viscera in patients presenting with CIPO with associated biliary and urinary tract dilation should be considered. Our case demonstrates the safety and adequacy of a full thickness rectal biopsy in making a diagnosis of SHVM.

© 2012 Thomson research. All rights reserved.

**Key words:** Visceral; Myopathy; Hollow; Pseudo-obstruction; Sporadic; Hepatobiliary dilation; Ureterohydronephrosis

Reddy SB, Hamerski CM, Gavankar SS, Singson ZJ, Deshmukh-

and eventually released under ransom in Tijuana. The patient was in her usual state of health upon her return to the United States for two weeks until she developed constant nausea, frequent bilious vomiting up to six times daily, diffuse abdominal discomfort, and watery diarrhea up to eight times daily. She had an associated thirty-pound unintentional weight loss. She initially presented to a community hospital in September 2010, where stool studies, esophagogastroduodenoscopy (EGD), and colonoscopy were unremarkable. The patient was discharged with anti-emetics and anti-diarrheal medications. The next day, she presented to our medical center.

On initial consultation, physical examination showed the following information: body temperature was 36.8°C, blood pressure 109/74, pulse 74, respirations 18 breaths per minute, weight 58 kg (128 pounds) and height 5 feet 5 inches (165 centimeters). She was a thin woman, in no distress with temporal muscle wasting. Her abdomen was distended and with diffuse tenderness to light palpation, but no rebound. The remainder of her exam was normal.

Laboratory tests were significant for low albumin (2.7 g/dL) and prealbumin (12.6 mg/dL), normocytic anemia (hemoglobin 9.6 g/dL, mean corpuscular volume 87 FL), elevated ferritin, low iron indices consistent with anemia of chronic disease, normal vitamin B12 and folate levels, vitamin D deficiency (total D2+D3=18 ng/mL, normal >30 ng/mL), positive anti nuclear antibody (>1:320), and positive anti-smith antibody (136 AU/mL). Complement levels were low on admission. Anti-double stranded deoxyribonucleic acid, SCL 70, and neuronal nuclear antibody were normal. Serologies were negative for Chagas disease, cytomegalovirus, Epstein Barr virus, entamoeba histolytica, human immunodeficiency virus, histoplasmosis, and viral hepatitis. Serum rapid plasma reagin and purified protein derivative subcutaneous test were negative and a serum quantitative tuberculosis gold was indeterminate. Stool studies were negative for clostridium difficile, shigella, salmonella, campylobacter, mycobacteria, ova and parasites, and giardia lamblia antigen. A 24 hour fecal fat was elevated to 20 g (normal 2-7 g/24 h). Computed tomography (CT) of the abdomen and pelvis was significant for diffuse, circumferential wall thickening and associated dilation of the small bowel, colon and rectum. There was also bilateral ureterohydronephrosis, thickened bladder with mild distention, distended biliary system, pleural effusions and ascites present. Magnetic resonance cholangiopancreatography (MRCP) confirmed distended gallbladder, common bile duct diameter up to 1.8 cm, dilation of intrahepatic ducts, and a pancreatic duct diameter up to 5 mm. There was sludge noted, but no evidence of biliary stones.

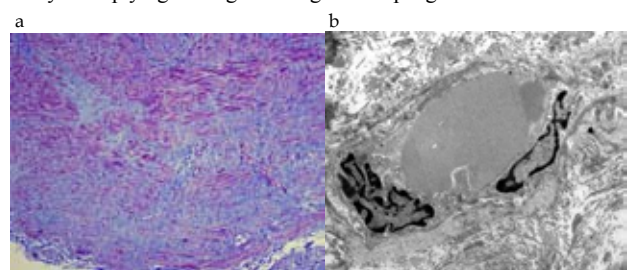


**Figure 1** Computed tomography: coronal view of patient's abdomen, demonstrating circumferentially thickened bowel and bladder wall. Diffuse distention throughout the bowel is notable.

The patient developed hematuria and dysuria several days after admission. Cystoscopy revealed moderate trabeculation of the bladder indicative of obstructive uropathy with no stones seen.

Biopsy of a lesion in the dome of the bladder showed mild, chronic inflammation. Urinalysis was positive for urinary tract infection. Bone marrow biopsy was unremarkable. A nuclear whole body ocreotide scan was negative for VIPoma. Diagnostic paracentesis showed a normal cell count and a serum ascites albumin gradient of 0.6, consistent with a non-portal hypertensive etiology. Cultures were negative including acid-fast bacilli. Two EGDs and colonoscopies were performed at our institution without significant mucosal disease endoscopically. Biopsies of the second portion of the duodenum showed mild nonspecific signs of inflammation with duodenal mild excess intraepithelial lymphocytes in villi, excess plasma cells, and moderate neutrophilic cells. Biopsies from the colonoscopy showed preserved architecture within the terminal ileum and right colon. Mild fibrosis was seen in the right colon submucosa. A surgical full thickness intestinal biopsy was deferred earlier in the hospital course over concern of her ability to heal after biopsy.

Given the patient's positive ANA and anti-Smith antibody, systemic lupus was considered. A renal biopsy revealed tubular vacuolar change, mild mesangial immunoglobulin, complement and electron dense deposits, possibly consistent with Class II lupus nephritis. Based on this biopsy result and that lupus may be a secondary cause of CIPO, a presumptive diagnosis of lupus enterocolitis was made and the patient was started on high dose intravenous (IV) steroids without response. She subsequently received cyclophosphamide 800 mg IV and rituximab 1 g IV without clinical improvement. All anticholinergic and opioid medications were held and the patient ambulated several times daily, without improvement in her symptoms. Neostigmine was given without significant effect. Despite this treatment, the patient failed to have resolution of nausea, vomiting, abdominal discomfort, or diarrhea. Imaging showed incomplete resolution of patient's diffuse bowel wall thickening and dilation. A gastric emptying study of liquids showed delayed emptying and significant gastroesophageal reflux.



**Figure 2** (a) Trichrome-stained section of specimen from transmural rectal biopsy showing interstitial fibrosis of outer longitudinal layer of muscularis propria (200X). (b) Electron micrograph showing homogeneous, electron-dense intracytoplasmic inclusion (8 µm x 4.6 µm) within degenerated myocyte (1100X).

Based on her failure to improve, the presumptive diagnosis of lupus enterocolitis was called into question and a full thickness transmural rectal biopsy was performed. This biopsy showed changes suggestive of visceral myopathy, in muscularis propria and muscularis mucosa encompassing extensive delicate and interstitial fibrosis, highlighted by trichrome and reticulin stains. The fibrosis was worst in the outer longitudinal layer of muscularis propria in the absence of inflammation and accompanied by vacuolar degeneration. A periodic acid-Schiff stain failed to reveal intracytoplasmic inclusions. There was associated neuronal hyperplasia in Henle plexus and Auerbach plexus and mild fibrosis of the rectal submucosa and perirectal fat. The rectal lamina epithelialis and lamina propria were normal. Electron microscopy showed extensive degeneration of myofibrils within myocytes. The degenerated myofibrils frequently aggregated into homogeneous electron-dense intracytoplasmic inclusions, which were

absent at conventional optical microscopy, even at retrospective review.

Based on this biopsy result, her correlating clinical picture, and lack of convincing secondary causes of visceral myopathy, this patient was diagnosed with sporadic hollow visceral myopathy.

After diagnosis, the patient was treated with rifaximin for presumed small bowel bacterial overgrowth (SIBO) and completed a fourteen-day course. She was started on erythromycin, metoclopramide, and octreotide without significant clinical improvement. A nasojejunal tube was placed, however even at a rate of 5 mL/h, the patient developed symptoms of nausea, vomiting, diarrhea, and worsening abdominal distention. Imaging confirmed worsened bowel distention after attempted feeding. Enteral nutrition was deemed a failure. A percutaneous endoscopic gastrostomy (PEG) tube was placed for venting purposes. An implantable venous access system was placed for long-term total parenteral nutrition (TPN). Patient was discharged home and upon follow up, was doing well off of enteral intake.

## DISCUSSION

Chronic intestinal pseudo-obstruction encompasses a varied group of disorders that may present diagnostic and treatment challenges to clinicians. This case demonstrates that a full thickness biopsy of affected bowel was essential to making a final diagnosis of sporadic hollow visceral myopathy. The full thickness biopsy allowed microscopic visualization of the myocytes within the affected viscera, which was crucial in making the diagnosis. The key histologic findings were extensive interstitial fibrosis and vacuolar degeneration, predominantly in the outer longitudinal layer of the muscularis propria under light microscopy. Intracytoplasmic inclusions within myocytes highlighted by periodic acid-Schiff stain described in a previous study<sup>[3]</sup> were absent in our case. However, electron microscopy demonstrated abundant homogeneous intracytoplasmic inclusions and aggregates of degenerated myofibrils and confirmed our diagnosis. The use of special stains such as trichrome and reticulin and electron microscopy. The key histologic findings were fibrosis in the muscularis propria and cytoplasmic inclusions within myocytes seen initially with trichrome and reticulin stains under light microscopy and confirmed by electron microscopy (EM). The use of immunohistochemical stains and EM will increase the sensitivity for diagnosing abnormalities<sup>[6]</sup>. As seen in this case, biopsies may be indicated in patients with severe intestinal motility disorders of unknown origin unresponsive to therapy or in patients who require either enteral or parenteral nutrition<sup>[7]</sup>. Concerns over poor healing in malnourished patients and possible septic complications in patients considered for full thickness intestinal biopsies can result in under-utilization of this diagnostic technique. In contrast, full thickness biopsies of the rectum, below the peritoneal reflection, may not carry the same risk of peritoneal complications. Therefore, full thickness rectal biopsies may serve as a more attractive option to clinicians and surgeons evaluating CIPO. Full thickness rectal biopsies to aid in diagnosing SHVM have been described previously in the literature<sup>[4]</sup>. This case adds to the current literature in encouraging transmural biopsies from an affected rectum for the diagnosis of SHVM.

Once SHVM was discovered, the patient's unresponsiveness to treatment for presumed lupus enterocolitis was understandable. SHVM is not felt to be an autoimmune process and immune modulating medications such as steroids, rituximab, and cyclophosphamide would not be expected to result in clinical improvement. Pro-motility agents such as erythromycin, metoclopramide, and octreotide were not effective due to the degree of fibrosis affecting this patient's GI tract muscularis propria. Symptomatically, she improved after a course

of rifaximin for presumed SIBO, abstinence of enteral nutrition, and routinely venting her gastrostomy tube. The malabsorption manifested by low albumin and prealbumin levels, along with high fecal fat content is likely a result of SHVM, exacerbated by SIBO. She may require further courses of antibiotics for SIBO. Her nutrition and hydration is maintained with TPN, which among its risks, carries a substantial possibility of venous catheter related infections and steatohepatitis that may lead to cirrhosis. SHVM is uncommon and there are no clear guidelines of how to approach therapy. In our review, we have found that pro-motility agents do not have a reproducible benefit for patients with SHVM<sup>[6,8]</sup>. Octreotide has shown some encouraging effect on patients with systemic sclerosis<sup>[9]</sup>, which is similar to SHVM in that it causes fibrosis within the muscularis propria. However, benefit for patients with SHVM requires further investigation. Decompressive stomas, rotating antibiotics to treat SIBO and urinary tract infections have been shown to be helpful<sup>[8]</sup>. There is no consensus regarding the treatment of patients with spontaneous visceral myopathy.

Our patient had involvement of the biliary system with elevated liver function tests with imaging evidence showing a distended gallbladder, intrahepatic and extrahepatic dilation. However, we do not have pathologic evidence of bladder or biliary duct muscularis propria to evaluate for fibrosis. Biliary involvement has been described in secondary<sup>[1,10]</sup> and primary, familial<sup>[11]</sup> visceral myopathies. We did not find published case reports of adult patients with new diagnosis of SHVM presenting with associated biliary involvement. In addition, bladder wall thickening and atony with resultant bilateral ureterohydronephrosis has been previously described in visceral myopathy<sup>[12-15]</sup>. SHVM may explain our patient's bladder atony causing stasis resulting in urinary tract infection and bilateral ureterohydronephrosis necessitating the placement of bilateral nephrostomy tubes. It is important to highlight these associations of biliary and urinary tract involvement with CIPO for several reasons. This triad may help assist in considering SHVM earlier in the patient's clinical course, prompting targeted diagnostic endeavors such as full thickness visceral biopsy and avoid costly, invasive procedures searching for other explanations for biliary, urinary, and intestinal dysfunction. Also, for management purposes biliary and urinary tract involvement prompts the clinician to be monitoring for signs of worsening liver and renal function as a result of cholestasis and hydronephrosis, respectively. Ultimately, because she has complete involvement of her GI tract, surgeries such as small bowel transplantation<sup>[11,16]</sup> and colectomy may also be considered in our patient. However, there is no strong evidence in the literature for the effectiveness of these treatments.

We have presented a unique case of abrupt onset of IPO, biliary and urinary tract dilation in an adult woman, initially thought to have presumed lupus enterocolitis, and after failure to respond to immune modulating therapy, diagnosed by full thickness rectal biopsy with SHVM. This case specifically demonstrates the utility of a full thickness rectal biopsy to provide the diagnosis when extensive diagnostic workup and therapeutic trials had failed. Unfortunately, treatment options for SHVM are limited, and patients may require long-term parenteral nutrition.

## REFERENCES

- 1 Chen YQ, Xue Q, Wang NS. Visceral muscle dysmotility syndrome in systemic lupus erythematosus: case report and review of the literature. *Rheumatol Int.*
- 2 Smith JA, Hauser SC, Madara JL. Hollow visceral myopathy: a light- and electron-microscopic study. *Am J Surg Pathol* 1982; **6**: 269-275.
- 3 Fogel SP, DeTar MW, Shimada H, Chandrasoma PT. Sporadic visceral myopathy with inclusion bodies. A light-mi-

- croscopic and ultrastructural study. *Am J Surg Pathol* 1993; **17**: 473-481.
- 4 Leon SH, Schuffler MD. Visceral myopathy of the colon mimicking Hirschsprung's disease. Diagnosis by deep rectal biopsy. *Dig Dis Sci* 1986; **31**: 1381-1386.
  - 5 Montalvo P, Paz L, Chiappa E, Aronne S, Novelli M, Biain ME. [Intestinal pseudo-obstruction due to sporadic visceral myopathy]. *Medicina (B Aires)* 2004; **64**: 525-528.
  - 6 Mann SD, Debinski HS, Kamm MA. Clinical characteristics of chronic idiopathic intestinal pseudo-obstruction in adults. *Gut* 1997; **41**: 675-681.
  - 7 De Giorgio R, Sarnelli G, Corinaldesi R, Stanghellini V. Advances in our understanding of the pathology of chronic intestinal pseudo-obstruction. *Gut* 2004; **53**: 1549-1552.
  - 8 Heneyke S, Smith VV, Spitz L, Milla PJ. Chronic intestinal pseudo-obstruction: treatment and long term follow up of 44 patients. *Arch Dis Child* 1999; **81**: 21-27.
  - 9 Nikou GC, Toumpanakis C, Katsiari C, Charalambopoulos D, Sfakakis PP. Treatment of small intestinal disease in systemic sclerosis with octreotide: a prospective study in seven patients. *J Clin Rheumatol* 2007; **13**: 119-123.
  - 10 Pardos-Gea J, Ordi-Ros J, Selva A, Perez-Lopez J, Balada E, Vilardell M. Chronic intestinal pseudo-obstruction associated with biliary tract dilatation in a patient with systemic lupus erythematosus. *Lupus* 2005; **14**: 328-30.
  11. Koh S, Bradley RF, French SW, Farmer DG, Cortina G. Congenital visceral myopathy with a predominantly hypertrophic pattern treated by multivisceral transplantation. *Hum Pathol* 2008; **39**: 970-974.
  - 12 Puri P, Lake BD, Gorman F, O'Donnell B, Nixon HH. Megacystis-microcolon-intestinal hypoperistalsis syndrome: a visceral myopathy. *J Pediatr Surg* 1983; **18**: 64-69.
  - 13 Bonsib SM, Fallon B, Mitros FA, Anuras S. Urological manifestations of patients with visceral myopathy. *J Urol* 1984; **132**: 1112-1116.
  - 14 Higman D, Peters P, Stewart M. Familial hollow visceral myopathy with varying urological manifestations. *Br J Urol* 1992; **70**: 435-438.
  - 15 Ghavamian R, Wilcox DT, Duffy PG, Milla PJ. The urological manifestations of hollow visceral myopathy in children. *J Urol* 1997; **158**: 1286-1290.
  - 16 Lauro A, Zanfi C, Ercolani G, Dazzi A, Golfieri L, Amaduzzi A, Pezzoli F, Grazi GL, Vivarelli M, Cescon M, Varotti G, Del Gaudio M, Ravaioli M, Cucchetti A, La Barba G, Zanello M, Vetrone G, Tuci F, Catena F, Ramacciato G, Pironi L, Pinna AD. Italian experience in adult clinical intestinal and multivisceral transplantation: 6 years later. *Transplant Proc* 2007; **39**: 1987-1991.

**Peer reviewers:** Niels Halama, National Center for Tumor Diseases, Department of Medical Oncology / Department of Internal Medicine VI, University Clinic Heidelberg, Im Neuenheimer Feld 460, 69120 Heidelberg, Germany; Philip H. Gordon, Professor Surgery and Oncology, McGill University and Jewish General Hospital, 3755 Cote St Catherine Road, Montreal Quebec H3T 1E2, Canada; Sung-Bum Kang, Department of Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 300 Gumi-dong Bundang-gu, Seongnam-si, Gyeonggi-do, 463-707, Korea.