STONY BROOK UNIVERSITY MEDICAL CENTER

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Retroflections

DIVISION OF GASTROENTEROLOGY

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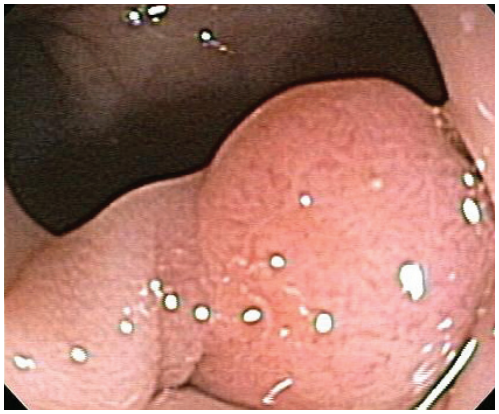
CUTTING-EDGE ENDOSCOPY

Chris E. Lascarides, MD

"The Never Failing Polypectomy"

On December 16, 2008, the first laparoscopic-assisted colonoscopic polypectomy was performed at Stony Brook University Medical Center. This was a groundbreaking, innovative collaboration between the Divisions of Gastroenterology and Colorectal Surgery to remove a large adenomatous polyp from the cecum of a patient using the combined techniques of colonoscopy with snare polypectomy and minimally invasive laparoscopy.

Colorectal adenomas are the precursors to colorectal cancer, and most are removed during colonoscopy. This is the backbone of colorectal



Large cecal polyp

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EDITOR'S NOTE

I am pleased to introduce this inaugural issue of *Retroflections*, the quarterly journal of the Division of Gastroenterology at Stony Brook University Hospital.

The mission of *Retroflections* is to highlight recent advances in gastroenterology in the form of brief reviews and case studies selected from our clinical material, and communicate the exciting advances that our Division is bringing to the practice of gastroenterology in our Hospital and, by extension, to Suffolk County and neighboring communities.

Retroflections is not just a catchy GI-related name but a symbol of what is the soul of our subspecialty: medical thinking, i.e., reflection on a patient's problem and technical skill. For those who are not gastroenterologists, an endoscopist will retroflex the endoscope to look back to better visualize the entire lumen of the intestine. Our completely reorganized Division focuses on these two principles, state-of-the-art endoscopy and high-level clinical scholarship.

Retroflections is the culmination of a lot of hard work of many individuals at our Medical Center. I thank Joyce Mormando, from our Endoscopy staff, who had the creativity to come up with the name of this journal; Bill Wertheim, whose participation in *Retroflections* and joint research with GI reflect the broad scope of our Division; and the contributors to this issue.

We hope to be part of your scholarly reading and spark improved patient care. I invite your feedback and comments and thank you for reading *Retroflections*. •

Chris E. Lascarides, MD
Assistant Professor of Medicine

CHIEF'S CORNER

Launching a new journal is no small undertaking under any circumstances. This is more so when a busy clinical service like GI is embarking on such an effort. The aptly named *Retroflections* has been conceived to provide a clinical and educational conduit linking our Division with our medical colleagues.

As Dr. Lascarides, the Editor-in-Chief, so eloquently describes in his inaugural note, the goals of *Retroflections* are both lofty and timely. Communication of events and ideas is now more important than ever. To remember the poet T.S. Eliot, it is evident from issue No. 1, that this journal provides not only information but also (and mainly) knowledge.

Retroflections is one of several recent developments in our Division. The many talented, energetic, and highly dedicated gastroenterologists that were recruited last year from leading schools have brought to our Division an expanded range of expertise and up-to-date clinical skills. More importantly, however, they have brought new energy and an enhanced sense of intellectual excitement. Indeed, with more recruitments underway and the expansion of our clinical activities the future of Gastroenterology at Stony Brook looks bright. We are now in a position to offer the best possible GI care in Suffolk County and beyond; support the broader gastroenterology community in the context of a leading academic center; and advance clinical knowledge in critical areas.

I want to congratulate all who contributed tirelessly and selflessly to this ambitious undertaking, and in particular Dr. Lascarides, who did a yeoman's job in putting this issue together. I am sure you will join me in wishing *Retroflections* the successful career it deserves.

Basil Rigas, MD, DSc
Professor and Chief
Division of
Gastroenterology
and Hepatology

CASE REPORT

Michael Harris, MD
Jonathan Buscaglia, MD

Endoscopic Pseudocyst Treatment

A 37-year-old man with history of idiopathic pancreatitis five months prior to admission presented with worsening left flank pain since his original diagnosis. The pain was described as dull, fluctuating, and worsened with movement. Physical exam revealed stable vital signs. He appeared well and his abdomen was soft without any palpable masses. Labs revealed normal LFTs and pancreatic enzymes. His white blood cell count was 14,000 cells/ml (normal 4.5-10 X 103) with a left shift. Abdominal/pelvic contrast enhanced CT revealed a cystic lesion adjacent to pancreatic tail measuring 5.7 X 2.3 cm *(Figure 1)*. ERCP revealed a normal caliber pancreatic duct and a "blush" near the tail suggestive of a communicating pseudocyst *(Figure 2)*. Transpapillary drainage was performed via sphincterotomy and placement of 5 Fr 3 cm pancreatic stent. The patient was discharged clinically improved.

He was then re-admitted two weeks later with worsening left sided flank pain associated with fever to 39.4 C. His white blood cell count was 25,000 cells/ml and repeat CT scan revealed slight enlargement of the pancreatic tail pseudocyst. Endoscopic ultrasound (EUS) examination revealed a large multi-lobulated heterogeneous cyst containing internal debris arising from the pancreatic tail *(Figure 3)*. A 19-gauge FNA needle was passed with a linear array therapeutic echoendoscope yielding thick viscous material resembling pus. A wire was passed into the cyst under fluoroscopy. The tract was dilated using a Soehendra Dilator™ up to 10 Fr followed by balloon dilatation to 12 mm. Following dilatation, pus could be seen entering the stomach via the cyst-gastrostomy tract. Two 10 Fr, 7 cm double pigtail stents were deployed with one end in the gastric lumen and the other in the cyst cavity *(Figure 4)*. His white blood cell count normalized and he continued to defervesce. He was sent home on oral antibiotics.

Discussion

The incidence of pancreatic pseudocyst development after acute pancreatitis is between 10 to 20% [1]. Although most resolve, persistent pseudocysts may develop leading to complications such as infection, hemorrhage, and biliary and gastric outlet obstruction. Drainage of these cysts can be performed surgically, percutaneously, or endoscopically. The latter can be done either transpapillary (TP) or transmurally (TM). Factors associated with successful endoscopic drainage include pseudocysts associated with chronic pancreatitis, cysts located in the pancreatic head, placement of multiple endoprostheses, and increasing experience of the endoscopist.[1] Although TP drainage is successful in 75 to 100% of patients[2,3] our patient failed therapy likely secondary to the distal location of the pseudocyst. TM drainage may be performed with or without EUS guidance. A recent prospective randomized trial[4] demonstrated significantly higher success with EUS compared to standard EGD. Finally, long-term follow up studies reveal treatment success up to 90% of patients treated with TM drainage.[5]

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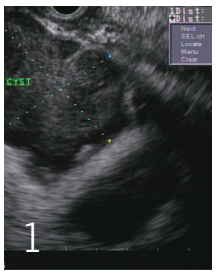
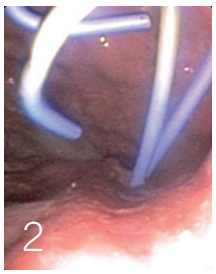
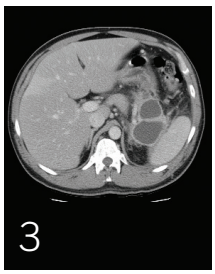
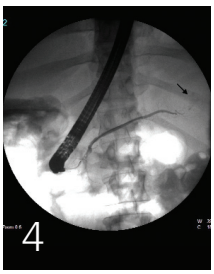




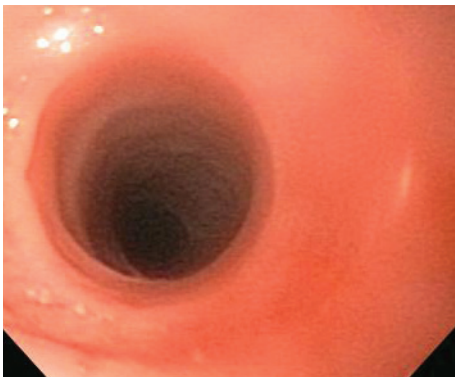




REVIEW ARTICLE

J. Brendan Wiggins, MD

Eosinophilic Esophagitis



Endoscopic view of eospinophic esophagitis

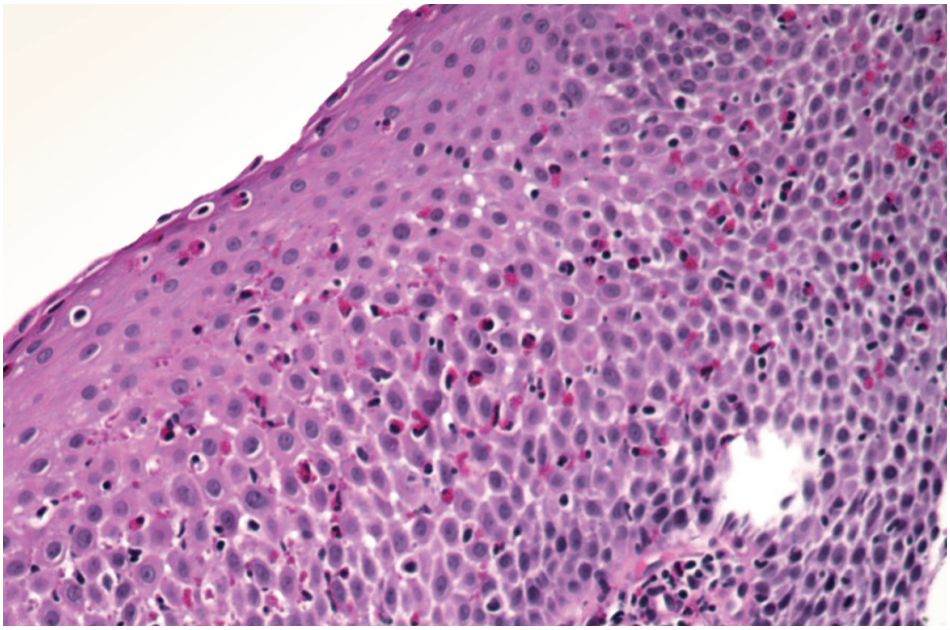
Eosinophilic esophagitis (EE), also known as allergic esophagitis, is an infiltrative disorder of the esophagus, which has been increasingly recognized as a cause for dysphagia and GERD symptoms unresponsive to anti-reflux measures. For reasons not understood, its incidence has been on the rise—with 4 individuals per 100,000 between 1986 and 1995 compared with 105 per 100,000 in 2007; a difference only partially explained by increased recognition. EE affects males more than females, and typically presents in the 20s and 30s. The exact pathogenesis of EE is unknown, but there is an association with allergies and atopic dermatitis.

The clinical manifestations of EE in adults include GERD and dysphagia with a significant proportion of patients experiencing food impaction. Esophageal dysmotility has also been observed, which may be suggestive of involvement of the muscular layers of the esophagus. Additionally, spontaneous esophageal perforation has been reported. The majority of patients have abnormal esophageal mucosal morphology by endoscopy, with the remainder showing only microscopic changes characteristic of EE.

Several morphologic features of EE have been described, with strictures (especially proximal strictures) being most common. Mucosal rings—single or multiple (so-called trachialization), linear furrowing, corrugation, whitish papules or granular exudates, and small caliber esophagus have all been described in the literature.

The diagnosis of EE should be considered for individuals with dysphagia but without objective evidence for GERD, and especially in young men with a history of food or environmental allergies. The diagnosis is generally based on the clinical presentation and presence of large numbers of eosinophils in the esophagus (>15 /HPF) in spite of acid suppression with PPI, as GERD itself has been associated with eosinophils in the distal esophagus. There are no diagnostic serum markers, although an association with elevated IgE has been reported. There are several histological features suggestive of EE including eosinophilic microabcesses, surface layering of eosinophils, papillary lengthening, degranulating eosinophils, basal cell hyperplasia, and lamina propria fibrosis. Several biopsies should be obtained along the whole length of the esophagus to maximize sensitivity.

Treatment of EE includes maximizing treatment with PPI as the first step. However, since PPI resistance is a cardinal feature of EE, further treatment is frequently needed. Fluticasone with MDI used without a spacer and swallowed (440 mcg BID) has been shown to be effective in both histologic and clinical improvement in a significant proportion of patients. Treatment should be continued for six to eight weeks. Several recent studies preliminarily have shown oral budesonide (as a viscous preparation) to be both more effective and with less side effects than fluticasone. Additional treatments that have shown some promise include food allergy testing and elimination of identified allergens, although the data is inconsistent. Relapse of symptoms is common upon discontinuation of treatment, and for those individuals, repeat treatment of four to six weeks is warranted, and long-term treatment may be needed. Endoscopic intervention may be needed for those requiring dilation; however, care must be taken as these individuals are at greater risk of esophageal rupture and deep mucosal tears. •



Histologic section showing eosinophilic esophagitis
Photo by Dr. Bernard Lane

Endosocpic Pseudocyst Treatment

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Comments

This case highlights the expanding role of EUS in therapeutic endoscopy. Transpapillary pancreatic stent placement in conjunction with pancreatic sphincterotomy is often insufficient in allowing for complete drainage of communicating pancreatic pseudocysts—especially in the setting of complicated cysts with internal necrotic or semi-solid debris, likely representing late pancreatic necrosis. For these patients, EUS is very helpful in facilitating safe access into the cyst cavity for transmural drainage and long-term fistula formation (i.e., cystgastrostomy or cystduodenostomy). Following endoscopic transmural decompression, patients are then followed clinically along with serial CT scans documenting resolution in the size of the pseudocyst and eventual endoscopic removal of the endoprostheses. •

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"The Never Failing Polypectomy"

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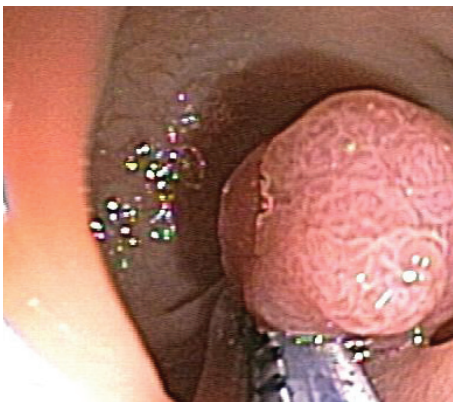


Endoscopic view of laparoscopic-assisted polypectomy

cancer screening and is the basis behind the risk reduction for colorectal cancer in a given individual. Some polyps, however, are not removed during colonoscopy. Polyps that are thought to be too large are not removed because of an increased risk for possible perforation during the polypectomy. Additionally, those polyps that are technically difficult to access are also left in place. Given the cancer risk of these lesions, patients in these clinical circumstances are subsequently referred to a colorectal surgeon for a partial colonic resection. These are generally straightforward procedures but are not without morbidity and mortality.

Chris Lascarides, MD, and Dr. Jonathan Buscaglia, MD, from the Division of Gastroenterology and Roberto Bergamaschi, MD, Chief of Colorectal Surgery, have fostered a close integrated relationship between these divisions since all three joined the faculty in mid 2008. This new close working relationship ignited the idea that perhaps something else could be done to spare a patient the potential morbidities and mortalities associated with a partial colon resection. In discussing the reasons for not removing these polyps, Dr. Bergamaschi suggested that he could help overcome these issues by combining a diagnostic laparoscopy with a colonoscopy done in the operating room. This dual approach allows for the mobilization of the colon to help align the polyp site in the proper safe orientation for the endoscopist to perform a complete polypectomy. Additionally any minor perforation can be detected on the spot and simply repaired by the laparoscopic surgeon using simple stapling techniques.

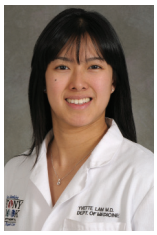
The sample taken from the polypectomy can be sent for a rapid frozen section pathologic assessment. If negative for carcinoma and high-grade dysplasia, the patient is closed and observed for 12 to 24 hours and sent home with his/her colon intact. If carcinoma or dysplasia is detected, then the procedure is converted into a partial colectomy with resection of mesentery and lymph nodes for tumor staging purposes. The patient does not need to come back for additional surgery.

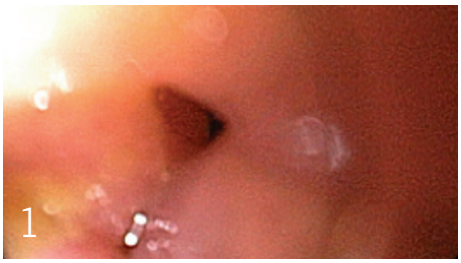
This index patient had a large polyp in the cecum that was tucked behind a fold. During diagnostic colonoscopy, the snare could not be safely placed around the entire polyp given its size and orientation. The polyp was left in place and the patient was brought to the OR on December 16 for laparoscopic-assisted colonoscopic polypectomy. The patient was prepped in the usual fashion for a diagnostic laparoscopy performed by Dr. Bergamaschi. The cecum and the terminal ileum were visualized and the terminal ileum was clamped to prevent back flow of air into the small bowel. At this point, colonoscopy was begun by Drs. Buscaglia and Lascarides and the colonoscope was advanced to the cecum. The polyp was in its usual suboptimal position but Dr. Bergamaschi was able to turn the cecum so that the polyp was flat in a six o'clock position. Submucosal saline injections were performed to help lift the polyp off the mucosa. The polyp was then easily removed in piecemeal fashion and recovered for pathologic evaluation. After determining that there was no significant bleeding and no perforation, the colonoscope was removed and the laparoscopy was completed. The patient tolerated the procedure well, was observed overnight, and sent home. •

CASE REPORT

A Duodenal Crohn's Disease Stricture

Yvette Lam-Tsai, MD
Ramona Rajapakse, MD





A 22-year-old Caucasian woman with a 6-year history of untreated upper GI and small bowel Crohn's disease presented with several months of worsening heartburn, left upper-quadrant abdominal spasms, early satiety, and 10 lb. weight loss. She denied dysphagia or odynophagia but she could only tolerate liquids without nausea or vomiting. She was previously treated with oral steroids and Pentasa® with mild improvement. Over the previous two years, she had turned to natural remedies for treatment. Her disease course had been complicated by rectovaginal fistula development four years ago. She continued to have 3 to 4 loose, non-bloody bowel movements daily.

Physical exam revealed a thin, young woman with mild epigastric tenderness. Laboratory data was normal. Upper endoscopy revealed a full stomach of residual food and liquid precluding complete evaluation. Repeat endoscopy revealed severe stenosis with erythema and edema at the pyloric channel which could not be intubated with a pediatric endoscope. Antral biopsies revealed moderate chronic inflammation but no granulomas or Helicobacter pylori. An upper GI series showed marked gastric distention with food debris *(Figure 1)* and a stricture with severe deformity of the duodenal bulb *(Figure 2)*. Patient was initiated on infliximab (Remicade®).

She underwent three consecutive upper endoscopies at monthly intervals with balloon dilation (up to a 15 mm dilator) and four-quadrant intramucosal triamcinolone injections at the pyloric channel stricture for treatment with successful results *(Figures 3-5)*. At six months follow up, the patient was able to eat a regular diet without difficulty and regained weight. During repeat endoscopy, the pyloric channel was patent and intubated with the endoscope *(Figure 6)*.

Discussion

Upper GI involvement of Crohn's disease is rare and occurs predominantly in younger patients. It has been reported in the literature to occur in 0.5% to 4% of patients with Crohn's disease who are diagnosed by clinical symptoms and radiological findings.[1,2] Most endoscopic findings are localized to the gastric antrum and duodenum. In this case, the patient presented with progressive signs of obstruction with early satiety, postprandial pain, nausea, vomiting, and weight loss. Aggressive treatment was indicated after discovery of the gastroduodenal stricture.

In the past, surgical intervention was considered the best option to manage gastroduodenal strictures with obstructive symptoms when conservative medical management, such as steroids and 5-ASA products, was unsuccessful. This was associated with greater complication and re-operation rates (27-38%, 33-70%).[6] A few case reports have reported that upper endoscopy with balloon dilation can be used successfully to treat Crohn's strictures.[3-5] This lowers morbidity rate, provides symptom-free intervals, and delays time to surgical intervention to allow for additional trials of medications to control active Crohn's disease.

Infliximab use in Crohn's strictures with proximal intestinal dilation is relatively contraindicated as it may worsen strictures. We therefore chose to combine Infliximab therapy with mechanical dilation using balloon dilators via the endoscope. This was highly successful in our patient who remains symptom free at one year without requirement for repeat dilations.

As treatment modalities for Crohn's disease become more sophisticated, the IBD specialist can, in many ways, intervene to prevent surgery. •

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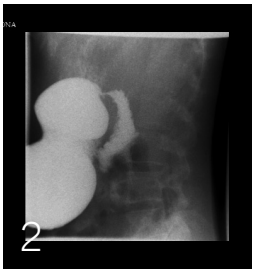
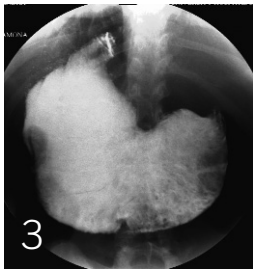
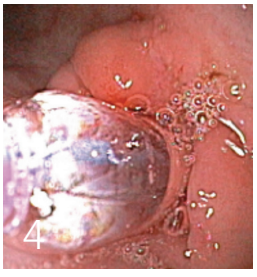
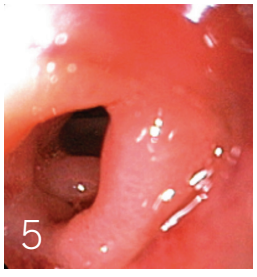
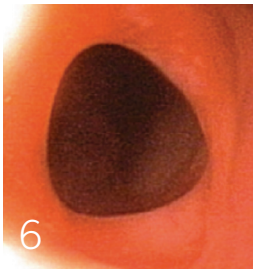
PHOTO KEY Figure 1: Pyloric channel stricture, Figure 2: Barium study demonstrating marked gastric distention with food debris, Figure 3: Tight ploric stricture with deformed bulb, Figure 4: Balloon dilatation, Figures 5 and 6: Post-procedure (immediately) and six-month results, respectively.





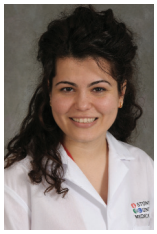






CASE REPORT

Leena Sayedy, MD
Robert Richards, MD



Unexplained Ascites

A 48-year-old Peruvian woman with a history of ESRD, initially requiring peritoneal dialysis for seven years then a cadaveric renal transplant presented with increasing abdominal distension since past two months. She denied having abdominal pain, nausea, vomiting, diarrhea, constipation, ankle edema, fevers, or chills. She was hospitalized four months ago for fluid retention for which she required hemodialysis for five days; the edema of her lower extremities improved but her abdominal distention persisted. During that hospitalization she had two large volume paracentesis and her SAAG was greater than 1.1 consistent with portal hypertension. The patient presented to us with prednisone 20 mg QD, Cellcept® 180 mg QD, Rapamune® 2 mg QD, Valcyte® 450 mg QD, Bactrim™ QIW, Lasix® 40 mg QD, Aldactone® 100 QD, Prevacid® 30 mg QD, and Procrit® 40,000 units once a week. Her other medical problems included HTN and surgical history consisted of cholecystectomy and right nephrectomy secondary to hematoma. She denied having a history of tobacco use, ETOH abuse, or IVDA. She denied having tattoos; was in a monogamist relationship and had received blood transfusions during her prior surgeries.

On physical exam her vital signs were stable. Her blood pressure was 137/72, her pulse was 97, her temperature was 97.9, her respiratory rate was 16, and she was oxygenating at 98% on room air. She was an otherwise thin woman with a distended abdomen. She had anicteric sclera, no jaundice, no spider angiomata, her lungs were clear, her heart sounds were normal, and her abdomen was soft, nontender, but distended with fluid shift; a caput medusa and hepatosplenomegally were not appreciated. There was no edema of her extremities.

Her pertinent laboratory data included a platelet count of 129, INR of 0.9, and albumin of 3.9. Her ANA, AMA, ASMA, hepatitis panel were all negative. Her ceruloplasmin level was normal and her transferrin sat was 66%. Peritoneal fluid showed a SAAG of 2.1; it was negative for malignancy and AFB. Her echocardiogram was normal. A RUQ sonogram with doppler flow showed a normal flow of hepatic and portal veins and no biliary dilatation. A CT of her abdomen showed large amount of ascites, and a normal size of liver and spleen. She then had a liver biopsy that showed hypertrophic and atrophic cells consistent with nodular regenerative hyperplasia. The pathology of her liver biopsy showed sinusoidal congestion, normal bile ducts, arteries, and portal veins. There was no necrosis, fibrosis, or inflammation seen.

Discussion

Nodular regenerative hyperplasia (NRH) is a non-cirrhotic cause of portal hypertension. It is characterized by rearrangement of hepatocytes into regenerative nodules, with minimal or no fibrosis. The condition is more common in the elderly. Autopsy studies show a prevalence of 0.72 to 2.6%. Under gross examination the liver consists of fine granules that are 1-3 mm in diameter. Under histological examination the nodules are composed of hypertrophic cells in the center with atrophic cells in the periphery. These nodules are clustered around the portal triads. The central veins are compressed by hypertrophied hepatocytes. There are a number of conditions associated with nodular regenerative hyperplasia. These include but are not limited to liver cancers, myeloproliperative disorders, Protein S deficiency, antiphospholipid syndrome, multiple myeloma, scleroderma, RA, SLE, atrial or ventricular septal defect, use of medications such as cyclophosphamide and azathioprine, or, as pertains to our patient, having a renal transplantation.

The pathogenesis of NRH is not fully known. One theory involves insufficiency of the portal vein as the cause of NRH. Thrombosis or occlusion of the portal vein due to hypercoagulability, endothelial injury, or autoimmune injury results in ischemia of liver and thereby hypertrophy and atrophy of hepatocytes. The clinical manifestations of NRH are related to portal hypertension such as ascites and varices. Most patients are asymptomatic and have normal liver synthetic functions. Encephalopathy is rare.

Treatment of NRH involves treating portal hypertension such as with diuretics and/or TIPS procedure. •

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FACULTY INTERVIEW

Interviewed by Juan Carlos Bucobo, MD

Jonathan Buscaglia, MD *Director of Endoscopy*

Each issue of *Retroflections* will include an interview with a member of the Stony Brook GI family. In this inaugural issue, we have chosen to interview one of our latest additions to the faculty and the new Director of Endoscopy at Stony Brook University Medical Center, Jonathan Buscaglia, MD. He specializes in advanced/therapeutic endoscopy and has brought an armamentarium of innovation to the University. He has a special interest in pancreatico-biliary disorders and performs various diagnostic and therapeutic procedures within the gastrointestinal tract.

Q How has your advanced endoscopy training at Johns Hopkins prepared you for what you have encountered at Stony Brook since joining the Division?

A "I feel that having done a two-year therapeutic endoscopy fellowship has really prepared me for the load of complex cases that I have been exposed to so far at Stony Brook. Although it often felt as though I would never finish my training, the second year of a third-tier fellowship was really helpful in solidifying my confidence in managing the most complex of cases that Hopkins had to offer."

Q The field of gastrointestinal endoscopy is rapidly growing, especially with the introduction of innovative diagnostic and therapeutic techniques. What do you see in the future for the field of gastroenterology?

A "The future of endoscopy, in my opinion, is headed further and further down the road of advanced intraluminal therapeutic techniques. Technology will continue to push our field forward, and it's up to us to use it in a manner that allows us to start better treating certain diseases in which we haven't been too successful in treating thus far. I think there will come a time when we begin to use endoscopic techniques to help manage such diseases and IBS and gastroparesis. This—I think—is the future of gastrointestinal endoscopy, and gastroenterology in general."

Q As the Director of Endoscopy at Stony Brook University Medical Center what changes are you making to keep up with emerging technologies?

A "Well, simply said, I want Stony Brook to serve as the outlet for local and regional gastroenterologists, oncologists, and surgeons to refer their most complex or difficult-to-manage cases. In order to do this, we need to be able to provide the skill, expertise, infrastructure, and equipment to handle such a population of patients. With significant support from the Medical Center, the School of Medicine, and the State, I have been able to acquire the most advanced endoscopic tools, and also hire additional faculty who are exceptionally competent in various aspects of GI endoscopy. Examples of this include our recent acquisition of the Spyglass™ direct visualization system for biliary and pancreatic ERCP, and expansion of our motility lab with esophageal impedance testing."

Q There is quite an interest in the emerging field of natural orifice transluminal endoscopic surgery (NOTES) within the surgical and GI communities. What are your feelings on NOTES? Do you think NOTES will become a commonly performed procedure by gastroenterologists?

A "I think the emergence of NOTES has done (and will continue to do) great things for gastrointestinal endoscopy. Although I think it's very unlikely that gastroenterologists will soon be performing outpatient cholecystectomy or appendectomy, I do think that NOTES will allow us to perform simple, straightforward diagnostic and therapeutic maneuvers in the peritoneal cavity such as staging peritoneoscopy in patients with cancer, or directed biopsy of certain abdominal organs. Furthermore, NOTES will push our limits in endoscopic research for treating those difficult to manage diseases like refractory GERD, achalasia, gastroparesis, etc."

Q It seems that your academic practice keeps you pretty busy. Do you have any time for activities outside the University? What are you hobbies?

A "Well, having three kids under the age of 6 years old doesn't leave much time for hobbies outside of medicine. I try and make it to the pool to swim laps about three days per week before coming into work, but that's sometimes easier said than done. When not working, I just enjoy being with my family and doing fun things with the kids." •

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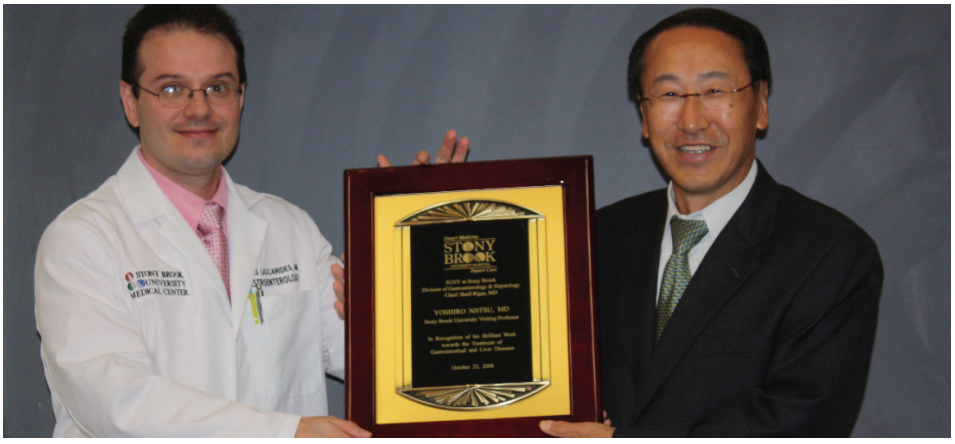
NEWSWORTHY

A Cure for Cirrhosis?

Stony Brook Hosts First U.S. Presentation of a New Treatment



Last December, Dr. Yoshiro Niitsu, an internationally recognized investigator, and Professor and Chairman, Department of Medicine, Sapporo University, Japan, was a Visiting Professor at Stony Brook University and a guest of our Division. Dr. Niitsu, pictured here receiving a plaque of recognition from Chris Lascarides, MD, presented his potentially revolutionary approach to the treatment of cirrhosis. In his talk, titled "Resolution of liver cirrhosis using siRNA against a collagen-specific chaperone," Dr. Niitsu presented how they used vitamin A-coupled liposomes to deliver small interfering RNA (siRNA) against gp46, the rat homolog of human heat shock protein 47, to hepatic stellate cells. Treatment with these siRNA-bearing liposomes resolved liver fibrosis and prolonged survival in rats with otherwise lethal liver cirrhosis.

Following their seminal publication in *Nature Biotechnology* (26:431-42; 2008), Dr. Niitsu's pioneering method received worldwide attention, including lengthy reports in major newspapers and the Internet. Dr. Niitsu's first talk in the U.S. on his novel treatment was at Stony Brook and was followed by a similar one at Harvard Medical School two days later. Our Division is currently exploring with Dr. Niitsu its participation in the planned first clinical trial of this treatment in humans. •