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The ACG Case Reports Journal was created to help fulfill ACG's commitment to providing growth and learning opportunities for GI fellows, and helps fellows meet core curriculum requirements for non-patient care activities. To this end, all case submissions must have a GI fellow or a resident interested in pursuing GI fellowship as the lead author. Cases authored by private practice clinicians and other members of the healthcare team who might traditionally face difficulty publishing with leading journals are also welcome.

PUBLISHER INFORMATION
Founded in 1932, the American College of Gastroenterology (ACG) is an organization with an international membership of more than 12,000 individuals from 86 countries. The College is committed to serving the evolving needs of physicians and other members of the health care team who might traditionally face difficulty publishing with leading journals.

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Colonoscopy showing a large cecal mass encompassing the majority of the cecum in a patient with ischemic colitis. (Image from Rabbanifard et al, page 100.)

MRCP showing native and graft pancreas. Graft pancreas divisum (large arrow) is confirmed with the duct of Santorini crossing over the bile duct stump of the graft (small arrow). The native pancreas and bile duct are seen in the conventional location cranially to the graft. (Image from Nawaz et al, page 103.)
LETTER FROM THE EDITOR

It is my pleasure to present the second issue of the ACG Case Reports Journal. This issue covers unusual but important clinical scenarios, interesting images, and novel endoscopic techniques. The members of the Editorial Board were again impressed with the number and quality of submissions. We are committed to providing an opportunity for young gastroenterologists and gastroenterology fellows to contribute to the literature, and are pleased by the overwhelmingly positive response to the Journal.

The current term for the Editorial Board will end in June 2014, and the invitation for new applications will be posted on our website within the next few weeks. I encourage all interested gastroenterology fellows who will still be in training through June 2015 to apply for a position. This experience will help prepare you for your future academic career by familiarizing you with the process and criteria of reviewing and publishing manuscripts. So far, it has been a fascinating experience to serve on the Editorial Board of a new journal. I have been honored to work in a friendly environment with other members of the Editorial Board and the ACG Publications Committee, and I am sure you will be delighted to be part of this too.

I hope you enjoy reading this issue of the ACG Case Reports Journal.

Mohammad Yaghoobi, MD, MSc, AFS
Editor-in-Chief
ACG Case Reports Journal
Unexpected Capsule Endoscopy Images Reveal Aspiration

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Case Report

An 83-year-old male inpatient was evaluated for iron-deficiency anemia after admission for near-syncope. He had prior history of mild occasional oropharyngeal dysphagia. Upper endoscopy and colonoscopy were normal. Video capsule endoscopy (VCE) was pursued.

The gastroenterologist who reviewed the VCE video 30 hours after administration quickly recognized images of the upper bronchi (Figure 1). The capsule remained in the bronchus throughout the entire 8 hours of recording. The patient, alert and in no distress, had reported difficulty swallowing the capsule; he also regurgitated it once before manually pushing it down his hypopharynx.

The video capsule was successfully removed from the right bronchus intermedius using flexible fiberoptic bronchoscopy. The patient tolerated the procedure well and recovered without further complications. He declined further endoscopic work up of his anemia. It was thought to be multifactorial due to chronic kidney disease and underlying myelodysplasia. He responded well to iron therapy and epoetin injections, with no further anemia. Few case reports exist in the literature of aspirated video capsules.1,2 This case serves to increase recognition of this possible adverse event.

Disclosures

Author contributions: H. Hussan wrote and edited the article, and is the article guarantor. TJ Paradowski obtained the images and wrote the article. CM Prather edited and approved the article.

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Informed consent was obtained for this case report.

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References

Chilaiditi’s Sign: A Rare Cause of Abdominal Pain

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Case Report

A 57-year-old woman with anxiety, depression, fibromyalgia, and bipolar disorder presented for evaluation of abdominal pain and constipation of 8 months duration. The pain was constant, gnawing, and occurred diffusely over her abdomen. The patient had associated increased gas and bloating. She had been having a bowel movement every 3 days without any bright red blood per rectum or melena. Bowel movements would improve the abdominal pain and bloating. There was no associated weight loss, fevers, or night sweats. Physical examination revealed a soft non-distended abdomen with normal active bowel sounds. The patient had diffuse tenderness supra-umbilically without any rebound or guarding. Laboratory tests, including a complete blood count, basic metabolic panel, and liver function tests, were unremarkable. CT scan of the abdomen revealed an abnormally malpositioned cecum and proximal right colon located within the right anterior subphrenic space immediately adjacent to the right lobe of the liver, consistent with Chilaiditi’s sign (Figure 1 and Figure 2). There was no evidence of obstruction or intraperitoneal free air.

Chilaiditi’s sign refers to a rare incidental radiologic finding where intestinal loops, especially colon, are malpositioned between the liver and the right hemidiaphragm. The incidence of Chilaiditi’s sign is less than 0.3% and the etiology may be congenital or acquired.¹ Acquired risk factors include chronic constipation, obe-
sity, multi-parity, ascites, liver atrophy, previous intestinal surgery, chronic lung disease, and paralysis of the right hemidiaphragm. Chilaiditi syndrome refers to the medical condition in which patients with Chilaiditi’s sign become symptomatic. The most common presenting symptoms are abdominal pain, distention, nausea, vomiting, and constipation. More morbid presentations include volvulus, cecal perforation, and perforated sub-diaphragmatic appendicitis. Rarely, patients present with respiratory symptoms including dyspnea and chest pain mimicking angina and require intensive care. The risk of an undiagnosed Chilaiditi’s sign is perforation during colonoscopy or liver biopsy. The best diagnostic imaging modality is CT scan. Conservative management should be attempted first to relieve constipation, pain, and distention. Surgery is rarely required and is reserved for patients who fail conservative management and in cases of obstruction, volvulus, or ischemia.

Disclosures
Author contributions: P. Jangouk acquired and interpreted the data, drafted the manuscript, and is the article guarantor. F Zaidi acquired the data and drafted the manuscript. JG Hashash acquired and interpreted the data, and drafted and critically reviewed the manuscript for important intellectual content.

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References
Pneumatosis Intestinalis: Do Not Excise These “Polyps”!

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Case Report

A 52-year-old male with a history of recurrent deep venous thrombosis underwent a CT scan of the chest investigating a suspected pulmonary embolism. The scan revealed thickening of the splenic flexure with foci of air adjacent to the colon (Figure 1). The patient reported mild nausea and chronic intermittent hemorrhoidal bleeding without abdominal pain. Physical exam and labwork were unremarkable. Colonoscopy to evaluate this radiographic finding demonstrated a corresponding cluster of cystic submucosal lesions of varying sizes with normal overlying mucosa consistent with pneumatosis intestinalis (Figure 2). The patient was discharged home and is being followed up in the gastroenterology clinic.

First described in 1783 by Du Vernoi, pneumatosis intestinalis is an uncommon but important condition in which gas is found in a linear or cystic form in the submucosa or subserosa of the bowel wall. Pneumatosis intestinalis is a sign rather than a disease, and is generally seen in the fifth to eighth decade of life. Although the exact etiology is not clear, multiple hypotheses have been proposed. The most popular theory posits dissection of gas into the bowel wall from either the intestinal lumen (as seen in necrotizing enterocolitis) or from the lungs via the mediastinum (as seen in patients with chronic obstructive pulmonary disease). Although up to 15% of cases may be benign with idiopathic etiology, this sign may be a harbinger of life-threatening pathologies such as bowel ischemia, obstruction, or toxic megacolon. On barium studies and endoscopy, it may appear similar to polyps; therefore, recognition of this condition is very important in order to avoid inadvertent resection that can potentially lead to complications such as frank perforation.

Disclosures

Author contributions: B. Shah wrote the manuscript and chose the images. K. Anna performed the procedure, assisted with images, and is the author guarantor. P. Sengodan formatted the images and wrote the
references. H. Kale supervised the process and made revisions to the manuscript.

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References

A Rare Case of Childhood Undifferentiated Embryonal Sarcoma of the Liver Managed Successfully

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Case Report

A 13-year-old boy presented with low-grade fever, upper abdominal pain, loss of appetite, and weight loss for 2 months, with a history of swelling in his upper abdomen for 15 days. On examination, a 17 x 20-cm intraabdominal, smooth, firm, non-tender swelling was noted occupying epigastric and left hypochondrium. The mass moved with respiration, and finger insinuation between mass and right coastal margin was not possible. There was no ascites and further examination was unremarkable. Liver function tests and α-fetoprotein were normal.

CT scan of the abdomen showed a homogenously enhancing mass lesion of 14.9 x 12.9 cm in the left lobe of the liver with multiple vascular structures traversing the lesion consistent with hepatocellular carcinoma (Figure 1). Non-anatomical left hepatectomy was done. Intraoperative examination revealed a 15 x 20-cm lesion arising from the inferior aspect of the left lateral segment of the liver, adhered to the stomach along the lesser curvature (Figure 2). Cut specimen showed solid tumor with cystic areas of hemorrhage and multiple vascular structures traversing the tumor (Figure 3).

Figure 1. CT scan of upper abdomen (axial and coronal sections) showing homogenously enhanced mass lesion of 14.9 x 12.9 cm in left lobe of liver, with multiple vascular structures traversing the lesion suggestive of hepatocellular carcinoma.
Postoperatively, 1 unit of packed red blood cell transfusion was given and the patient was discharged on postoperative day 8. Histopathological examination reported a tumor predominantly showing spindle cells arranged in sheets embedded in myxoid stroma. Vimentin was strongly positive. Desmin, carcinoembryonic antigen, and α-fetoprotein were negative. This suggested undifferentiated embryonal sarcoma of liver (UESL; Figure 4), a rare, highly malignant neoplasm that is more common in children. Bone scan was normal. Adjuvant chemotherapy was given. The patient is now asymptomatic on regular follow-up. We stress the role of histopathology and IHC in diagnosing UESL and of timely en bloc resection and postoperative chemotherapy in improving survival rates.

Disclosures

Author contributions: All the authors contributed to evaluating and managing the case and to writing the manuscript. GR Gondu is the article guarantor.

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Enterocutaneous Fistula From A Billroth II Afferent Limb: Successful Closure With Endoclips

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Abstract

Recently, indications for endoscopic clips have expanded to include closure of gastrointestinal fistulae and perforations. A 62-year-old man with remote history of surgery for peptic ulcer underwent right hemicolectomy for a large hepatic flexure mass with proximal colonic dilatation. During surgery, inadvertent pinpoint duodenotomy of the afferent Billroth II limb resulted in a duodeno-cutaneous fistula. Despite total parental nutrition, cutaneous bile drainage persisted. The duodenal fistula was closed during upper endoscopy using three endoclips. Cutaneous bile drainage stopped, and the abdominal wall defect healed. This is the first published case of endoclip closure of an iatrogenic duodenal fistula from a Billroth II afferent limb.

Introduction

Use of endoscopic clips was first described in 1975 as a novel method for management of gastrointestinal bleeding.1 Over the next 2 decades, endoclips were extensively employed in Europe and Japan, and they are now widely used in the United States.2,3 No consensus guidelines exist for the use of endoclips for other indications. Recent case reports describe more expanded utility to include closure of gastrocutaneous fistulae and viscus perforations.4-7 The ability to treat such breaches in intestinal continuity endoscopically and avoid surgery has great potential for shortening hospital stays and decreasing patient morbidity and mortality. We report a patient with prior Billroth II surgery who developed a duodeno-cutaneous fistula following laparotomy to resect a hepatic flexure colon mass. Spontaneous closure of the fistula did not occur after several months of conservative treatment including total parenteral nutrition. Another surgery for fistula closure was contemplated. Prior to operation, upper endoscopy to assess the duodenum was requested by the surgical service.

Case Report

A 62-year-old man was first seen in the gastroenterology clinic complaining of abdominal pain and weight loss. He had a history of partial gastrectomy and vagotomy performed 25 years earlier for treatment of peptic ulcer disease. He reported 6 months of mild postprandial epigastric pain and 15 pounds of unintentional weight loss. He denied nausea, vomiting, melena, hematochezia, and change in bowel habits. Five years earlier, upper endoscopy revealed Billroth II anatomy consistent with his reported ulcer surgery. Colonoscopy performed at that time was significant for a 30-mm tubulovillous adenoma in the descending colon, which was completely resected via snare polypectomy.

Physical examination revealed evidence of prior abdominal surgery and mild tenderness to palpation in the right upper quadrant without guarding or rebound. On colonoscopy, there was an obstructing, near circumferential...
Closure of Enterocutaneous Fistula with Endoclips

Voellinger et al

Figure 1. (A and B) Large polypoid appearing mass at the hepatic flexure. (C) Fistula orifice originating from afferent Billroth II duodenal limb. (D) Three standard endoclips deployed with successful closure of fistula orifice.

mass at the hepatic flexure (Figure 1A and Figure 1B) preventing further advancement of the colonoscope. Multiple biopsies of the mass were taken. CT scan of the abdomen performed on the same day reported a 4.9 x 2.9-cm hepatic flexure mass with circumferential narrowing and a dilated, air-filled colon proximal to the lesion. Endoscopic biopsies of the mass showed normal colonic mucosa. Repeat colonoscopy 3 weeks after the initial procedure showed a similar endoscopic appearance, and biopsies of the mass were again negative for neoplasia.

The case was presented at the institution’s tumor board, and a collective decision was made to perform an open right hemicolectomy, given radiologic and endoscopic appearance suggesting a hepatic flexure colon cancer. At surgery, both the afferent limb of the duodenum and the gallbladder were tightly adherent to the colon in the area of the hepatic flexure, and the gallbladder contained multiple gallstones. During the right hemicolecctomy and cholecystectomy procedure, a pinpoint duodenotomy occurred. The duodenal perforation was sutured, and a percutaneous drain was placed in the gallbladder fossa adjacent to the duodenotomy site. Pathology of the resected colon showed marked acute and chronic serositis with associated fibrosis, but no malignancy or neoplasia was evident.

Significant percutaneous drainage of bile occurred in the immediate postoperative period and persisted over the next 2 months, despite a trial of total parenteral nutrition. Fistulogram revealed an enterocutaneous fistula arising from the afferent limb of the Billroth II anastomosis with contrast entering the stomach via the gastojejunostomy. Upper endoscopy was performed in anticipation of surgery to close the fistula, and the duodenal opening of the fistula was easily identified in the afferent limb of the Billroth II anastomosis (Figure 1C). Three standard endoclips were used to approximate the fistula opening (Figure 1D), resulting in immediate and lasting cessation of percutaneous bile drainage. The patient was discharged from the hospital 2 days after endoscopic clipping. At 1 month follow-up, the patient reported no leakage of intestinal contents, and the abdominal wall fistulous site had closed.

Discussion

Postoperative enterocutaneous fistulae present a therapeutic challenge. Traditionally a complication requiring surgical intervention, development of a number of endoscopic devices/therapeutics, including fibrin tissue sealant/adhesive and endoclips, has led to several non-surgical methods for management of enterocutaneous fistulae.

Endoscopically-placed endoclips for management of small gastrointestinal perforations was initially described in 1995 when Wewalka et al successfully closed a small esophageal perforation that developed after pneumatic dilatation for achalasia.4 In 2003, Familiari et al described endoclip closure of a colocutaneous fistula, which occurred following an episode of necrotizing pancreatitis.5 Gastrocutaneous fistula, which occasionally occurs after removal of a percutaneous gastrostomy tube, also lends itself to endoclip closure.6,9 In our case, extensive adhesions secondary to the patient’s prior Billroth II surgery and chronic cholecystitis resulted in a complex mass involving the hepatic flexure of the colon, the gallbladder, and the duodenal portion of the Billroth II afferent limb. Extensive dissection to free these organs resulted in an injury to the duodenum, which was not successfully repaired and continued to drain bile externally for 2 months through a surgical drain placed in the gallbladder fossa. Successful endoscopic closure of our patient’s duodenal fistula with endoclips obviated the need for additional surgery. To our knowledge, this is the first report of endoclip closure of an iatrogenic duodenal fistula in a Billroth II afferent limb. Use of endoscopically-placed endoclips should be considered as a non-surgical therapeutic option when dealing with small breaches in upper gastrointestinal viscus integrity.

Disclosures

Author contributions: All authors contributed significantly to the creation and review of all parts of the manuscript. All take full responsibility for the work presented in the paper. MT Voellinger is the article guarantor.

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References
Transnasal Endoscope Locked in a Bent Position Causing Difficult Withdrawal

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Abstract
We report a rare but severe complication of routine transnasal esophagogastroduodenoscopy (EGD). The tip of a transnasal endoscope was locked in a bent position. Since the bent tip was unable to be returned to a neutral position, the snare from another endoscope inserted transorally was used to straighten it, which allowed the transnasal endoscope to be withdrawn with only mild injury to the gastric mucosa. Endoscopists should be aware of this complication and how to manage it.

Introduction
Transnasal endoscopy is a widely used technique for routine, unsedated endoscopic examination of the upper gastrointestinal tract because scope insertion is well tolerated. We describe an unusual complication during routine transnasal endoscopy involving an instrument whose tip became locked in a coiled position and was difficult to withdraw.

Case Report
A 37-year-old Japanese man was undergoing transnasal esophagogastroduodenoscopy (EGD) without sedation for evaluation of epigastric discomfort. Endoscopic examination of the upper gastrointestinal tract did not reveal any gastric ulcers or cancer, but a small gastric polyp was detected in the cardia and biopsy was attempted. The tip of a transnasal endoscope (Fujinon EG-530N2; Fujifilm Corporation, Tokyo, Japan) that had been in daily use for 3.5 years with appropriate regular maintenance was bent to reach the cardiac polyp. When the handle was forcefully rotated to achieve a very sharp angle, the bent tip of the instrument became locked in position despite release of the handle. After this maneuver, the handle could be turned freely but this did not change the position of the instrument tip, which could not be returned to a neutral position. We attempted to withdraw the scope slowly, expecting the scope to straighten during the withdrawal process, but the tip remained bent and pressed against the gastric wall, causing pain while the instrument was being retracted.

The patient was transferred to an X-ray room with the scope still inserted. X-ray examination showed that the tip of the scope was coiled (Figure 1A, red arrow). We inserted another endoscope transorally (Olympus GIF-Q260; Olympus Corporation, Tokyo, Japan, Figure 2A). The tip of the transnasal scope was grasped with a snare from the transoral endoscope and pulled forcefully (Figure 2B, green arrow). After several initial unsuccessful attempts, the bent tip of the transnasal scope, through which biopsy forceps were inserted to encourage a straightened configuration, returned to the neutral position (Figures 1B and 2C). The straightened transnasal endoscope was finally withdrawn with only mild injury to the gastric mucosa (Figure 2D). No surgical procedure was required.

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After the transnasal endoscope was removed, it was inspected by the manufacturer to determine the cause of this phenomenon. When the base of the endoscope is opened, there is usually a stopper (Figure 3A, red arrow), located next to the sleeve (Figure 3A, blue arrow) of the wire that controls the direction of bending. This stopper prevents overbending. In the present case, the stopper was broken and the sleeve slid under the broken stopper (Figure 3B, red and blue arrows). Since this part is encased in a metallic frame (Figure 3A and 3C, yellow arrows), abnormal movement of the sleeve probably disabled the handle’s ability to control the tip of the instrument.

Discussion
The use of transnasal endoscopy without sedation as a routine endoscopic examination procedure is increasing due to its safety and patient tolerability. However, this case shows that a rare but severe complication can occur during this procedure. To date, the only major complication reported was one case of esophageal perforation. Tatsumi et al reported difficult scope withdrawal in 0.12% of approximately 13,000 cases performed in 14 Japanese institutions. Whereas difficult withdrawal was mainly due to a narrow nasal cavity in their study, the inability to withdraw the scope in the present case was due to an unexpected fixed bend in the instrument.

The appropriate way to resolve a fixed bend similar to the one in the present case was discussed with the endoscope manufacturer. The best approach is to cut the wire at the bottom of the endoscope (Figure 3A, green dotted line) after opening the base of the endoscope. This will release the tension in the wire that maintains the bend, thus allowing the tip to straighten during a slow withdrawal. This procedure can be done while the scope was inserted in the patient, because the base of the endoscope is in the endoscopist’s hand. However, it requires the base of the endoscope to be opened. The tool to open this part will be provided from the manufacturer. Alternatively, the fiber of the endoscope can be cut easily with scissors, although this would render the scope non-functional for further use. Extreme rotation of the handle should be avoided to prevent this complication.

In conclusion, fixed coiling of the transnasal endoscope is a possible severe complication of transnasal EGD. Endoscopists should be aware of this complication and how to manage it. Improvements in endoscope design to prevent this complication are under development by the manufacturer.
Disclosures

Author contributions: H. Toyoda participated in patient care and technical analysis, and is the article guarantor. Y. Hisanga participated in patient care. T. Kumada supervised the manuscript creation.

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Informed consent was obtained for this case report.

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References

Severe Ulcerative Esophagitis Induced by Crizotinib Therapy

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Abstract
Crizotinib is an oral tyrosine-kinase inhibitor that inhibits anaplastic lymphoma kinase (ALK) in gene-rearranged non-small cell lung cancer (NSCLC). In 2011, the Food and Drug Administration approved crizotinib for treatment of locally advanced or metastatic ALK-positive NSCLC. The crizotinib adverse events profile included esophageal disorders in 11% of patients treated during trial phases I, II, and III, but none of them had severe events. We describe the development of severe ulcerative esophagitis secondary to crizotinib therapy and the re-introduction of therapy at a lower dose without recurrence of esophageal symptoms.

Introduction
In 2011, the Food and Drug Administration (FDA) approved the Vysis ALK Break-Apart FISH Probe Kit for the detection of anaplastic lymphoma kinase (ALK) gene rearrangements in non-small cell lung cancer (NSCLC), while concurrently granting approval for an agent directed at this target. Crizotinib was granted accelerated approval by the FDA for the treatment of locally advanced or metastatic NSCLC testing positive for the ALK rearrangement. The approval of crizotinib was based on 2 single-arm studies. Within both studies, the most commonly reported adverse reactions included visual disturbance, nausea, vomiting, diarrhea, constipation, and edema. Currently available studies have not specifically reported on the incidence of esophagitis associated with crizotinib treatment.¹² Severe esophagitis attributed to crizotinib was reported by Srivastava et al earlier this year; however, crizotinib therapy was not re-introduced to that patient due to tumor progression.³ The current report describes the development of severe esophagitis secondary to crizotinib therapy and the re-introduction of therapy at a decreased dose.

Case Report
A 74-year-old Caucasian male, a never smoker, presented to his primary care provider complaining of right hip and back pain for few months and cough for few weeks. Chest imaging was obtained and showed a left upper lobe mass with multiple additional masses within the lungs. Further imaging by PET scan revealed extensive disease with bone and lymph node metastasis. A biopsy of left scalene lymph node showed metastatic well-differentiated mucinous carcinoma of pulmonary origin. The tumor cells were 68% positive for ALK rearrangement. The patient was started on crizotinib 250 mg capsules twice per day.

The patient did well initially, but within 1 week started to complain of progressive dysphagia. He denied odynophagia, fever, or chest pain. During the second week of crizotinib therapy, he presented to the emergency room...
with severe dehydration, weakness, poor oral intake, and 2
days of small volume hematemesis. The patient was admit-
ted to the hospital, and crizotinib treatment was held. Sup-
portive care with intravenous fluids and pantoprazole drip
was started. Hemoglobin level at presentation was 12.0 g/
dL and decreased to 9.8 g/dL within 2 days. Esophagoga-
troduodenoscopy (EGD) demonstrated a diffusely ulcerated
esophagus from the cricopharyngeus to the gastroesopa-
geal junction, with blood actively oozing from the entire
esophagus secondary to severe ulcerations (Figure 1 and
Figure 2). Biopsy was deferred because of active esophageal
bleeding. The patient was started on total parenteral nutri-
tion to allow the esophagus to heal. His swallowing started to
improve 1 week after crizotinib was held, and within 2 weeks
of his presentation he was able to resume oral intake.

Because of the severity of the inflammation and ulcerations
on EGD, a clinical decision was made to re-introduce crizo-
tinib therapy at half dose (250 mg daily) and monitor the
patient closely for recurrence of esophagitis. The patient re-
ported tolerating therapy at a follow-up visit after 3 months.
Endoscopy was not repeated given the resolution of patient’s
symptoms.

Discussion
Camidge et al presented an updated analysis of the phase
I crizotinib study with regards to its activity and safety. Gas-
trointestinal and visual events, with the majority grade 1 or
2, were reported as some of the more frequently occurring
adverse events. Overall, crizotinib was reported to be well-
tolerated, with no reports of esophagitis.

Treatment emergent esophageal disorder—widely defined
as dyspepsia; dysphagia; epigastric discomfort, pain, or
burning; esophagitis; esophageal obstruction, pain, spasm,
or ulcer; gastroesophageal reflux; odynophagia; and reflux
esophagitis—was reported in 20% of patients in both trials,
leading to the approval of crizotinib. Only half of these inci-
dences were categorized as treatment related, and no grade
3 or 4 toxicity occurred.

A recent phase III study by Shaw et al compared crizotinib
therapy with standard chemotherapy in 347 patients with
ALK-positive NSCLC. The adverse effects profile seen was
similar to previously reported studies. Gastrointestinal ef-
fects were reported as similar to previous findings with no
specific cases of esophagitis reported.

Park et al described 2 cases of esophagitis associated with
crizotinib therapy, attributing the incidences to pill-induced
esophagitis. These cases differ from our case in that the
ulceration was confined to mid-esophagus, which supports
the diagnosis of pill esophagitis compared to the diffuse dis-
ease in our patient.

Our case describes the development of EGD-proven severe
ulcerative and diffuse esophagitis within 2 weeks of the ini-
tiation of crizotinib. Given the timing of initiation of therapy
and the onset of symptoms, the severe esophagitis was at-
tributed to the initiation of crizotinib therapy. Treatment was
discontinued, and the patient’s symptoms of esophagitis re-
solved. Additionally, the patient tolerated re-introduction of a
half dose of crizotinib therapy.

Although an infectious etiology could not be excluded with
absolute certainty in our patient without obtaining biopsies,
the clinical presentation and endoscopic examination were
not supportive of such etiology. Most patients with infectious
esophagitis present with odynophagia in addition to dysphagia. EGD was not consistent with typical findings of infectious esophagitis. Cytomegalovirus (CMV) and Candida are 2 commonly identified causes of esophagitis. However, CMV most commonly causes multiple, deep ulcers at the lower esophageal sphincter, and Candida infection results in white mucosal plaque-like lesions.6,7 The patient was not felt to be immunosuppressed enough to place him at increased risk of these infections. Herpes simplex virus infection usually affects the distal esophagus with well-circumscribed ulcers and normal-appearing intervening mucosa.8 Our patient had superficial, diffuse ulcerations of esophagus with no white mucosal lesions.

Camidge et al describe the role of ALK in the development of gut and visual systems of other organisms. While the role and function of ALK is not well-known in humans, they suggest the predominance of gastrointestinal and visual side effects seen with crizotinib therapy may be accounted for by the anti-ALK effects within these tissues.2

Given the severity of disease experienced by our patient and the high percentage of ALK expression in the tumor cells, we postulate that the severity and diffuse nature of the esophagitis represents an on-target anti-ALK phenomenon.

Disclosures

Author contributions: A. Abdel Jalil and J. Craig acquired, analyzed and interpreted the data. A. Abdel Jalil, J. Craig, R. Bajaj, and T. Spurling drafted and critically revised the manuscript for important intellectual content. AA Abdel Jalil is the article guarantor.

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References

Rapunzel Syndrome in a Postpartum Patient after Caesarian Delivery

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Abstract
A trichobezoar is an immobile, indigestible collection of hair or hair-like fibers that accumulates within the GI tract. Rapunzel syndrome is a rare variant in which a trichobezoar extends into the small intestine, potentially causing obstruction. We describe the first case, to our knowledge, of Rapunzel syndrome occurring in a postpartum patient after delivery by Caesarian section.

Introduction
A trichobezoar is an immobile, indigestible collection of hair or hair-like fibers that accumulates within the GI tract. The first reported case of trichobezoar was by Baudamant in 1779. Trichobezoar is typically the result of trichotillomania and trichophagia, or the pulling and eating of one’s own hair. Rapunzel syndrome is a rare variant in which a trichobezoar extends into the small intestine, potentially causing obstruction. We describe the first case, to our knowledge, of Rapunzel syndrome occurring in a postpartum patient after delivery by Caesarian section.

Case Report
A 27-year-old woman presented to the hospital with acute onset of abdominal pain, nausea, and vomiting for 1 day. The patient was recently pregnant, and underwent uncomplicated Caesarian delivery 2 months prior to presentation. The patient suffered from chronic abdominal pain, nausea, and vomiting throughout her pregnancy, and required multiple admissions to the hospital during her pregnancy for what was thought to be hyperemesis gravidarum. Two weeks following delivery, the patient was again admitted for severe abdominal pain, nausea, and vomiting. Evaluation at that time included a CT scan of the abdomen showing a large amount of heterogeneous material in the stomach (thought to be recently ingested food), a new umbilical hernia, and no other abnormalities. The patient was discharged home after evaluation by surgical services. The patient described her current symptoms as being similar to those she had throughout her pregnancy and in the 2 weeks after her delivery.

Her past medical history was significant for a gunshot wound to the face 1 year prior, requiring multiple facial surgeries and resulting in chronic opioid dependence. She had recently been weaned off opioids, and her chronic medications at home included naltrexone, ibuprofen as needed for pain, and promethazine as needed for nausea. The patient had 2 other young children from whom she was estranged. On physical exam, the patient appeared nervous and anxious and was hiding underneath the blankets in her hospital bed. Her abdomen was
markedly tender to palpation in the epigastrum and right upper quadrant with no palpable masses. Laboratory testing was unremarkable. CT of the abdomen again showed a large amount of material in the gastric lumen with gastric distension (Figure 1).

The patient admitted that she had been ritualistically eating her own hair for the last 6 years, and had been seeing a therapist as an outpatient with poor follow-up.

Upper endoscopy revealed hair in the oropharynx and esophagus, and a large trichobezoar filling the entire stomach that prevented passage of the endoscope beyond the proximal gastric body (Figure 2). Due to the size and nature of the trichobezoar, general surgery was consulted for surgical resection. The patient underwent laparotomy with gastrotomy and removal of the trichobezoar, which was described by the surgeons as a cast of the entire stomach made entirely of hair that extended partially into the duodenum. The specimen removed measured 23.0 x 6.0 x 5.0 cm (Figure 3).

Discussion

Only 2 cases of Rapunzel syndrome occurring during the peripartum have been reported to date: one occurring in the second trimester, and one after spontaneous vaginal delivery.3 We describe the third known case of Rapunzel syndrome occurring in the peripartum, and the first such case diagnosed after Caesarian section delivery. The significance of the patient’s Caesarian delivery is that her recent surgery provided one more attributable cause of her abdominal pain. The layered history of a recent pregnancy, recent surgery, and complex social history provided several possible explanations for her symptoms. As a result, it took multiple presentations to the emergency department before it became clear that further investigation was necessary. The emotional and physical stress of pregnancy, Caesarian delivery, and care for a new infant likely exacerbated the patient’s trichotillomania and trichophagia to the point that the ingested hairs accumulated and ultimately impacted in her upper digestive tract.
Human hair is resistant to digestion and peristalsis due to its smooth surface. When hair is ingested, it accumulates between mucosal folds in the stomach. With the aid of peristalsis, the strands of hair can become entwined to form a mesh. Over time, continued ingestion of hair leads to impaction mixed with mucus and food, forming a trichobezoar, which ultimately takes the shape of the stomach. Trichobezoars form in only 1% of patients who have trichotillomania with trichophagia. The diagnosis is most common in young women and children. Typically, patients have an underlying psychiatric disorder, mental retardation, or pica. Carpet and clothing fiber can also accumulate in the GI tract and form trichobezoars if ingested in large amounts.

Rapunzel syndrome is a rare variant in which a trichobezoar extends past the pylorus and into the small intestine. It is named after the enchanting German fairy tale of Rapunzel, written by the Brothers Grimm in 1812. Rapunzel had hair so long that she could lower it down to her prince from high up in her prison tower to allow him to climb up to her window and rescue her. Similarly, there are reported cases of Rapunzel syndrome with trichobezoars extending as distal as the transverse colon.

Gastroparesis is a risk factor for developing gastric bezoars. Patients with diabetes, end-stage renal disease, prior gastric surgery, and patients on mechanical ventilation are all at greater risk for bezoar formation. Patients typically present with abdominal pain (37%), nausea and vomiting (33.3%), obstruction (25.9%), or peritonitis (18.3%). Physical exam may reveal a palpable abdominal mass. Diagnosis of trichobezoar is best screened by imaging modalities such as CT scan, and is best confirmed by upper endoscopy. Small trichobezoars may be managed conservatively, but larger trichobezoars are best managed by laparotomy with gastrotomy and removal. Complications of trichobezoar and Rapunzel syndrome include ulceration or perforation of the stomach or intestine, intussusception, small bowel obstruction, jaundice, and even pancreatitis due to obstruction at the ampulla of Vater.

Trichobezoar is a rare diagnosis that should be considered in patients with nonspecific abdominal pain, nausea, and vomiting, especially in young women with prior or suspected concurrent psychiatric diagnoses. Trichobezoar should also be considered in the differential diagnosis for a pregnant woman with abdominal pain, intractable nausea, and vomiting. Effective communication and a good relationship between the patient and medical provider are essential in making an early diagnosis of trichobezoar. Preventing recurrence is just as important as active treatment of trichobezoar. Patients diagnosed with trichobezoar should have close follow-up with psychiatry post-operatively to prevent recurrence. Parental or spousal counseling may be beneficial. Follow-up endoscopy or contrast study may be indicated if symptoms recur, or if trichotillomania and trichophagia is suspected. Patients may deny persistent or recurrent trichotillomania and trichophagia, which is all the more reason to establish a strong relationship with such patients early on.

**Disclosures**

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**References**

Nodular Lymphoid Hyperplasia in a Patient Initially Believed to Have Familial Adenomatous Polyposis

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Abstract

A 50-year-old male was initially thought to have familial adenomatous polyposis (FAP) after innumerable small nodules in the upper GI tract were discovered upon endoscopic retrograde cholangiopancreatography for common bile duct stone extraction. ERCP was unsuccessful due to inability to find the major papilla amongst the nodules found in the duodenum. Biopsy of the nodules was consistent with nodular lymphoid hyperplasia. The patient was later found to have common variable immunodeficiency.

Introduction

Common variable immunodeficiency (CVID) is the second most prevalent primary immunodeficiency disorder after selective immunoglobulin A deficiency. Nodular lymphoid hyperplasia (NLH) of the gastrointestinal tract is a rare disorder associated with immunodeficiency syndromes, and characterized by numerous visible mucosal nodules. We report a patient with CVID and NLH initially mistaken for familial adenomatous polyposis (FAP).

Case Report

A 50-year-old male with past medical history of hypertension, polio infection, and cholecystectomy was referred for evaluation of persistent abdominal pain for the past 5 weeks. The patient complained of gastrointestinal reflux and sharp pain localized to the right upper quadrant exacerbated by fatty meals. Laboratory tests revealed an alkaline phosphatase (ALP) of 461 U/L, aspartate aminotransferase (AST) of 297 U/L, alanine aminotransferase (ALT) of 599 U/L, and a total bilirubin level of 0.6 mg/dL. Abdominal CT showed a common bile duct diameter of 1 cm. Initial attempt at endoscopic retrograde cholangiopancreatography (ERCP) was unsuccessful due to the inability to find the major papilla amongst the innumerable, 5–8-mm nodules found within the upper GI tract (Figure 1).

With familial adenomatous polyposis (FAP) as the working diagnosis, repeat ERCP resulted in successful biliary cannulation and extraction of CBD stones with resolution of the abdominal pain and normalization of the liver chemistry abnormalities. Biopsy of the nodules showed prominent hyperplastic lymphoid follicles with a reduced number of plasma cells in the lamina propria, consistent with nodular lymphoid hyperplasia. Further lab tests showed low levels of IgM, IgA, and IgG (11 mg/dL [34–214], <6 mg/dL [83–407], and 246 mg/dL [680–1,445], respectively), and the patient was referred to an immunologist. The patient admitted to annual episodes of sinusitis and bronchitis, and had persistently low levels of IgA and IgG. He was diagnosed with common variable immune deficiency (CVID) and treatment with intravenous immunoglobulin was initiated.


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Discussion

Nodular lymphoid hyperplasia (NLH) is a lymphoproliferative disease that has been reported in patients with CVID, a disorder characterized by impaired B cell differentiation with defective immunoglobulin production. It is the most prevalent form of severe antibody deficiency affecting both children and adults. The clinical manifestations include recurrent sinopulmonary infections, autoimmune disorders, gastrointestinal disease, increased susceptibility to lymphoma, and a decreased immunogenicity to protein and polysaccharide vaccines. Histologically, there is enlargement of the mucosal B cell follicles, a normal-appearing mantle zone, and hyperplastic lymphoid follicles with large germinal centers within the lamina propria and superficial submucosa. Mahsa et al reported a case of NLH mimicking FAP wherein they attributed the misdiagnosis to similarities in the polyp-like appearance on endoscopy and large lymphoid follicles in the lamina propria on histology. Studies have shown that infection with *Giardia lamblia* may create a nodular mucosal pattern.

There have been suggestions that NLH is a risk factor for intestinal and extra-intestinal lymphoma. Abolhassani et al emphasized the need for an endoscopic surveillance protocol for gastric cancer in addition to immunoglobulin replacement therapy. They suggest looking for risk factors in CVID patients, such as *Helicobacter pylori* infection, pernicious anemia, or dyspepsia, prior to initiating screening esophago gastroduodenoscopy (EGD). Frequency of follow-up EGD would be based on site and extent of gastric lesions.

Disclosures

Author contributions: S. Altafi contributed to acquisition of data, drafting and revising of case report, and is the author guarantor. A. Volfson contributed to analysis of data and revising of case report. M. McKinley contributed to conception, acquisition, and analysis of data, and revising of case report.

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References

Bannayan Ruvalcaba Riley Syndrome

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Abstract

A 63-year-old male with history of prostate cancer treated with radiation presented for a colonoscopy for small volume hematochezia. The colonoscopy revealed numerous polyps, which were found to be ganglioneuromas on histological examination. He was referred to medical genetics with suspicion for hamartomatous polyposis syndrome and was found to have a mutation in the PTEN gene. Based on this and suggestive clinical findings, he was diagnosed with Bannayan Ruvalcaba Riley syndrome.

Introduction

Bannayan Ruvalcaba Riley syndrome (BRRS) is an autosomal dominant hamartomatous polyposis syndrome, findings of which can include intestinal polyposis in up to 45% of patients. Polyps are predominantly in the distal ileum and colon, but any part of the GI tract may be involved. BRRS is associated with a germline mutation of the tumor suppressor gene PTEN, although there does not appear to be an increased incidence of colorectal cancer or other gastrointestinal cancers in patients with BRRS. We report a patient found to have BRRS following diagnostic colonoscopy.

Case Report

A 63-year-old Caucasian male presented for colonoscopy for evaluation of intermittent small volume hematochezia. He denied any abdominal or perianal pain, constipation, diarrhea, or weight loss. His past medical history was significant for a thyroidectomy 20 years ago for an unknown thyroid disorder and prostate cancer, which was diagnosed 3 years prior and treated with radiotherapy. At colonoscopy, he was noted to have multiple (>30) 1–10 mm sessile polyps throughout the entire colon, all of which were resected via snare polypectomy except those in the sigmoid colon due to the duration of the procedure (Figure 1). He also had changes consistent with radiation proctopathy, thought to be the likely source of hematochezia, and was treated with argon plasma coagulation. Histopathologic examination of the colonic polyps showed evidence of spindle cell proliferation composed of Schwann cells expanding the lamina propria and distorting the overlying colonic crypts. Within the spindled stroma, numerous ganglion cells were identified (Figure 2), suggestive of mucosal ganglioneuromas.

Given the suspicion for a hamartomatous polyposis syndrome, he was referred to the genomic medicine service. During this evaluation, the patient reported that his birth weight was over 10 pounds and he has always needed to wear extra-large hats. He also reported pigmented macules on his glans penis. There were no café-
au-lait spots, inguinal or axillary freckling, or cutaneous neurofibromas to suggest neurofibromatosis. His family history was significant for a 37-year-old son with learning delays and a 4-year-old grandson with concerns for muscle weakness and autism. Neither had undergone genetic evaluation. The patient had a 67% chance of having a PTEN mutation based on a clinical scoring system. Genetic testing demonstrated the presence of a pathogenic mutation (c.632dupG) on one copy of the PTEN gene. Based on clinical manifestations and the presence of the PTEN mutation, he was diagnosed with Bannayan Ruvalcaba Riley syndrome (BRRS). Genetic counseling of at-risk family members was also recommended.

Discussion

BRRS is an autosomal dominant hamartomatous polyposis syndrome that encompasses 3 previously described disorders including Riley-Smith syndrome, Bannayan-Zonana syndrome, and Ruvalcaba-Myhre-Smith syndrome. BRRS has an incidence of 1 in 200,000. Patients tend to be diagnosed early in life, and manifestations may include macrocephaly, lipomatosis, hemangiomas, pigmented macules of the penis, high birth weight, proximal myopathy, joint hyperextensibility, pectus excavatum, and scoliosis, as well as developmental delay and intellectual deficiency. Intestinal polyposis is seen in up to 45% of patients predominantly in the distal ileum and colon, though any part of the GI tract can be involved. Thyroid pathology findings can be benign or malignant and include multinodular goiter, follicular adenoma, or follicular and papillary carcinoma. BRRS is associated with germline mutations of the tumor suppressor gene PTEN, which has a significant role in the molecular pathway of cellular proliferation, migration, and apoptosis. Mutations in PTEN are seen in up to 65% of patients with a suspected diagnosis. If a mutation is confirmed, asymptomatic, at-risk first and second degree relatives should be offered genetic counseling and testing if appropriate.

There are 3 other clinically distinct syndromes associated with PTEN mutations, collectively referred to as PTEN hamartoma tumor syndrome (PHTS). These allelic disorders include Cowden syndrome, Proteus syndrome, and Proteus-like syndrome, and all have established diagnostic criteria. The diagnosis of Cowden syndrome can be made using either pathognomonic findings (facial trichilemmomas, acral keratosis, papillomatous papules, and mucosal lesions) or a combination of major criteria (breast cancer, thyroid cancer, macrocephaly, endometrial cancer, and Lhermitte-Duclos disease) and minor criteria (non-malignant thyroid lesions, mental retardation, hamartomatous intestinal polyps, fibrocystic breast disease, lipomas, fibromas, and genitourinary tumors or malformations). Diagnostic criteria for Proteus syndrome include malformations and hamartomatous overgrowths of multiple tissue, connective tissue nevi, and epidermal nevi, while tumors including ovarian cystadenoma, testicular tumors, central nervous system tumors, and parotid adenomas have been observed in a subset of patients. Patients with features of Proteus syndrome but not meeting diagnostic criteria are given the diagnosis of Proteus-like syndrome.

No such criteria exist for BRRS, but the syndrome is suspected in the presence of macrocephaly, hamartomatous intestinal polyposis, and pigmented macules of the glans penis in males, all of which were present in our patient. In addition, he had a presumably associated benign thyroid manifestation. In the absence of definitive diagnostic criteria for BRRS, a scoring system has been developed to assess the likelihood of a PTEN mutation based on the constellation of clinical findings in a patient suspected of having the condition. It should be noted that some authorities feel that

Figure 1. Endoscopic photograph of colonic polyps.

Figure 2. (A) Photomicrograph of resected polyp showing a large ganglioneuroma. (B) Immunohistochemical stain with S-100 highlighting the Schwann cells and sparing the ganglion cells.
Cowden syndrome and BRRS are varying spectrums of the same syndrome, while others feel that these are distinct entities. There has been no reported increased incidence of colorectal cancer or other gastrointestinal cancers in patients with BRRS to date, though this is a rare condition with few data from large patient cohorts. Patients with BRRS should undergo screening and surveillance for gastrointestinal malignancies, including colorectal cancer, as per guidelines for average risk patients. Polyps without malignant potential (such as our patient’s ganglioneuromas) do not require heightened surveillance. Patients with BRRS and PTEN mutations may have an undefined increased extra-intestinal cancer risk, and it has been suggested they follow the same surveillance recommendations as patients with Cowden syndrome, with screening for breast cancer, thyroid cancer, and uterine cancer.

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References
CASE REPORT | COLON

A Rare Case of Nephrocolic Fistula Resulting from Radio Frequency Ablation (RFA) of Renal Cell Carcinoma

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Abstract
Nephrocolic fistula is a rare, abnormal fistulous connection between the urinary system (kidney/ureters) and colon. Different benign and malignant etiologies are implicated in the formation of a nephrocolic fistula. Even though conservative treatment options have been tried recently (especially for benign etiologies), surgical resection has been the treatment of choice and should be pursued if conservative management fails. We report the first case of a nephrocolic fistula after a radiofrequency ablation of a renal cell carcinoma, which required surgical resection after conservative management failed.

Introduction
Nephrocolic fistula is an abnormal fistulous connection between the urinary system (kidney/ureters) and colon. Approximately 43 cases of nephrocolic fistula have been described in literature. Common reported causes of nephrocolic fistula are staghorn calculi, Crohn’s disease, malignancy, surgical complications, and, rarely, renal tuberculosis.1–6 Colovesical fistulas and ureterocolonic fistulas are most frequently caused by diverticulitis, and in the latter, the left ureter is most commonly affected.7–9 Radiation therapy has been implicated as a cause of vesicovaginal, ureterovaginal, and vesicoileal fistulas. This is the first report of a nephrocolic fistula after radiofrequency ablation (RFA) for a renal cell carcinoma (RCC).

Case Report
A 63-year-old, obese Caucasian male presented to a primary care clinic with pneumaturia and fecaluria for one month. The patient had recurrent urinary tract infections for the last 2 months, which were treated with oral antibiotics. He denied hematuria. Four months prior to presentation, he had CT-guided RFA for a left upper pole renal cell carcinoma. Based on clinical presentation and history of RFA, a presumptive diagnosis of nephrocolic fistula was made.

An abdomen/pelvis CT scan showed a fluid collection around the left kidney with extensive scar formation, thickening of left Gerota’s fascia, moderate pericolonic edema/inflammation, and air in the urinary bladder (Figure 1). Colonoscopy revealed a fistulous tract opening in the descending colon 45 cm from the anal verge (Figure 2 and Figure 3). A retrograde pyelogram showed contrast extravasation from the middle calyx of the left kidney into the colonic system; a ureteral stent was then placed (Figure 4). The patient had persistent fecaluria and pneumaturia with no improvement over the next month. Total parenteral nutrition was initiated to provide...
Repeat CT scan showed no inflammation or air around the left kidney indicating resolution of fistula (Figure 5).

**Discussion**

Although a case of nephroduodenal fistula has been reported as a consequence from RFA, nephrocolic fistula is not a known complication of RFA treatment for renal cell carcinoma. Usually, the nephrocolic fistula manifests as a late result of chronic inflammation and is not seen in early stages on a CT scan. In our case, the CT scan did not show the fistulous tract, but clinical findings were suspicious for nephrocolic fistula. Diagnosis was confirmed by retrograde pyelogram (Figure 4).

bowel rest and to optimize nutritional status prior to surgery. Surgical resection of nephrocolic fistula and resection of 8 cm of descending colon with end-to-end anastomosis was performed. The post-operative course was uneventful and the patient recovered well, with no recurrence of symptoms.

Traditionally, nephrocolic fistulae have been treated with surgical excision but, recently, conservative approaches (antibiotics, ureteral stent, treatment of underlying diseases like tuberculosis) have been successfully tried. Our patient did not improve on conservative management; this may be because of extensive scar formation that required resection. Surgical interventions (partial bowel resection, fistulectomy, and possibly nephrectomy) should be pursued in cases of failed conservative management, complex fistulae, sepsis, renal failure, or bleeding.

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Figure 4. Retrograde pyelogram.

References

Synchronous Small Cell Neuroendocrine Carcinoma and Adenocarcinoma of the Colon: A Link for Common Stem Cell Origin?

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Abstract
Synchronous carcinomas have been recognized for over a century, with synchronous primary adenocarcinoma of the colon reported to range from 2–11% of cases involving this type of malignancy. Small cell carcinomas occur frequently with colorectal adenomas; however, despite these reports and a known adenoma-to-carcinoma sequence, scarce literature exists on synchronous colorectal adenocarcinoma and small cell carcinomas. We present a rare cancer of synchronous small cell neuroendocrine carcinomas and discuss a possible link between these two cancers.

Introduction
Colorectal adenocarcinoma is the most common colorectal malignancy. Small cell neuroendocrine carcinomas (SCNC) are rare entities accounting from 0.1–3.9% of colorectal cancers.1,2 The estimated prevalence of synchronous primary adenocarcinoma of the colon is 2–11%.3 SCNC is frequently associated with adjacent colorectal adenomas, but it is rarely associated with colorectal adenocarcinoma.4,5 Histologically, SCNC is largely heterogeneous, ranging from glandular to squamous in differentiation supporting derivation from a pluripotent stem.6,7 We describe a rare case of a synchronous SCNC and adenocarcinoma of the colon and review the current literature discussing a possible pathogenetic link between these two entities.

Case Report
A 63-year-old African American male with a history of HIV and chronic HCV presented to the emergency room with malaise, abdominal pain, hematochezia, constipation, and a 50-pound weight loss over the prior 5 months. The abdominal pain was diffuse, located primarily in the right lower quadrant, constant, burning, non-radiating,
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and not associated with meals. His pain was rated a 5–6 on a pain scale to 10. Blood in the stool was first noted intermittently several months ago and was now noticed with every stool. The patient noted a change in bowel habits from daily stools to 1 stool every 3–4 days. He reported a 30 pack-year smoking history. He denied any history of gastrointestinal malignancies or previous surveillance colonoscopy. Physical exam revealed right lower quadrant pain and mild hepatomegaly. Laboratory tests demonstrated a white blood cell count of 8.4 K/mm³, hemoglobin 14.8 K/mm³, hematocrit 42.9%, platelets 475K/mm³, and a carcinoembryonic antigen of 10.9 ng/mL. His CD4 count was 471 cells/mm³ with a viral load less than 47 copies/mL. His basic metabolic profile was within normal limits and liver-related tests were significant for an alkaline phosphatase level of 518 mg/dL.

A contrast CT scan of the abdomen/pelvis revealed two masses: one in the ascending colon and the other in the cecum, with diffuse abdominal lymphadenopathy and several hepatic areas of low attenuation (Figure 1 and Figure 2). A colonoscopy revealed masses in the cecum and ascending colon. Biopsies revealed a well-differentiated adenocarcinoma of the ascending colon (Figure 3), and an SCNC of the cecum (Figure 4). Due to progressive obstructive symptoms and uncontrolled bleeding, the patient underwent right hemicolectomy (Figure 5) with lymph node dissection revealing 18 of 28 positive nodes for adenocarcinoma. Biopsy of the hepatic lesion was compatible with metastatic SCNC. The patient was diagnosed with synchronous stage IIIB adenocarcinoma and stage IV SCNC of the colon.

Discussion

Neuroendocrine tumors of the colon and rectum are divided into either carcinoid tumors with low-grade atypia and malignancy or neuroendocrine cell carcinomas with high-grade atypia and malignancy. Histologically, neuroendocrine tumors are classified based on tumor differentiation (well vs. poorly differentiated) and tumor grade (grade 1–3). Differentiation, tumor grade, Ki-67 proliferation index and mitotic counts are used to assess aggressiveness and prognosis. High-grade neuroendocrine carcinomas include both SCNC and large cell neuroendocrine carcinoma.

SCNC of the gastrointestinal tract were first described by Mckewon in 1952, when he published two cases of esophageal tumors morphologically indistinguishable from SCNC found in the lung. Colonic SCNCs were later introduced into the medical community by Gould in 1978. The most common site of metastasis is the liver, followed by the lymph nodes, bones, and bone marrow. In one study, the highest
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incidence of colonic neuroendocrine tumors occurred in the cecum (48%), followed by the ascending (16%), sigmoid (13%), descending (11%), and then transverse colon (6%).12

Synchronous carcinomas have been recognized for over a century, first described in the 1880s by Billroth,13 Czerny,14 and Fenger.15 The estimated prevalence of synchronous primary adenocarcinoma of the colon is 2–11%.2 Cunliffe et al16 theorized that the entire colorectal mucosa is unstable and at risk for malignant change in those found to have synchronous and metachronous colorectal carcinomas. One study showed colorectal adenomas in 35% of patients with synchronous colorectal adenocarcinomas compared with only a 15% occurrence rate in those with isolated colorectal adenocarcinoma.15 Colorectal neuroendocrine tumors are frequently associated with secondary primary tumors, with an annual incidence reported of 3–15%.17,18

The typical clinical presentation is similar to other colonic masses and includes hematochezia, abdominal pain, altered bowel habits, and signs of bowel obstruction. SCNC may, rarely, secrete hormones such as vasoactive intestinal peptide, antidiurectic hormone, calcitonin, serotonin, parathyroid hormone related protein, or adrenocorticotropic hormone.11 Morphologically, SCNC is indistinguishable from small cell carcinoma of the lung; occasionally, immunohistochemical staining for thyroid transcription factor-1 (TTF-1) can help distinguish the two. These malignant cells typically contain minimal cytoplasm, fusiform cell shape, granular nuclear chromatin, and small or absent nucleoli. Positive neuroendocrine markers for this tumor include neuron-specific enolase, chromogranin, synaptophysin, and CD56 (neural cell adhesion molecule). Despite these markers, the diagnosis of SCNC remains morphological rather than immunohistochemical due to the rarity of the disease.2 One case series reports LMWK, CK 19 and pancytokeratin, TTF-1 negative stain may be helpful to differentiate SCNC from pulmonary small cell carcinomas, and additional stains CDX2, mCEA, CD56, synaptophysin, NSE, and chromogranin to differentiate high-grade neuroendocrine from non-endocrine poorly differentiated adenocarcinoma.19

Treatment for gastrointestinal SCNC is derived from case reports and small retrospective series with no existing expert panel guidelines. The histopathological similarity between SCNC of the colon and lung has led many clinicians to treat SCNC of the colon identically to that of the lung. Treatment is usually surgical for localized disease, whereas metastatic and non-resectable disease is treated with radiation therapy and a backbone of cisplatin, etoposide, cyclophosphamide, and doxorubicin.11 Gastrointestinal SCNC is highly aggressive and, without appropriate treatment, survival is usually measured in weeks.13

The histogenesis of gastrointestinal SCNC is largely debated, with a number of theories linking neuroendocrine carcinoma and adenocarcinomas. Contrary to the initial hypothesis by Pearse et al that neuroendocrine carcinoma origin is derived from the amine precursor uptake and decarboxylation cell from neural crest cells,20 several reports link SCNC with adenomatous colorectal adenomas, suggesting a common stem cell origin similar to that seen in colorectal adenocarcinoma.4,5,21,22 The morphological differentiation of SCNC from squamous to glandular suggests a divergent differentiation from pluripotent stem cells derived from the endoderm.5,6 Recent studies indicate that colonic endocrine cells originate from an endodermal stem cell capable of multidirectional differentiation.4 Reports of admixed endocrine cells...
residing in colonic adenocarcinomas, as well as reports of amphiocrine tumors with both exocrine and endocrine characteristics in the same cell support this theory.4

Vortmeyer et al theorized that a progenitor stem cell could differentiate into two or more diverse cell lines and could account for the development of synchronous, yet histologically different, tumors along the gastrointestinal tract.23 He demonstrated through genetic analysis that poorly differentiated neuroendocrine carcinoma and associated adenocarcinoma appears to be derived from the same cell origin. Although neuroendocrine tumors are easily distinguishable from adenocarcinomas histologically, it is not uncommon to find adenocarcinomas lesions with sections of neuroendocrine differentiation.17 Kato et al reported a CK20 positive (a common marker found in colorectal adenocarcinoma) large cell neuroendocrine tumor that occurred synchronously to a colorectal adenocarcinoma.24 Several cancer predisposing syndromes—such as Li-Fraumeni—promote the development of multiple, histologically different malignancies. These findings support the theory that different types of gastrointestinal neoplasm might originate from a common stem cell clone and/or may share a similar genetic mutation(s) during early oncogenesis.

In conclusion, we believe our case may support a common link between the pathogenesis of these two distinct entities and possible future research in this area.

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References
Ischemic Colitis, the Great Imitator: A Mass Completely Resolved

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Abstract

Ischemic colitis (IC) is the most common type of intestinal ischemia, with a vast clinical spectrum of injury ranging from mild and transient ischemia to acute fulminant colitis. The pattern of injury is usually segmental, but it is mainly dictated by individual anatomy, duration of ischemia, and degree of re-perfusion injury. Analysis of clinical presentation, early endoscopic evaluation, and biopsy are all essential for prevention of misdiagnosis. We present a unique case of IC with mass-like features on regular imaging, emphasizing the importance of endoscopy and biopsy for accurate diagnosis.

Introduction

Ischemic colitis (IC) is a common disorder of the large bowel. It is frequently seen in older patients, and is the most common form of intestinal ischemic injury. It accounts for about 50–60% of all gastrointestinal ischemic episodes, most often in the absence of major vessel occlusion.1–4 IC is a result of inadequate blood flow to the colon, causing mucosal injury that is mediated by hypoxia, followed by reperfusion injury.4 The pattern of injury is usually segmental, mainly involving the “watershed” zones of the splenic flexure, descending colon, and the rectosigmoid junction; however, any part of the colon can be affected, including isolated right-sided colon, which carries a higher morbidity and mortality rate.2 Common clinical manifestations include sudden presentation of abdominal pain that is usually located over the affected area of the colon, followed by bright red blood per rectum.4 The severity of clinical symptoms varies, including fever, diarrhea, peritonitis, and septic shock, depending on the extent of colonic injury. We report a unique presentation of IC and stress the significance of endoscopy and biopsy for accurate diagnosis and therapy.

Case Report

A 76-year-old Caucasian male with a past medical history of tobacco use, hypertension, and chronic kidney disease stage III, not on dialysis, presented to the emergency room with acute right lower abdominal pain and non-bloody diarrhea. He reported a history of a previous colonoscopy with 1 polyp removed 2 years ago at an outside hospital. In the emergency department, he was febrile to 102°F and tachycardic. Physical exam revealed a well-developed and well-nourished male in no acute distress with a tender right lower quadrant with no rebound or guarding. Other systems were normal. Laboratory findings were remarkable for a white blood cell count of 12.1 x 10^3/L and a creatinine of 1.9 mg/dL.

CT scan of the abdomen revealed annular thickening of the cecum, concerning for malignancy (Figure 1). The patient was admitted and treated supportively with intravenous fluids and pain management. Colonoscopy showed a large, necrotic-appearing mass encompassing the majority of the cecum (Figure 2). Pathology revealed fragments of necrotic colonic mucosa, fibrinopurulent exudates, and partial viable tissue and associated repara-
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Figure 1. CT abdomen/pelvis showing segmental abnormal mucosal thickening in an annular fashion involving the cecum, highly suggestive of a colonic malignancy.

tive changes without evidence of malignant cells (Figure 3). IC was diagnosed when these findings were correlated with the clinical findings. The patient was treated conservatively with resolution of his symptoms. He was discharged 1 week later with outpatient gastroenterology follow-up. A repeat colonoscopy done 2 months later showed complete resolution of the mass (Figure 4).

Discussion

IC is the most common manifestation of ischemic bowel disease and is important to recognize, especially in the elderly population. Commonly seen risk factors among patients with IC include coronary artery disease, hypertension, chronic kidney disease, diabetes, and hyperlipidemia. Ischemia typically affects the colon in a segmental manner secondary to the pattern of vascular supply to the colon. Colon ischemia has many causes, most often associated with an acute change in blood flow to the colon, usually in the absence of major vessel occlusion. Isolated right-sided colon ischemia, as seen in this case, accounts for about 25% of cases. It is usually precipitated by reduction in circulating blood volume, marked fluid shift, and hypotension, which could lead to superior mesenteric artery (SMA) vasoconstriction. Patients usually present with symptoms of non-specific abdominal pain but lack the bloody diarrhea seen in classic IC affecting the splenic flexure or “watershed area.” There is higher morbidity and mortality with right-sided colon involvement compared to the other segments of the colon. This is hypothesized to be due to insufficient collateralization and blood flow to the right side of the colon. Given the vague symptoms and higher morbidity and mortality, early recognition and treatment is critical.

Endoscopic manifestations of IC are vast and range from mild erythema to pseudo-tumor, as reported in this case. Lymphocytic and neutrophilic infiltration along with edema and ulceration of the superficial mucosa are seen in mild forms of ischemia. In such cases, the glandular architecture of the deep mucosa is preserved. Gland degeneration and fibrinopurulent exudate are seen in more severe ischemia. Pseudo-tumor can be attributed to submucosal hemorrhage, which can create a mass-like appearance when severe. Given that there is no widely accepted diagnostic criteria for IC, clear recognition and knowledge of the clinical, endoscopic, and pathologic characteristics is crucial in making an accurate diagnosis and providing timely treatment.
This case emphasizes that, while preliminary radiographic imaging may be suggestive for malignancy, it is essential to perform colonoscopy with biopsies to distinguish ischemic colitis from carcinoma. After confirmation of IC, performing a follow-up endoscopy is important to ensure resolution of the ischemic area and to rule out other colonic pathology obscured by the initial ischemia. Generally, conservative management is recommended since surgery portends a higher mortality. Therefore, it is imperative to have a high index of suspicion for ischemic colitis because a misdiagnosis with colon cancer has a significant risk of unnecessary adverse events, including surgery.

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References
Recurrent Acute Pancreatitis Secondary to Graft Pancreas Divisum in a Patient with Modified Multi-Visceral Transplant

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Abstract
A patient with modified multivisceral transplant developed recurrent acute pancreatitis (RAP) 1 year after transplant and was found to have graft pancreas divisum with otherwise negative work-up for identifying the etiology of RAP. Endoscopic retrograde cholangiopancreatography was performed with minor papilla sphincterotomy and pancreatic duct stent placement of the graft pancreas. The patient’s symptoms resolved following endotherapy for a follow-up period of 2 years. This is a unique case of graft pancreatitis secondary to pancreas divisum.

Introduction
Composite visceral transplantation (including combined liver/small bowel and multivisceral grafts) is the standard of care in patients with irreversible intestinal failure secondary to short bowel syndrome, abdominal vascular catastrophe, or major abdominal trauma. Multivisceral (MV) grafts include transplantation of the stomach, duodenum, pancreas, liver, and intestine, and are indicated in conditions such as hollow visceral myopathy/neuropathy, GI polyposis, and extensive mesenteric desmoid tumors. This procedure may be modified (modified MV) to contain all of these organs except the liver. Pancreaticobiliary complications including graft pancreatitis (GP) and rejection have been frequently reported in patients with modified MV transplant. The prevalence of such complications is far less when the pancreas is included as a component of a multivisceral graft as opposed to isolated pancreas transplantation.

Herein we describe a unique case of a patient with modified MV transplant who developed recurrent GP secondary to pancreas divisum. The patient provided consent for enrollment in an institutional review board–approved prospective cohort study and was included in a prior published series.

Case Report
A 40-year-old female with history of modified MV transplantation for hollow visceral myopathy presented 1 year after the transplant with recurrent acute pancreatitis (RAP). She had severe attacks of characteristic epigastric pain with concurrent lipase elevation that required hospitalization. Upon initial evaluation, her vital signs were normal. Physical exam showed upper abdominal tenderness to palpation without guarding. She had a lipase level of 625 IU/L (upper limit of normal <200) consistent with acute pancreatitis. Initial work-up, including review of medications, family history of acute pancreatitis, tobacco and alcohol use, serum triglyceride and ionized calcium level, celiac serologies, and right upper quadrant ultrasound was unrevealing. Abdominal MRI showed graft pancreas divisum to be the etiology of the recurrent GP (Figure 1).
Endoscopic retrograde cholangiopancreatography (ERCP) to treat the graft pancreas divisum was performed. The transplanted minor papilla was identified and successfully cannulated (Figure 2). Minor papilla sphincterotomy with pancreatic duct stent placement was then successfully performed. The patient did not develop any subsequent attacks of GP in 2-year clinical follow-up.

**Discussion**

In the presented case, a modified multivisceral technique was performed, where the graft stomach, duodenum, pancreas, and small intestine were transplanted *en bloc* with the native pancreas and liver preserved. This technique has been increasingly utilized over the past decade with significant improvement in outcome. However, pancreaticobiliary complications are relatively common after composite visceral transplantation. In a study of 271 patients with 289 composite visceral grafts, 19 patients developed pancreatic complications (6 patients had edematous pancreatitis, 7 had necrotizing pancreatitis, and 6 had pancreatic duct fistulae). Five patients experienced combined biliary and pancreatic complications.

Pancreas divisum is the most common congenital anomaly involving the pancreatic ductal system, with a reported prevalence between 2.7–22%. It is characterized by failure of fusion between dorsal and ventral pancreatic ducts during embryonic development. This condition is usually asymptomatic. Pancreas divisum is an uncommon cause of RAP. Secretin-enhanced MRCP is considered the gold standard imaging modality to diagnose pancreas divisum, but its sensitivity remains modest at 73% with a specificity of 96%.

The treatment of pancreas divisum causing RAP includes ERCP with minor sphincterotomy and stenting. Based on a recent meta-analysis, the pooled response rate of pancreatic endotherapy in patients with recurrent acute pancreatitis and pancreas divisum was 79%. This response rate was higher when compared to response rate of pancreatic endotherapy for patients with chronic pancreatitis (69%) or for pain only in the setting of pancreas divisum (54%).

We describe a unique case of pancreas divisum of the graft pancreas causing RAP in a patient with modified MV transplant. Clinicians treating patients with otherwise unexplained recurrent pancreatitis should have a low threshold to obtain secretin-enhanced MRCP to assess for pancreas divisum, which may be amenable to endoscopic intervention.

**Disclosures**

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Pancreatitis Secondary to Celiac Trunk Dissection

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Abstract

Dissection of the visceral arteries happens infrequently, with the superior mesenteric artery being the most commonly affected. Isolated dissection of the celiac trunk is rare, and only a few cases have been reported in the medical literature. We report the case of a 51-year-old male who presented with abdominal pain and was subsequently diagnosed with a celiac trunk dissection with secondary pancreatitis and pancreatic infarction. The patient’s symptoms improved with conservative medical management. We review the current literature involving celiac trunk dissection and its management, and provide discussion regarding this unrecognized complication of pancreatitis.

Introduction

Spontaneous visceral artery dissection is a rare event. The majority of dissections involve the superior mesenteric artery, but celiac trunk dissection can account for a minority of these cases, representing approximately 4% of visceral artery dissections.1 Approximately half of celiac trunk dissections are symptomatic and present with abdominal pain but with unremarkable physical exam and laboratory findings.2,3 Many patients are asymptomatic, but complications such as ischemia, infarction, and hemorrhage do occur. It is not routinely considered in the differential of acute abdominal pain, but is being diagnosed more frequently given advanced imaging modalities. Pancreatitis secondary to celiac trunk dissection is a complication that has only been reported a few times in the medical literature.4 We report the case of a 51-year-old male who presented with abdominal pain, nausea, and vomiting, and was subsequently diagnosed with pancreatitis secondary to celiac trunk dissection.

Case Report

A 51-year-old African-American male with no significant past medical history presented to the emergency department with 1 day of acute epigastric abdominal pain, nausea, and vomiting. His abdominal pain was sharp, constant, and radiated into his left flank. His vital signs were normal on presentation and his physical exam was notable for mild epigastric tenderness, hypoactive bowel sounds, and no rebound or guarding. Initial laboratory work was notable for a normal complete blood count, renal function, and hepatic function. Amylase and lipase were elevated to 524 U/L and 3,473 U/L, respectively. The patient underwent a CT abdomen/pelvis (with oral and IV contrast), which revealed a celiac trunk dissection with a flap extending from the origin of the celiac trunk to the celiac trifurcation (Figure 1 and Figure 2). The CT scan was also notable for a 1.8-cm hypodense lesion in the tail of the pancreas with peri-pancreatic fat and soft tissue stranding (Figure 3). The lesion in the tail of the pancreas was consistent with a pancreatic infarct secondary to the dissection. His presenting symptoms were determined to be due to a combination of the dissection and secondary pancreatitis. The patient was managed conservatively with bowel rest, pain control, blood pressure control, and IV hydration. Other etiologies of pancreatitis such as alcohol use, medications, hypertriglyceridemia, and trauma were ruled out. His symptoms improved, his diet was advanced back to a normal diet, and he was discharged home after 6 days of hospitalization.
Pancreatitis Secondary to Celiac Trunk Dissection

Discussion

Pancreatitis is inflammation of the pancreas and has multiple well-known causes, including gallstones, ethanol, hypertriglyceridemia, trauma, infection, autoimmune, medications, and post-ERCP complications. Ischemia is a rare cause of pancreatitis, in part due to the multiple vessels that supply blood to the pancreas. The head of the pancreas is supplied by the superior pancreaticoduodenal artery (from the common hepatic artery) and the inferior pancreaticoduodenal artery (from the superior mesenteric artery). The neck, body, and tail of the pancreas receive blood from the pancreatic branches of the splenic artery. The celiac trunk has three main branches (common hepatic artery, splenic artery, and left gastric artery; Figure 4). A dissection of the celiac trunk leads to a disruption in the perfusion of the pancreas with subsequent development of ischemia, inflammation, and infarction of pancreatic tissue. Given the multiple branches of the celiac trunk, complications such as splenic infarction, intestinal ischemia, and intraperitoneal hemorrhage can also be seen. To date, there have only been 2 case reports in the medical literature reporting pancreatitis as a result of celiac trunk dissection.4,5

The first reported case of spontaneous visceral artery dissection was by Baurersfeld in 1947.6 Celiac trunk dissection is an uncommon form of visceral artery dissection, with one report estimating it to account for 4% of all visceral artery dissections.1 Since Baurersfeld’s original report, there has been a paucity of cases reported in the medical literature, with one recent study quoting 33 reported cases of celiac trunk dissection based on a Medline database search.4 Spontaneous arterial dissection is more common in males (5:1) with an average age of 55 years.7 Causes of arterial dissection include hypertension, atherosclerosis, trauma, pregnancy, iatrogenesis, syphilis, vasculitis, cystic medial degeneration (Marfan’s syndrome), and other congenital disorders of the vascular wall (e.g., Ehler’s-Danlos syndrome).8 Our patient had none of these risk factors.

CT angiogram is considered to be the diagnostic modality of choice, given that this method can provide details of the mesenteric vasculature.7 Management strategy is often based on the presence of complications. Conservative medical therapy with pain control and hypertension management is recommended in patients without intestinal ischemia or hemorrhage.4 Some authors advocate for anticoagulant therapy for 3–6 months given the risk for thromboembolic complications associated with visceral artery dissection.9 Surgery and endovascular procedures may be considered...
when a patient is hemodynamically unstable, has persistent abdominal pain, when medical therapy fails to control blood pressure, and when the dissection is progressing. Although rare, celiac trunk dissection is now more frequently reported due to improvement in imaging modalities and should be considered in the differential of unexplained abdominal pain and pancreatitis of unclear etiology.

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References

Undifferentiated Carcinoma with Osteoclast-Like Giant Cells of the Pancreas in a Patient with New Diagnosis of Follicular Non-Hodgkin’s Lymphoma

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Abstract
Pancreatic tumors with osteoclast-like giant cells are rare, with only 50 cases published to date. We report a case of a 67-year-old male with a new diagnosis of follicular non-Hodgkin’s lymphoma with an incidental pancreatic body mass on abdominal imaging. Cytology from the pancreatic mass obtained via endoscopic ultrasound-directed fine-needle aspiration (EUS-FNA) revealed an undifferentiated carcinoma with osteoclast-like giant cells.

Introduction
Undifferentiated carcinoma with osteoclast-like giant cells (UCWOGC) is a rare abdominal tumor that is estimated to account for 1% of pancreatic tumors.1,2 Although this cytologic variant has been identified in other tissues such as the skin, thyroid gland, ovary, and breast,3 it has been most commonly reported in the pancreas and was first described by Rosai in 1968.1,4 The tumor is often found on imaging and typically appears as a large heterogeneous mass with well-demarcated hyper- and hypoechoic areas that represent necrotic areas and cystic structures, respectively.1,5 About 50 reports of this tumor have been described, and most have been in Asia.6

Case Report
A 67-year-old Caucasian male presented with a non-tender, submandibular “lump.” He reported no fatigue, night sweats, weight loss, or abdominal pain. His past medical history was unremarkable. The clinical examination revealed an enlarged submandibular lymph node and tenderness in the right upper abdominal quadrant. Biopsy of the submandibular lymph node showed pathology consistent with follicular non-Hodgkin’s lymphoma. He then underwent treatment with rituxan and bendamustine. A PET scan performed to stage the patient’s lymphoma showed focal fluoro-2-deoxy-d-glucose (FDG) uptake in the body of the pancreas. An MRI revealed a multi-locular cystic mass with multiple intrallesional septations in the pancreatic body; endoscopic ultrasound revealed a 4.9 x 4.1-cm solid mass in the body of the pancreas with anechoic complex structures and a regular border without vascular involvement (Figure 1). EUS-FNA with 4 aspiration passes obtained a specimen that consisted of atypical spindle cells admixed with multi-nucleated giant cells (Figure 2). The spindle cells were positive for CAM 5.2 and vimentin. The giant cells were positive for CD68. The morphology and immunohistologic profile supported a diagnosis of UCWOGC in the setting of grade III intraductal papillary mucinous neoplasm with no ovarian-type stroma.

The patient underwent a radical distal pancreatectomy and pathology was consistent with UCWOGC (Figure 2).
The gross specimen appeared as an 11 x 5.5 x 4-cm mass with a focally softened solid portion and a portion of multiple smooth-walled cysts containing mucoid material. The patient did well postoperatively without adjuvant chemotherapy.

**Discussion**

UCWOGC is classified as a rare variant of ductal adenocarcinoma with two distinct cell lines, including a mononuclear cell line population and osteoclastic tumor cells. The tumor is further described by the Stanford Surgical Pathology Criteria as multinucleated giant cells with malignant background cells. Due to the poor differentiation of the underlying tumor cells, it is unclear where these neoplastic cells originate. Many authors favor an epithelial origin while others favor a mesenchymal origin.

UGWOGC is thought to have an equal male–female predominance with an average age of incidence around 60 years. The presentation is variable depending on the location of the tumor within the pancreas; pancreatic head masses present with jaundice and weight loss, and pancreatic body and tail tumors present with abdominal pain. Patients typically present with advanced disease. Imaging, including abdominal ultrasound, CT, and MRI are used for diagnosis of these tumors. These masses are typically further evaluated by EUS-FNA of the mass, as in this case, or through mass resection. In patients with UCWOGC, numerous reports have shown that treatment choice is resection if possible, though resection can rarely be performed since the disease typically presents in advanced stage.

The prognosis of UCWOGC is poor, but it is better than that of ductal carcinomas and pleomorphic giant cell tumors of the pancreas. In some studies, 10-year survival with UGWOGC has been reported, which shows that this tumor may have a better prognosis than undifferentiated carcinoma of the pancreas without osteoclast-like giant cells. In general, the average survival has been shown to be about only 20 months. There have been trials investigating the use of chemotherapeutic agents, such as gemcitabine, but no conclusive evidence has been found to indicate their use.

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**References**

A Rare Case of Icteric Acute Hepatitis C Infection Acquired Through Intranasal Methamphetamine Use

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Abstract
Most patients with acute hepatitis C (HCV) infections are asymptomatic, while 15% present with jaundice. Intranasal drug use can uncommonly transmit HCV via contaminated instruments and nasal epithelial breakdown. Given a 15% prevalence of HCV infection in chronic methamphetamine users, recognition of potential transmission routes is important to target prevention and screening efforts in this population.

Introduction
Most patients with acute hepatitis C (HCV) infection are asymptomatic, while only about 15% present with jaundice. Although uncommon, acute icteric hepatitis is important to recognize because the accompanying intense immune response is associated with higher rates of spontaneous clearance of the infection. The most common route of HCV transmission is intravenous drug use, but up to 20–40% of individuals have unidentified routes of transmission.1,2 We present a rare case of acute icteric HCV infection acquired through intranasal methamphetamine use.

Case Report
A 38-year-old male presented with a 1-month history of generalized body aches, nausea, pruritus, and dark-colored urine. He drank a pint of bourbon daily. He reported intranasal methamphetamine use 6 weeks previously by sharing a straw with his mother who had known chronic HCV. He denied intravenous (IV) drug use, hepatotoxic medications, or herbal products. His vital signs were normal, and physical examination findings included icteric sclera and mild hepatomegaly. He was alert and oriented without asterixis. Laboratory data showed total bilirubin 6.2 mg/dL, direct bilirubin 5.4 mg/dL, aspartate aminotransaminase (AST) 1,735 U/L, alanine aminotransferase (ALT) 1,647 U/L, alkaline phosphatase 184 U/L, and INR 0.9. He had an undetectable acetaminophen level, normal serum ceruloplasmin 36.8 mg/dL, normal total IgG 703 mg/dL, and negative results for antinuclear antibody, anti-smooth muscle antibody, hepatitis A IgM, hepatitis B surface antigen, hepatitis B core IgM, EBV PCR, CMV PCR, and hepatitis C antibody (Ab). An abdominal ultrasound with Doppler was unremarkable, with no signs of vascular occlusion.

Repeat laboratory testing after transfer to our institution revealed positive HCV Ab and HCV RNA >6,000,000 IU/mL. His AST and ALT peaked at 2,698 U/L and 1,916 U/L, respectively. A liver biopsy (Figure 1) showed moderate to severe portal-based active hepatitis with moderate interface and lobular activity, consistent with acute HCV infection without fibrosis or steatohepatitis (<5%). Testing for the IL28B genotype returned as ho-
mozygous C/C. His transaminases started to decline, and he was monitored for potential spontaneous viral clearance. Four weeks after discharge, his HCV RNA level was 461 IU/mL, and 9 months after his initial presentation, his HCV RNA PCR (quantitative) and HCV TMA (qualitative) assays were both negative, indicating successful spontaneous clearance of the virus.

Discussion

We report what may be the first documented case of HCV transmission from intranasal methamphetamine use via a shared straw. Although the most common route of transmission of HCV is injection drug use, 20–40% of individuals have unidentified sources of infection. Potential transmission modalities include intranasal drug use, sharing of drug pipes, tattoos, or other instrumentation with unsterilized equipment. HCV is present in nasal secretions of infected individuals. Active drug sniffing can increase nasal secretions and irritate the nasal epithelium, causing ulcerations and perforations. Instruments used for intranasal drug use can transfer secretions that contain the virus.

In their case–control study of risk factors for HCV transmission from intranasal methamphetamine use via a shared straw, the authors found that intranasal cocaine use was independently associated with a 4.5 increased odds of HCV transmission. Prior studies have reported HCV transmission via intranasal cocaine and/or heroin use; however, we did not find any clearly documented cases of HCV transmission in the context of intranasal methamphetamine use. Our patient's lack of IV drug use and the temporal association of straw sharing with an HCV-infected individual support this route as the most likely source of his infection. Other causes of markedly elevated transaminases, including acute ischemic injury to the liver ("shock liver"), drug or toxin ingestion, other acute viral hepatitis, autoimmune hepatitis, and Budd-Chiari syndrome were ruled out. Our patient was actively consuming alcohol, but alcoholic hepatitis classically results in much more moderate transaminase elevations.

His clinical presentation and work-up, including laboratory values (with noted HCV Ab seroconversion), imaging, and biopsy results, strongly support acute icteric HCV infection as the cause of his acute liver injury. Our patient presented with jaundice, which is a less common but paradoxically favorable sign because it represents an intense immune response that predicts a higher likelihood of spontaneous clearance of the virus. In addition, his favorable IL28B genotype has been shown to predict spontaneous clearance of acute HCV infection compared with the T/T or T/C genotypes. This case highlights the importance of polymerase chain reaction (PCR) testing for HCV as the diagnostic test of choice in an acute phase of the illness since seroconversion of HCV Ab takes 20–150 days.

Conclusion

Although rare, HCV can be transmitted via contaminated instruments and nasal epithelial breakdown from intranasal drug use. Given a 15% prevalence of HCV infection in chronic methamphetamine users, recognition of potential transmission routes is important to target education, prevention, and screening efforts in this population.

Disclosures

Author contributions: C. Chou wrote and proofread the manuscript, researched data, and is the article guarantor. KK Yimam, RT Frederick, and SL Swenson wrote and proofread the manuscript, and researched data. All authors drafted the manuscript and provided critical revision of the manuscript for important intellectual content.

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Sorafenib-Induced Grade Four Hepatotoxicity in a Patient with Recurrent Gastrointestinal Stromal Tumor (GIST): A Case Report and Review of Literature

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Abstract

Gastrointestinal stromal tumor is a rare mesenchymal tumor. Sorafenib is an effective medication in these tumors based on two phase II clinical trials and a retrospective analysis. We report a rare case of a 57-year-old male with acute hepatotoxicity from sorafenib. He was treated conservatively with IV fluids and prednisolone. Liver function tests improved over 2 months. We conclude that sorafenib could cause life-threatening hepatotoxicity and patients taking sorafenib need to be closely monitored.

Introduction

Mesenchymal tumors including gastrointestinal stromal tumors (GIST) are rare tumors of the GI tract and comprise less than 1% of primary GI tumors. These tumors can involve any part of the GI tract, omentum, and mesentery. The primary treatment is surgical resection of a tumor larger than 2 cm. The majority of tumors have C-kit mutation and some contain a platelet-derived growth factor receptor polypeptide gene (PDGFR-A) mutation. The kit mutation is thought to drive the tumor. The risk of progressive disease is high in a tumor larger than 2 cm and >5 mitoses per 50 microscopic high-power field (HPF) in tissue sections. There are 3 FDA-approved drugs for metastatic GIST: imatinib, sunitinib, and regorafenib. Sorafenib is a recommended treatment option based on National Comprehensive Cancer Network (NCCN) guidelines. We report a case of NCIC common toxicity criteria (CTC) grade 4 hepatotoxicity caused by sorafenib in a patient with GIST and review the literature for sorafenib-induced severe hepatotoxicity.

Case Report

A 57-year-old Vietnamese male with history of coronary artery disease status post-percutaneous coronary intervention 8 years ago with consequent systolic heart failure (ejection fraction of 35–40%) presented to the hospital with abdominal pain. He did not drink alcohol and his medications include metoprolol, quinapril hydrochloride, tamsulosin, aspirin, and atorvastatin. CT scan of the abdomen demonstrated small bowel obstruction resulting from a 9.9 x 6.4-cm mass arising from the small bowel. During emergent surgery, the tumor was removed with en bloc resection of small bowel, sigmoid colon, and portion of rectum. The pathologic specimen confirmed multifocal GIST with a high Ki-67. The tumor was C-kit (CD 117-stem cell factor receptor) positive.

He was offered adjuvant imatinib but he declined due to concerns for side effects. Surveillance CT scan 6 months later showed recurrence of disease. He was given imatinib, and, 1 month later, developed severe NCIC CTC grade 3 diarrhea and abdominal pain with normal liver function tests (LFTs). The imatinib was stopped.
Sunitinib is often used in patients who are resistant to or intolerant to imatinib, but can worsen underlying heart failure and was avoided in this patient. His LFTs were normal when he was prescribed sorafenib 200 mg twice daily. He reported feeling better after 1 month; side effects included grade 1 fatigue and dizziness but no diarrhea or hand-foot syndrome. His LFTs remained normal.

Two months later, he noticed darkening of urine color and worsening abdominal pain. He developed frank jaundice within a few days but no mental status alteration. He was admitted to the hospital for supportive care. Blood serology revealed normal alpha 1 antitrypsin, ceruloplasmin, and no evidence of viral hepatitis, Epstein-Barr virus, cytomegalovirus, or autoimmune hepatitis. Triple phase CT showed hepatic steatosis and pelvic masses consistent with his known recurrent GIST. Biopsy of the liver showed moderate acute hepatitis with parenchymal necrosis, prominent canalicular cholestasis, and lymphocytic infiltrate (Figure 1). His ALT and AST levels peaked to 1,193 U/L and 766 U/L, respectively, prior to total bilirubin peak at 23 mg/dL (direct bilirubin 20 mg/dL) after 2 weeks (Figure 2). His prothrombin time increased to 15.7 seconds and INR to 1.25. His alkaline phosphatase increased to 285 U/L.

He was treated with IV fluids and prednisolone, and his sorafenib was discontinued. His liver function tests normalized over the course of 10 weeks. He subsequently was given sunitinib after complete normalization of his liver function tests.

**Discussion**

Sorafenib (Nexavar®) is a small molecule multi-tyrosine kinase inhibitor (TKI) that inhibits RAF kinase; vascular endothelial factor receptor 1, 2, and 3; and other tyrosine kinases. Sorafenib is metabolized primarily by oxidative metabolism in the liver (mediated by CYP3A4) and glucuronidation (mediated by UGT1A9). Common side effects (any grade in >30% of patients) are diarrhea, rash, fatigue, and hand-foot syndrome. Some of these side effects are dose limiting.
lar carcinoma. This explanation is supported by the absence of hepatotoxicity in a randomized phase III trial of axitinib versus sorafenib in metastatic renal cell cancer.¹⁴ Unlike these two large clinical trials, 2% of patients had grade IV increase in AST and ALT when sorafenib was compared to tivantinib.¹⁵ Nineteen percent of patients in the sorafenib arm had liver metastases, but the status of liver metastases in patients who had elevation of transaminases is not clear from publication.

Gupta-Abramson et al reported a phase II trial of sorafenib in advanced thyroid cancer. One patient developed worsening LFTs 8 weeks after commencement of treatment; despite stopping treatment and supportive care, the patient died 3 months later from liver failure. The patient refused liver biopsy and there were no reported drug–drug interactions or other clear etiology for the liver failure except sorafenib.¹³ One patient with metastatic renal cell carcinoma who had a normal liver with no metastases when he was given sorafenib as part of SORCE trial developed a severe idiosyncratic reaction 7 weeks after starting treatment. He later on died of fulminant hepatic failure. The autopsy revealed lobular hepatitis and hepatocyte necrosis.¹⁶ Our patient's liver toxicity also happened between 6-8 weeks after initiation of the drug.

This review of literature suggests relative increased risk of hepatotoxicity in patients with underlying liver damage by liver cirrhosis, hepatocellular carcinoma, or hepatic metastases.¹⁵ However, our case illustrates that hepatotoxicity is also possible in patients with normal liver function. It is not clear what increases the risk of hepatotoxicity, as the reported phase III RCC trials do not detail whether there were drug interactions, underlying liver metastases, or liver disease in patients who developed hepatotoxicity. Sorafenib is commonly used in hepatocellular and renal cell carcinoma, and we suggest careful, regular monitoring of liver function tests during treatment.

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