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World J Gastroenterol 2017 August 14; 23(30): 5451-5644



**EDITORIAL**

- 5451** Wilson's disease: Prospective developments towards new therapies

Ranucci G, Polishchuck R, Iorio R

- 5457** Are our endoscopy patients at risk for pyogenic liver abscess?

Cerwenka H, Schemmer P

REVIEW

- 5460** Pancreatitis: Preventing catastrophic haemorrhage

Evans RPT, Mourad MM, Pall G, Fisher SG, Bramhall SR

MINIREVIEWS

- 5469** Treating children with inflammatory bowel disease: Current and new perspectives

Guariso G, Gasparetto M

- 5486** Influence of gut microbiota on neuropsychiatric disorders

Cenit MC, Sanz Y, Codoñer-Franch P

ORIGINAL ARTICLE**Basic Study**

- 5499** Everolimus halts hepatic cystogenesis in a rodent model of polycystic-liver-disease

Temmerman F, Chen F, Libbrecht L, Vander Elst I, Windmolders P, Feng Y, Ni Y, De Smedt H, Nevens F, van Pelt J

- 5508** MicroRNA profile in neosquamous esophageal mucosa following ablation of Barrett's esophagus

Sreedharan L, Mayne GC, Watson DI, Bright T, Lord RV, Ansar A, Wang T, Kist J, Astill DS, Hussey DJ

- 5519** Expression of Interleukin-26 is upregulated in inflammatory bowel disease

Fujii M, Nishida A, Imaeda H, Ohno M, Nishino K, Sakai S, Inatomi O, Bamba S, Kawahara M, Shimizu T, Andoh A

- 5530** Autophagic cell death induced by reactive oxygen species is involved in hyperthermic sensitization to ionizing radiation in human hepatocellular carcinoma cells

Yuan GJ, Deng JJ, Cao DD, Shi L, Chen X, Lei JJ, Xu XM

- 5538** Yangzheng Sanjie decoction regulates proliferation and apoptosis of gastric cancer cells by enhancing let-7a expression

Deng HX, Yu YY, Zhou AQ, Zhu JL, Luo LN, Chen WQ, Hu L, Chen GX

Case Control Study

- 5549 Crohn's disease environmental factors in the developing world: A case-control study in a statewide catchment area in Brazil

Salgado VCL, Luiz RR, Boechat N, Schorr BC, Leão IS, Nunes T, Zaltman C

Retrospective Cohort Study

- 5557 Postoperative bleeding in patients on antithrombotic therapy after gastric endoscopic submucosal dissection

Sato C, Hirasawa K, Koh R, Ikeda R, Fukuchi T, Kobayashi R, Kaneko H, Makazu M, Maeda S

Retrospective Study

- 5567 Serous pancreatic neoplasia, data and review

Dietrich CF, Dong Y, Jenssen C, Ciaravino V, Hocke M, Wang WP, Burmester E, Möller K, Atkinson NSS, Capelli P, D'Onofrio M

- 5579 Pancreaticoduodenectomy for duodenal papilla carcinoma: A single-centre 9-year retrospective study of 112 patients with long-term follow-up

Lian PL, Chang Y, Xu XC, Zhao Z, Wang XQ, Xu KS

Clinical Trials Study

- 5589 Efficacy and safety of Xiangsha Liujunzi granules for functional dyspepsia: A multi-center randomized double-blind placebo-controlled clinical study

Lv L, Wang FY, Ma XX, Li ZH, Huang SP, Shi ZH, Ji HJ, Bian LQ, Zhang BH, Chen T, Yin XL, Tang XD

Observational Study

- 5602 Combination of acoustic radiation force impulse imaging, serological indexes and contrast-enhanced ultrasound for diagnosis of liver lesions

Sun XL, Yao H, Men Q, Hou KZ, Chen Z, Xu CQ, Liang LW

Prospective Study

- 5610 Incidents and adverse events of endoscopic ultrasound-guided fine-needle aspiration for pancreatic cystic lesions

Du C, Chai NL, Linghu EQ, Li HK, Sun YF, Xu W, Wang XD, Tang P, Yang J

SYSTEMATIC REVIEWS

- 5619 Systematic review of giant gastric lipomas reported since 1980 and report of two new cases in a review of 117110 esophagogastroduodenoscopies

Cappell MS, Stevens CE, Amin M

- 5634 Acute colonic pseudo-obstruction: A systematic review of aetiology and mechanisms

Wells CI, O'Grady G, Bissett IP

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Systematic review of giant gastric lipomas reported since 1980 and report of two new cases in a review of 117110 esophagogastroduodenoscopies

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Abstract

AIM

To systematically review the syndrome of giant gastric lipomas, report 2 new illustrative cases.

METHODS

Literature systematically reviewed using PubMed for publications since 1980 with following medical subject heading/keywords: ("giant lipoma") AND ("gastric") OR [("lipoma") and ("gastric") and ("bleeding")]. Two authors independently reviewed literature, and decided by consensus which articles to incorporate. Computerized review of pathology/endoscopy records at William Beaumont Hospitals, Royal Oak and Troy, Michigan, January 2005-December 2015, revealed

2 giant gastric lipomas among 117110 consecutive esophagogastroduodenoscopies (EGDs), which were thoroughly reviewed, including re-review of original endoscopic photographs, radiologic images, and pathologic slides.

RESULTS

Giant gastric lipomas are extremely rare: 32 cases reported since 1980, and 2 diagnosed among 117110 consecutive EGDs. Average patient age = 54.5 ± 17.0 years old (males = 22, females = 10). Maximal lipoma dimension averaged $7.9 \text{ cm} \pm 4.1 \text{ cm}$. Ulcerated mass occurred in 21 patients. Lipoma locations: antrum-17, body-and-antrum-4, antrum-intussuscepting-into-small-intestine-3, body-2, fundus-1, and unspecified-5. Intramural locations included submucosal-22, subserosal-2, and unspecified-8. Presentations included: acute upper gastrointestinal (UGI) bleeding-19, abdominal pain-5, nausea/vomiting-5, and asymptomatic-3. Symptoms among patients with UGI bleeding included: weakness/fatigue-6, abdominal pain-4, nausea/vomiting-4, early-satiety-3, dizziness-2, and other-1. Their hemoglobin on admission averaged $7.5 \text{ g/dL} \pm 2.8 \text{ g/dL}$. Patients with GI bleeding had significantly more frequently ulcers than other patients. EGD was extremely helpful diagnostically ($n = 31$ patients), based on characteristic endoscopic findings, including yellowish hue, well-demarcated margins, smooth overlying mucosa, and endoscopic cushion, tenting, or naked-fat signs. However, endoscopic mucosal biopsies were mostly non-diagnostic (11 of 12 non-diagnostic). Twenty (95%) of 21 abdominal CTs demonstrated characteristic findings of lipomas, including: well-circumscribed, submucosal, and homogeneous mass with attenuation of fat. Endoscopic-ultrasound showed characteristic findings in 4 (80%) of 5 cases: hyperechoic, well-localized, mass in gastric-wall-layer-3. Transabdominal ultrasound and UGI series were generally less helpful. All 32 patients underwent successful therapy without major complications or mortality, including: laparotomy and full-thickness gastric wall resection of tumor using various surgical reconstructions-26; laparotomy-and-enucleation-2; laparoscopic-transgastric-resection-2; endoscopic-mucosal-resection-1, and other-1. Two new illustrative patients are reported who presented with severe UGI bleeding from giant, ulcerated, gastric lipomas.

CONCLUSION

This systematic review may help standardize the endoscopic and radiologic evaluation and therapy of patients with this syndrome.

Key words: Esophagogastroduodenoscopy Lipoma; Gastric; Giant; Melena; Upper gastrointestinal bleeding; Systematic review

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Core tip: Systematic literature review of giant gastric lipomas revealed 32 reported cases since 1980, with 2 new cases reported among 117110 esophagogastroduodenoscopies. Two authors independently reviewed literature, and decided by consensus which articles to incorporate. Average-patient-age = 54.5 ± 17.0 years (males = 68.8%). Mean-maximal-lipoma-diameter = $7.9 \text{ cm} \pm 4.1 \text{ cm}$. Lipoma locations: antrum-17, antrum and other gastric segments-7, other-8. Lipomas were submucosal-92%, subserosal-8%. Presentations included: acute upper gastrointestinal (UGI) bleeding-19, abdominal pain-5, nausea/vomiting-5, asymptomatic-3. Esophagogastroduodenoscopy was extremely helpful diagnostically; findings included: yellowish hue, well-demarcated margins, and smooth overlying mucosa. Endoscopic biopsies were infrequently diagnostic. Twenty of 21 abdominal CTs demonstrated characteristic lipoma findings: well-circumscribed, submucosal, and homogeneous mass with fat attenuation. Endoscopic-ultrasound showed characteristic findings in 80%. All patients underwent successful therapy without major complications/mortality, including: laparotomy-with-full-thickness-gastric-wall-resections-26; and other-6. Two newly reported patients presented with severe UGI bleeding from giant, ulcerated, gastric lipomas. This review may help standardize work-up of these patients.

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INTRODUCTION

Gastric lipomas are rare, constituting < 3% of benign gastric tumors, and < 1% of all gastric tumors^[1], and giant gastric lipomas ($\geq 4 \text{ cm}$) are extremely rare, with only 32 cases reported since 1980 (Table 1)^[1-33]. Although small gastric lipomas are usually asymptomatic, giant gastric lipomas typically produce major symptoms from GI obstruction, tumor ulcers, or acute upper gastrointestinal (UGI) bleeding, with 19 cases of UGI bleeding reported since 1980 (Table 1). Due to its extreme rarity, all prior studies of giant gastric lipomas have comprised single case reports. This work systematically reviews the literature since 1980, and collates the case reports scattered among various and sometimes obscure journals, to semi-quantitatively describe the clinical presentation, endoscopic and radiologic findings, and therapy of the disease; and to report two new illustrative cases who presented with massive, life-threatening UGI bleeding among 117110

Table 1 Comprehensive review of the 32 giant gastric lipomas reported since 1980

Ref.	Age, sex, clinical presentation, PMH, signs and lab abnormalities	Diagnostic work-up	Treatment, pathology	Outcome and follow-up
Upper GI bleeding Current case report 1	63 y. o. M with previous medical history of hypertension and hyperlipidemia presented with melena and dyspnea on exertion for 3 d and epigastric pain, early satiety and 10-kg weight loss during the last 6 mo. BP = 144/77 mm/Hg, pulse = 87/min. Hgb = 6.2 g/dL	EGD: 13-cm-wide, submucosal, yellowish, gastric mass in antrum covered by smooth mucosa except for focal ulceration Abdominal CT: well-circumscribed, uniform 13.4 cm × 8.4 cm × 8.2 cm mass, with attenuation characteristic for fat	Laparotomy: Resected by subtotal gastrectomy extended by partial bulbar duodenectomy with Billroth II reconstruction Pathology: Homogeneous, submucosal, soft, 14.5 cm × 8.7 cm × 7.5 cm mass. Lipoma with spindle cell variant by CD34 positivity by immunohistochemistry	Did well postoperatively with no complications. Asymptomatic at 8 wk of follow-up
Current case report 2	78 y. o. F presented with melena for 3 d, associated with weakness and orthostatic dizziness. BP = 124/67 mmHg, pulse = 68/min. Rectal exam-melena. Hgb = 7.1 g/dL	Abdominal CT: submucosal, 9.5 cm × 6.0 cm × 4.5 cm, antral mass. EGD: large, focally ulcerated, antral gastric mass, exhibiting a positive cushion sign	Laparotomy: large, 9.0 cm × 6.0 cm × 4.5 cm, submucosal mass excised by distal gastrectomy. Pathology: lipoma	Patient discharged 5 d postoperatively with no further bleeding Did well postoperatively with uneventful recovery
Ramdass <i>et al</i> ^[1] , 2013	37 y. o. F with epigastric pain, melena, vomiting and weakness for 4 d. Pallor and epigastric tenderness. Hgb = 5.9 g/dL. Transfused 6 units packed erythrocytes	EGD: submucosal mass with 1 cm central ulcer in gastric body	Gastric body. Laparotomy: 4 cm × 3.5 cm × 3.2 cm mass at junction of body and antrum removed surgically Pathology: lipoma	Remained well at 9 mo follow-up
Almohsin <i>et al</i> ^[2] , 2015	61 y. o. M presented with hematemesis, melena, epigastric pain, and fatigue	EGD: Gastric mass with an ulcer. Endoscopic biopsies: benign tissue. EUS: large, hyperechoic, antral, submucosal lesion. Abdominal CT: 8.5 cm × 5 cm submucosal, well-encapsulated antral lesion with density of fat with ulcerated overlying mucosa	Laparotomy: enucleation of lesion and overlying mucosa. Pathology: lipoma	Remained well at 9 mo follow-up
Beck <i>et al</i> ^[3] , 1997	13 y. o. M with hematemesis, melena and abdominal pain for 2 d. Occasional nausea and vomiting for several years. Benign abdomen Hgb = 10.5 g/dL	Abdominal radiograph: polypoid mass. EGD: 8 cm × 3 cm × 4 cm soft and compressible, polypoid mass with basal ulceration on anterolateral wall of antrum. Endoscopic mucosal biopsy: normal antral tissue. Abdominal CT: smooth, uniform intraluminal mass with low attenuation in submucosal layer	Endoscopic polypectomy: Unsuccessful due to thick polyp stalk and patient pain during attempted polypectomy Surgery: Excision of polyp Pathology: lipoma	Uneventful postoperative course. Patient asymptomatic
Bijlani <i>et al</i> ^[4] , 1993	70 y. o. M presented with acute hematemesis. Physical examination revealed pallor. Hgb = 7.0 g/dL	EGD: Protruding mass in antrum. Could not traverse endoscope beyond mass. Endoscopic biopsies: normal UGI series: space-occupying lesion in antrum Abdominal USD: normal	Laparotomy: soft, yellowish mass in antrum stretching the serosa. Mass enucleated <i>via</i> serosal approach Pathology: lipoma	Uneventful post-operative recovery. Asymptomatic at 6 mo of follow-up N.A
Bloch <i>et al</i> ^[5] , 1974	55 y. o. F with 1 episode of melena Nausea, epigastric fullness, and belching for 7 mo. Physical exam reveals grapefruit-sized epigastric mass N.A	Supine abdominal radiograph: Well-demarcated, large epigastric mass UGI series: huge, sharply demarcated, mass in distal two-thirds of stomach with 2 cm × 3 cm ulcer at apex of mass	Distal two-thirds of stomach on anterior wall. Laparotomy: huge, grapefruit size submucosal lipoma arising from anterior wall with shallow central ulcer Surgical resection: not documented	Uneventful postoperative course and asymptomatic at 1 yr
Chu <i>et al</i> ^[6] , 1983	61 y. o. F with previous medical history of gastric ulcer and hiatal hernia diagnosed 2 yr earlier presented with melena and weakness for several days. Rectal exam: fecal occult blood. Hgb = 6.0 g/dL. Transfused 3 units of packed erythrocytes	UGI series: sliding hiatal hernia, and golf-ball-sized mass protruding from lesser curve in antrum. Mass moved in and out of pylorus EGD: well-circumscribed, submucosal, 5 cm × 3 cm-mass protruding along lesser curve in antrum. Positive cushion sign	Laparotomy: 5 cm × 4 cm × 3 cm mass in pre-pylorus. Underwent resection of mass with adjacent lesser curvature, and pyloroplasty Pathology: lipoma	Uneventful postoperative course and asymptomatic at 1 yr
Kibria <i>et al</i> ^[7] , 2009	44 y. o. F with hematemesis and melena for 1 d. Hgb = 8.6 g/dL	EGD: Soft, broad-based, 5 cm × 3 cm mass on greater curvature of stomach. Two ulcers on mass. Positive cushion sign. Abdominal CT: 4.5 cm × 3.0 cm gastric mass with attenuation of fat projecting into lumen. Doppler-assisted EUS: submucosal mass of mixed echogenicity	Greater curvature of stomach Surgical resection, 4.8 cm × 3.2 cm, mature adipocytes with ulceration and necrosis of overlying mucosa	Uneventful recovery. Unremarkable EGD at 6 mo of follow-up

Kumar <i>et al</i> ^[8] , 2015	72 y. o. previously healthy M presented with presyncope associated with diaphoresis and pallor. Rectal exam revealed melena. Hgb = 9.9 g/dL	Abdominal CT: 4.3-cm-wide polypoid mass in antrum consistent with gastric lipoma. EGD: large, submucosal mass in gastric antrum with central ulcer with overlying clot. Ulcer injected with dilute epinephrine	Laparotomy: Gastrostomy with wide excision of antral lesion along anterior wall. Pathology: lipoma	Good postoperative recovery and discharged 3 d after surgery
López Cano <i>et al</i> ^[9] , 1991	76 y. o. M with recent NSAID use, and hypertension presented with acute melena. Hgb = 6.8 g/dL	EGD: posterior wall of antrum 3.5-cm-wide lesion with overlying smooth mucosa. Central ulceration. Endoscopic biopsy: gastritis. Abdominal ultrasound with water-filled stomach: 4-cm-wide, echogenic submucosal mass	Partial gastrectomy Pathology: lipoma	No postoperative complications
Myint <i>et al</i> ^[10] , 1996	54 y. o. F presented with hematemesis and melena for 1 wk. BP = 70/50 mmHg. Benign abdominal exam. Hgb = 4.0 g/dL.	EGD: 4 cm × 3 cm ulcerated submucosal mass in antrum Endoscopic biopsies: nondiagnostic. Abdominal CT: gastric mass with attenuation value of lipoma	Laparotomy: 6 cm × 6 cm mass in posterior wall of gastric antrum with central ulceration. Pathology: lipoma	Patient alive with no evident disease 6 mo after surgery
Ortiz de Solórzapo Aursua <i>et al</i> ^[11] , 1997	60 y. o. F. PMH: vitiligo, acute pancreatitis, duodenal ulcer presented with melena, postprandial pain, nausea, vomiting and early satiety. Pallor. Rectal exam: melena. Hgb = 12.8 g/dL	EGD: antral deformity. No active bleeding. Gastric volvulus? Abdominal USD: 5.8 cm × 3.4 cm pedunculated antral mass intussuscepting into duodenum. Abdominal CT: 4 cm × 3 cm × 3-cm-wide, well-defined, submucosal mass	Surgery; Underwent partial gastrectomy for antral mass intussuscepting into duodenum. Pathology: lipoma	Did well for 6 mo of follow-up
Paksoy <i>et al</i> ^[12] , 2003	71 y. o. M with acute hematemesis and melena. BP = 110/70 mmHg, Pulse = 100/min Hematocrit = 27%	EGD: 4 cm-wide mass with superficial ulcer on posterior gastric wall. Endoscopic biopsies: "benign" lesion Abdominal CT: 4 cm lesion of lipid density in inferioposterior wall of stomach	Inferioposterior wall of stomach Surgery: laparoscopic transgastric resection of 4 cm intramural lipoma Pathology: intramural lipoma	Discharged 6 d postoperatively without complications
Pérez Cabañas <i>et al</i> ^[13] , 1990	73 y. o. M presented with melena and hematemesis for 2 d. Recent NSAID use. PMH: hypertension. Physical exam: pallor, rectal exam-melena. Hgb = 8.6 g/dL. Transfused 5 units of packed erythrocytes	EGD: gastric mass on posterior wall and greater curve with superficial overlying ulcer, small hiatal hernia. Abdominal ultrasound: normal stomach. UGI series: large filling defect, from submucosal lesion	Surgery: Wedge resection for 5 cm × 4 cm submucosal mass Pathology: ulcerated lipoma	Did well after surgery
Priyadarshi <i>et al</i> ^[14] , 2015	46 y. o. M with melena for 1 yr. Palpable, soft epigastric lump. Mild epigastric tenderness Hgb = 5 mg/dL; coagulation parameters and chemistry WNL	EGD: large mass arising from posterior wall antrum with superficial ulceration. Unable to traverse pylorus due to obstruction. Abdominal CT: huge mass with lobulated surface projecting into gastric lumen with density consistent with fat. Tumor extended into pylorus and caused gastric outlet obstruction	Posterior wall of gastric antrum Laparotomy: Billroth I partial gastrectomy; 14 cm × 11 cm × 5 cm sessile broad based submucosal lipoma; path = mature adipocytes	No reported complications
Rao <i>et al</i> ^[15] , 2013	60 y. o. M presented with melena, fatigue and pallor. Hgb = 7.2 g/dL	EGD: large, smooth, submucosal bulge along lesser curvature of stomach. Contrast enhanced abdominal CT: Well-defined, encapsulated, submucosal mass with attenuation of fat along lesser curvature of stomach	Laparotomy: large submucosal tumor excised <i>via</i> anterior gastrotomy Pathology: 15 cm × 12 cm submucosal tumor with a focal ulcer. Microscopy demonstrates submucosal lipoma	Presently asymptomatic
Regge <i>et al</i> ^[16] , 1999	52 y. o. M presented with hematemesis and melena. Hgb = 5.5 g/dL	EGD: 3.5-cm-wide, round, pale-pink formation on anterior gastric antrum with oozing superficial ulcer. Hemostasis achieved with dilute epinephrine injection. Abdominal USD: 4-cm-wide hyperechoic antral lesion with distinct margins. Abdominal CT with IV contrast: 4-cm-wide, well-circumscribed, antral lesion with density of fat. Abdominal MRI: Confirmed fat-tissue signal in mass by hyperintensity on T1-weighted images and marked signal reduction on sequences performed with fat suppression	Laparotomy: Antrectomy and gastrojejunal anastomosis <i>via</i> a Roux-en-Y loop. Pathology: lipoma	N.A
Sadio <i>et al</i> ^[17] , 2010	44 y. o. M with medical history of hypertension, obesity, and sleep-apnea, presented with fatigue and intermittent melena for 1 mo. Physical exam revealed pallor. Hgb = 7.8 g/dL	EGD: 4-cm-wide, yellowish, submucosal mass in gastric fundus with central overlying ulceration. EUS: hyperechoic submucosal mass. Abdominal CT: homogeneous, well-circumscribed mass in fundus with density of fat	Surgery: partial gastric resection Pathology: submucosal lipoma	Did well and discharged 10 d postoperatively

Singh <i>et al</i> ^[18] , 1987	40 y. o. M with melena, pyrexia, chills, and weakness. BP = 100/70 mmHg, pulse = 106/min, temp = 39 °C, abdomen-soft, nontender, no palpable mass. Hgb = 4.0 g/dL	EGD: huge polypoid tumor in gastric body along greater curve. Multiple small superficial ulcers in antrum EGD biopsies: Mildly inflamed, mature adipose tissue UGI series: large gastric tumor	Gastric body along greater curve Laparotomy: smooth mass in gastric body and antrum. Multiple small ulcerations. Underwent subtotal gastrectomy and gastrojejunostomy. Pathology: 18 cm × 10 cm × 10 cm encapsulated lipoma	Discharged 2 wk postoperatively. Asymptomatic for 1 yr.
Youssef <i>et al</i> ^[19] , 1999	54 y. o. nonalcoholic F presented with melena and dizziness Physical exam: stable vital signs, abdominal tenderness without peritoneal signs. Hgb = 9.2 g/dL	EGD: submucosal protrusion with mucosal erosion along greater curvature in body and antrum Abdominal USD: homogeneous, hyperechoic mass in submucosa of posterior gastric wall. Abdominal CT: homogeneous, 5.1 cm × 3.7 cm lesion with density of fat in posterior gastric wall	Laparotomy: with full-thickness resection of lesion Pathology: 5.2 cm × 3.8 cm × 3.2 cm submucosal lipoma	Uneventful recovery
Abdominal pain Alberti <i>et al</i> ^[20] , 1999	11 y. o. F with periumbilical and RLQ abdominal pain for 3 yr. Outpatient UGI series revealed multiple filling defects in gastric antrum and body. Normal physical examination. Abdomen was soft with no palpable mass. No fecal occult blood. Normal routine blood studies. Normal iron studies	EGD: multiple, large, soft, masses protruding into gastric body and antrum with normal overlying mucosa. Gastric biopsies: normal mucosa. Abdominal USD: multiple, homogeneous, well-encapsulated, submucosal masses with attenuation characteristic of fat. Abdominal MRI: solid, hyperintense formations with signal characteristic of fat in gastric body and antrum. Percutaneous transgastric ultrasound guided biopsy: features of lipoma with mild inflammatory infiltrate	Gastric body and antrum. No treatment because became asymptomatic	"Pain progressively relieved" Follow-up MRI of abdomen: no change
Hamdane <i>et al</i> ^[21] , 2012	51 y. o. M with epigastric pain N.A	EGD: soft, large, ulcerated, submucosal mass in antrum Endoscopic biopsies: nonspecific inflammation of gastric mucosa. Abdominal CT: Round, well-circumscribed, low-attenuation, 9-cm-wide, gastric mass	Surgery: total gastrectomy. Pathology: 9 cm × 7.5 cm × 5 cm., mature adipocyte proliferation with variation of cell size in a fibro-myxoid background. Immunohistochemistry: positive to anti-HGMA2, but not S-100, or CD34, No MDM2 or CDK4 amplification, consistent with lipoma	Uneventful recovery. No symptoms at 1 yr follow-up
Neto <i>et al</i> ^[22] , 2012	63 y. o. M history of dyslipidemia, and hypertension with upper abdominal pain. Physical exam reveals a palpable, moveable upper abdominal mass Normal routine laboratory tests	Abdominal USD: large echoic mass compatible with an expansive lesion in gastric antrum. EGD: large bulging mass in posterior gastric wall with three ulcerated areas Endoscopic biopsies: necrotic mucosa Abdominal CT: well-defined, homogeneous, oval mass located within the posterior gastric wall that compressed descending duodenum and had the density of fat	Posterior gastric wall. Laparotomy with a subtotal gastrectomy and D1 lymphadenectomy with Roux-en-Y reconstruction: 12 cm × 8 cm × 6 cm, lipoma with mature, well differentiated adipocytes surrounded by a fibrous capsule with 3 ulcerative lesions of 0.5 cm, 1 cm, and 1.4 cm Antrum	Uneventful recovery with discharge 7 d postoperatively
Ramaraj <i>et al</i> ^[23] , 2012	52 y. o. M with dyspepsia, anorexia, and early satiety for 6 mo. Gastric ulcer 5 yr earlier. Iron deficiency anemia: Hg = 11.5 g/dL, ferritin = 5 ng/mL	Colonoscopy: within normal limits. EGD: Extrinsic indentation in distal stomach with smooth overlying mucosa. Endoscopic biopsy: normal mucosa CT abdomen: 15 cm × 14 cm fatty tumor in distal stomach	Subtotal gastrectomy: Submucosal antral lipoma with central ulceration	No postoperative complications. Asymptomatic at 4 wk of follow-up
Zak <i>et al</i> ^[24] , 2006	58 y. o. M with intermittent upper abdominal discomfort, early satiety, smoking, hyperlipidemia, obesity, PTSD, and depression. Has iron deficiency anemia	EGD: 10 cm × 6 cm smoothly lobulated, submucosal mass in gastric antrum along greater curvature. Chronic inflammation and intestinal metaplasia of gastric mucosa. EUS: hypoechoic submucosal mass surrounded by a hyperechoic layer in posterior wall of stomach, consistent with encapsulated lipoma. Abdominal CT: homogeneous, round, sharply-defined, encapsulated, submucosal lesion with characteristic density of fat	Gastric antrum along the greater curvature Laparotomy: resection only of the encapsulated mass Pathology: 10 cm × 6 cm lipoma	Uneventful recovery with discharge on day 7. Follow-up abdominal CT 2 mo later revealed no abnormalities
Predominantly nausea and vomiting or obstructive symptoms				

Aslan <i>et al</i> ^[25] , 2015	77 y. o. M with nausea and vomiting, and dyspepsia. Complete blood count and comprehensive metabolic panel: WNL	EGD: submucosal mass with normal overlying mucosa extending into antrum along lesser curve	Endoscopic submucosal resection of 9-cm-long lipoma with an intact capsule	Discharged after 3 d. Resolution of symptoms at 6 mo of follow-up. Repeat endoscopy did not reveal a mass
Lin <i>et al</i> ^[26] , 1992	77 y. o. F with nausea, vomiting, abdominal pain for 3 wk and 7-kg-weight-loss. Dehydrated and generalized mild abdominal tenderness. Rectal exam: fecal occult blood	UGI series: large polypoid gastric mass intussuscepting into duodenum. Abdominal USD: suspected intussusception. EGD: inadequate examination. Differential of gastric torsion <i>vs</i> intussusception	Laparotomy: large necrotic polypoid intussuscepting mass arising in stomach. Polyp resected at its base. Pathology: large polypoid lipoma	Ultimately recovered and was discharged
Mouës <i>et al</i> ^[27] , 2002	72 y. o. M with anorexia, early satiety, nausea, and involuntary weight loss. No overt GI bleeding. Left lung lobectomy for bronchial lung cancer 10 yr earlier. Hemoglobin = 4.7 g/dL	EGD: gastric mucosal hypertrophy extending into duodenum. Abdominal USD: hyperechoic mass in small intestine, consistent with lipoma, with likely intussusception. CT abdomen: low attenuation intraluminal tumor compatible with small intestinal lipoma	Laparotomy: large pedunculated tumor intussuscepting into jejunum. Mass reduced back into stomach. Gastrostomy revealed 10 cm × 5 cm superficially ulcerated gastric lipoma. Mass excised. Pathology: mature adipose tissue	Uneventful recovery
Nasa <i>et al</i> ^[28] , 2016	56 y. o. F with dyspepsia and occasional vomiting for 1 yr. Mild epigastric tenderness	EGD: smooth 5-cm-wide antral bulge with overlying normal mucosa. Positive cushion sign. Endoscopic biopsy: chronic active gastritis from <i>Helicobacter pylori</i> . EUS: homogeneous, hyperechoic, mass arising from layer 3 of gastric wall, compatible with lipoma. Abdominal CT: homogeneous, 6-cm-wide, oval mass in antropyloric region, with density of fat	Antrum and pylorus along lesser curve Laparotomy: Excision of 6 cm wide, encapsulated tumor along lesser curve of stomach	Did well and discharged. Asymptomatic at 6 mo
Treska <i>et al</i> ^[29] , 1998	61 y. o. M with intermittent vomiting for several days. History of gastric ulcer N.A	UGI series: spherical, smooth, 4.0 cm × 4.5 cm defect in gastric antrum. EGD: protruding, yellowish tumor in prepylorus. Two ulcers above tumor. Abdominal ultrasound: 7 cm × 6 cm × 5 cm echogenic defect in wall of gastric antrum. Abdominal CT: prepyloric intramural lipoma	Gastric antrum. Laparotomy: 7.0 cm × 6.0 cm tumor in prepylorus. Tumor resection of lipoma with performance of Billroth II	Discharge 12 d postoperatively. No GI symptoms 8 mo after surgery
Lipoma discovered incidentally in work-up for other condition				
Al Shammari <i>et al</i> ^[30] , 2016	41 y. o. M presented for morbid obesity with a BMI of 43.9 kg/m ² and history of obstructive sleep apnea. Normal routine blood tests	Abdominal ultrasound: liver span of 18.8 cm. EGD: rounded 3 cm × 3 cm mass in antrum with normal overlying mucosa. Positive cushion sign. Abdominal CT: 3.5 cm × 3.0 cm lesion in stomach suspicious for lipoma	Antrum. Laparoscopy: Intragastic submucosal mass excised from inside stomach after gastrostomy. Sleeve gastrectomy then performed for morbid obesity. Pathology: 4 cm × 3 cm × 2 cm lipoma	Discharged 4 d postoperatively. Asymptomatic at 2 wk of follow-up
Hyun <i>et al</i> ^[31] , 2002	22 y. o. M who underwent abdominal CT as preoperative evaluation of retroperitoneum before orchiectomy for testicular cancer. N.A	Abdominal CT: large gastric mass with attenuation of fat projecting into gastric lumen. EGD: large, soft, sessile mass on greater curve of stomach with overlying pink mucosa. Positive cushion sign. Endoscopic biopsies: normal mucosa. EUS: Submucosal mass with less echogenicity than expected for lipoma	Surgical resection: 12 cm × 9 cm × 2.5 cm mobile mass resected. Pathology: Submucosal gastric lipoma	Doing well at 2 mo follow-up
López-Zamudio <i>et al</i> ^[32] , 2015	59 y. o. M who underwent abdominal CT performed during episode of acute alcoholic pancreatitis revealed probable pyloroduodenal intussusception of a tumor with attenuation suggestive of fat. Hgb = 9.3 g/dL	EGD: 8 cm long polypoid mass impeding flow near pylorus. EGD biopsy: gastritis and incomplete intestinal metaplasia. Repeat EGD: greater curve posterior wall large pedunculated polyp with central ulceration Repeat EGD biopsies: chronic gastritis, focal ulceration intestinal metaplasia and <i>Helicobacter pylori</i> infection. EUS: 5.6 cm × 4.9 cm mass in gastric antrum in muscular layer	Surgery: 5 cm × 5 cm tumor in anterior wall of gastric antrum. Underwent antroduodenectomy with gastroduodenal anastomosis and Roux-en-Y	No postoperative surgical complications. Asymptomatic at 18 mo of follow-up

PMH: Previous medical history; GI: Gastrointestinal; y.o.: Years old; M: Male; F: Female; Hgb: Hemoglobin; BP: Blood pressure; EGD: Esophagogastroduodenoscopy; CT: Computerized tomograph; EUS: Endoscopic ultrasound; UGI: Upper gastrointestinal; USD: Ultrasound; N.A: Not applicable; NSAID: Nonsteroidal anti-inflammatory drug; WNL: Within normal limits; IV: Intravenous; MRI: Magnetic resonance imaging; RLQ: Right lower quadrant; PTST: Post traumatic stress disorder; BMI: Body mass index.

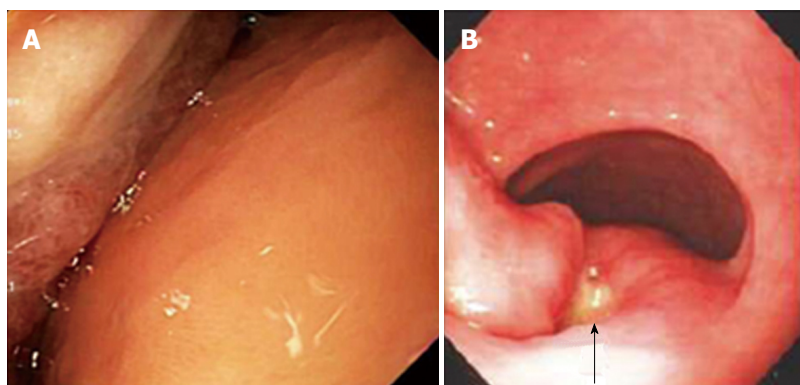


Figure 1 Findings at esophagogastroduodenoscopy in two patients with giant gastric lipomas. A: Patient 1. Esophagogastroduodenoscopy (EGD) in a 63-year-old male who presented with melena and a hemoglobin decline to 6.2 g/dL that required transfusion of 2 units of packed erythrocytes, showing the distal body and antrum with a huge mass folded upon itself occupying most of the lumen and an 8 mm wide, nonbleeding, acute mucosal ulcer without stigmata of recent hemorrhage embedded deep in the valley (fold) between the right and left parts of the mass. The ulcer was attributed to friction from the opposing surface. The mass was 13-cm-wide, submucosal, yellowish, and covered by smooth mucosa except for focal ulceration, findings consistent with a gastric lipoma; B: Patient 2. EGD in a 78-year-old woman, who presented with melena for 3 d, orthostatic dizziness, and a hemoglobin decline to 7.1 g/dL requiring transfusion of 2 units of packed erythrocytes, revealed an acute 1-cm-wide prepyloric ulcer (arrow) with a white exudate but without stigmata of recent hemorrhage between the right and left lobes of a large, well-demarcated, submucosal, mass covered by otherwise normal, superficial mucosa. This endoscopic photograph shows only a part of the mass.

analyzed esophagogastroduodenoscopies (EGDs) at two large hospitals.

MATERIALS AND METHODS

The literature was systematically reviewed using PubMed for articles published since 1980 with the following medical subject heading (MeSH) or keywords: ("giant lipoma") AND (gastric) OR [("lipoma") and ("gastric") and ("bleeding")]; and by reviewing the section on gastrointestinal lipomas in standard pathology textbooks or monographs. Two authors independently reviewed the literature, and decided by consensus which articles to incorporate in this review. After reviewing one case from 1974^[5], cases reported before 1980 were selectively excluded because the preoperative evaluation at the time frequently used relatively obsolete tests such as UGI series and often lacked currently mandatory tests such as EGD. Four case reports, written in Spanish^[9,11,13,32], were professionally translated into English. Case reports of large gastric adenomas which did not satisfy the minimal size criteria of giant gastric lipomas (≥ 4 cm) were systematically excluded^[3,34]. A video publication was excluded because clinical details were not reported^[35]. A clinical series of 16 gastric lipomas were excluded because this series lumped together medium-sized and giant lipomas^[36].

Computerized review of the pathology records at William Beaumont Hospitals at Royal Oak and at Troy, Michigan from January 2005–December 2015 using the computerized system of PowerPath (Tamtron) and SOFTPath with the software terms ("lipoma" or "lipomas") AND ("gastric" or "stomach") revealed 2 cases of giant gastric lipomas. Computerized review of the EGD reports using ProVations did not reveal any

further cases. These 2 cases were thoroughly reviewed based on medical records, including re-review of the original endoscopic photographs by an expert endoscopist, radiologic images by an expert radiologist, and pathologic slides by an expert pathologist. This dual case report received exemption/approval by the IRB at William Beaumont Hospital, Royal Oak, on October 17, 2016.

Illustrative case reports

Case 1: A 63-year-old, nonalcoholic, man with a medical history of hypertension treated with lisinopril, amlodipine, and nifedipine, and hyperlipidemia treated with lovastatin, presented with epigastric pain, early satiety, and involuntary 10-kg-weight-loss during the last 6 mo, and melena and dyspnea on exertion for 3 d. The vital signs were stable, with a blood pressure of 144/74 mmHg, and pulse of 87/min. The abdomen was soft, nontender, and without hepatosplenomegaly or palpable masses. Rectal examination revealed melena. The hemoglobin was 6.2 g/dL, blood urea nitrogen was 27 mg/dL, and creatinine was 1.40 mg/dL. He had 496000 platelets/mL, a normal international normalized ratio (INR), and normal partial thromboplastin time (PTT). He was transfused two units of packed erythrocytes.

EGD revealed a 13-cm-wide submucosal, yellowish, gastric mass primarily in the antrum, covered by smooth mucosa except for focal ulceration (Figure 1A), and exhibiting the pillow sign, of indentation of the mass with moderate pressure applied *via* a closed forceps^[37,38]. Microscopic examination of multiple mucosal biopsies of the ulcer margin revealed superficial ulceration, granulation tissue, and no malignancy. Abdominal computerized tomography (CT) revealed a well-circumscribed, homogeneous, 13.4 cm \times 8.4

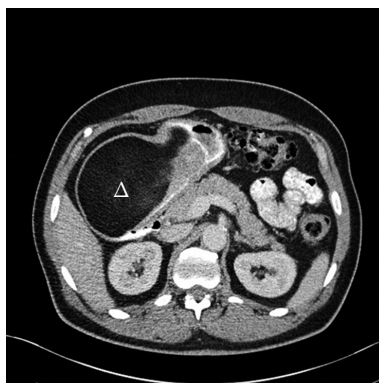


Figure 2 Abdominal computerized tomography findings in patient 1. A 63-year-old male (patient 1) presented with acute melena and hemoglobin decline to 6.2 g/dL, and esophagogastroduodenoscopy revealed a huge, submucosal mass with a smooth overlying surface and exhibiting the pillow sign characteristic of a submucosal lipoma. Illustrated abdominal computerized tomography shows an approximately 13.4 cm × 8.2 cm × 8.4 cm mostly homogeneous, hypodense mass with a characteristic attenuation of fat (-90.2 Hounsfield units) extending from proximal gastric body through entire antrum. The normal-appearing very proximal stomach is filled with oral contrast without a mass, and leads to a very narrow, compressed, distal and dorsal, gastric channel containing oral contrast that passes into the duodenum. Triangle: antral giant gastric lipoma which has the characteristic hypodense attenuation of fat.

cm × 8.2 cm mass, with attenuation characteristic of fat, arising from the gastric antrum and producing a mass effect on the proximal duodenum (Figure 2). A 7-mm-wide lesion in the body of the pancreas was also suspected to be a lipoma based on its characteristic attenuation. The patient underwent laparotomy due to the recent bleeding of the giant lipoma. It was resected *via* subtotal gastrectomy extended by partial bulbar duodenectomy due to lipoma extension into duodenal bulb, with Billroth II reconstruction. Gross pathology revealed a homogeneous, soft, submucosal mass with a cut surface exposing yellowish, greasy tissue, measuring 14.5 cm × 8.7 cm × 7.5 cm (Figure 3A), which microscopically revealed lipoma (Figure 4A). Immunohistochemical staining revealed positivity for CD34 (Figure 4B), a finding highly consistent with a spindle cell variant lipoma^[39]. The patient was discharged 8 d postoperatively, and had no complications during 8 wk of follow-up.

Case 2: A 78-year-old, nonalcoholic, woman with a medical history of atrial fibrillation, peripheral neuropathy, hypertension, dyslipidemia, diabetes, chronic renal insufficiency, and hysterectomy for uterine fibroids, presented with melena for three days, associated with fatigue and orthostatic dizziness. Medications included warfarin, furosemide, metoprolol, diltiazem, atorvastatin, pioglitazone, amitriptyline, and glimepiride. Physical examination revealed stable vital signs, with a blood pressure of 124/67 mmHg, and pulse of 68/min. There was a heart murmur, and bilateral 3+ lower extremity edema. The abdomen was

soft, and non-tender, with normoactive bowel sounds, and no organomegaly. Rectal examination revealed melena. The hemoglobin was 7.1 g/dL, INR was 4.9, platelet count was 306000/mL, and PTT was 42.5 s. The blood urea nitrogen was 44 mg/dL and creatinine was 1.8 mg/dL. An electrocardiogram revealed atrial fibrillation without acute ischemic changes.

She was transfused 2 units of packed erythrocytes and 2 units of fresh frozen plasma. Two-dimensional echocardiography revealed mild mitral valve regurgitation, moderate-to-severe right atrial dilatation, and severe tricuspid valve regurgitation. Abdominal CT revealed a submucosal, antral, gastric mass measuring 9.5 cm × 6.0 cm × 4.5 cm. EGD revealed a large, focally ulcerated, smooth, antral gastric mass, exhibiting the cushion sign (Figure 1B). Microscopic examination of multiple mucosal biopsies of the ulcer margin revealed superficial ulceration, granulation tissue, and no malignancy. The patient underwent surgery due to the recent bleeding of the giant lipoma. At laparotomy, the submucosal mass was excised by distal gastrectomy. Gross pathology of the resected mass revealed a relatively homogeneous, 9.0 cm × 6.0 cm × 4.5 cm, focally ulcerated, mass with a greasy, tan-yellow cut surface (Figure 3B), which microscopically was a lipoma (Figure 4C and D). The patient was discharged 5 d postoperatively with no further GI bleeding^[37-39].

RESULTS

Systematic literature review revealed that giant gastric lipomas are rare, with only 32 cases reported since 1980 (Table 1), and only 2 cases currently identified among 117110 EGDs performed during 11 years at William Beaumont Hospital, Royal Oak, one of the five largest hospitals in the United States, and at William Beaumont Hospital, Troy. The 32 reported patients were on average 54.5 ± 17.0 years old. Thirty were adult patients, and two were pediatric patients. Twenty-two were male, and 10 were female. Twenty-one patients had an ulcerated mass. The lipomas averaged 7.9 cm ± 4.1 cm in maximal dimension. Lipoma locations included antrum-17, body and antrum-4, antrum intussuscepting into small intestine-3, gastric body-2, fundus-1, and unspecified-5. This data confirms previous reports that giant gastric lipomas most commonly occur in the antrum^[40]. Intramural locations included submucosal-22, subserosal-2, and unspecified-8. This data confirms previous reports that giant gastric lipomas are generally submucosal, but occasionally subserosal^[22,36].

Nineteen patients presented with acute UGI bleeding, including melena-11, hematemesis and melena-7, and hematemesis-1. Giant lipomas can ulcerate and bleed secondary to venous stasis^[14], friction and trauma

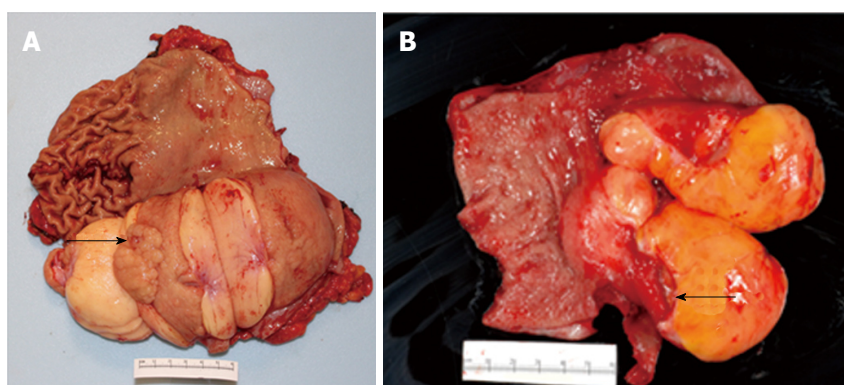


Figure 3 Gross pathologic findings in gastrectomy specimens in two patients with giant gastric lipomas. A: Patient 1. Patient 1 presented with acute melena and hemoglobin decline and had an ulcer detected at esophagogastroduodenoscopy (EGD) within a huge, lipomatous gastric mass. Gross pathologic view of the gastrectomy specimen after it is opened to expose the luminal surface shows a well-circumscribed, lobulated, 14.5 cm × 9.0 cm × 7.5 cm lipomatous mass extending from the gastric body (left) to antrum (right). A small ulcer (round depression, arrow) is present on the mucosa overlying the lipomatous mass. Normal gastric rugae are present above the mass on the upper left, but have been effaced on the upper right, likely because of chronic compression/pressure from the giant lipomatous mass located below (on the contralateral gastric wall before opening the stomach). Vertical incisions show a homogeneous yellow-tan cut surface, indicative of a lipomatous tumor; B: Patient 2. Patient 2 presented with melena for 3 d, orthostatic dizziness, and a hemoglobin decline to 7.1 g/dL requiring transfusion of 2 units of packed erythrocytes and had at EGD a large, yellowish, smooth, well-circumscribed antral mass. Gross pathologic view of distal gastrectomy specimen after it is opened to expose the luminal surface shows normal gastric antral tissue at left and a lobulated, well-circumscribed, yellow-tan, 9.0 cm × 6.0 cm × 3.5 cm lipomatous tumor at right, with a deep, clean-based, ulcer (arrow) on the mucosa overlying the mass.

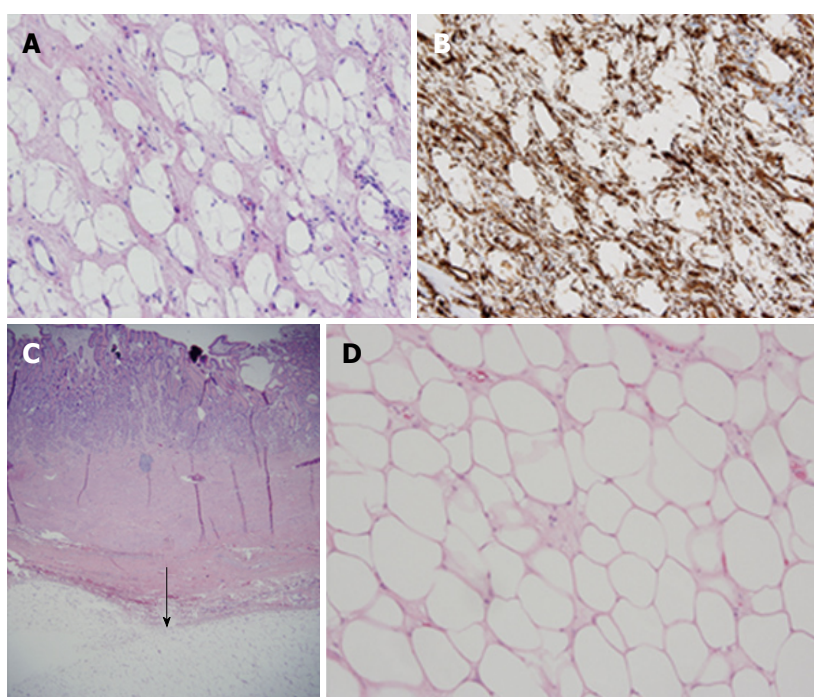


Figure 4 Histopathologic findings in gastrectomy specimens in two patients with giant gastric lipomas. A: Patient 1-standard histochemistry. Medium power photomicrograph of a hematoxylin and eosin stain of a tissue section from the resected gastric mass in patient 1 reveals large adipocytes filled with clear, homogeneous, cytoplasm and tiny, compressed, peripheral nuclei. No lipoblasts are detected. Note the spindle-shaped stroma surrounding the adipocytes, findings consistent with spindle cell lipoma, as proven by immunohistochemistry (B); B: Patient 1-immunohistochemistry. Medium power photomicrograph of immunohistochemistry, using an antibody to CD34, reveals within tumor in patient 1 extensive staining in a spindly pattern of the stroma surrounding characteristically clear adipocytes, a characteristic staining pattern for spindle-shaped lipoma; C: Patient 2-standard histochemistry-low power. Low power photomicrograph of a hematoxylin and eosin stain of a tissue section from resected gastric mass in patient 2 reveals a well-circumscribed, submucosal layer composed of adipocytes with clear cytoplasm (arrow) and scant loose, myxoid stroma; D: Patient 2-standard histochemistry-medium power. Medium power photomicrograph of a hematoxylin and eosin stain of a tissue section from resected gastric mass in patient 2 reveals sheets of large, adipocytes filled with clear, homogeneous, cytoplasm and tiny, compressed, peripheral nuclei, with scant loose, myxoid stroma. No lipoblasts are detected. These histologic findings are characteristic of lipomas.

Table 2 Risks factors for upper gastrointestinal bleeding among 32 patients with giant gastric lipomas

Parameter	mean ± SD of parameter in patients with bleeding	mean ± SD of parameter in patients without bleeding	Patients with bleeding: <i>n</i> with parameter/ total <i>n</i> (% with parameter)	Patients without bleeding: <i>n</i> with parameter/ total <i>n</i> (% with parameter)	<i>P</i> value	OR	95%CI	Statistical test
Continuous variables								
Patient age	54.9 ± 15.5 yr	53.8 ± 19.6 yr	-	-	0.87	NA	NA	Student's <i>t</i> test
Lipoma size	7.1 cm ± 4.4 cm	9.3 cm ± 3.1 cm	-	-	0.16	NA	NA	Student's <i>t</i> test
Dichotomous variables								
Male sex	-	-	12/19 (63.2)	10/13 (76.9)	0.47	0.51	0.08-3.17	χ^2 test
Ulcer overlying lipoma	-	-	16/19 (84.2)	4/13 (30.8)	0.004	12.0	1.72-101.9	Fisher's exact test

UGI: Upper gastrointestinal; *P*: Probability; NA: Not available.

of the lipoma tip against the wall contralateral to the lipoma attachment site, or, least likely, from outgrowing their blood supply. Among 19 patients presenting with acute GI bleeding, the hemoglobin on admission averaged 7.5 g/dL ± 2.8 g/dL (unavailable in 2 patients). Symptoms in the 19 patients included: weakness/fatigue-6, abdominal/epigastric pain-4, nausea and vomiting-4, epigastric fullness/early satiety-3, dizziness/presyncope-2, and belching-1. Signs included: pallor-7, epigastric tenderness-3, epigastric mass-3, tachycardia-2, and one each with diaphoresis or hypotension. Among four analyzed variables including age, sex, lipoma size, and lipoma ulceration, only lipoma ulceration was statistically significantly different (more common) in patients presenting with UGI bleeding, than in patients with other presentations (*P* = 0.004; Table 2). This difference emphasizes the importance of lipoma ulceration in the pathogenesis of bleeding.

Five patients presented predominantly with abdominal pain, without acute UGI bleeding, including 2 presenting with iron deficiency anemia. Additional symptoms in these 5 patients included early satiety-2, and anorexia-1. Five patients presented with nausea and vomiting. These patients had additional symptoms including dyspepsia/abdominal pain-3, weight loss-2, anorexia-1, and early satiety-1. Three patients had asymptomatic giant gastric lipomas incidentally detected: by EGD before bariatric surgery for morbid obesity; by abdominal CT in the evaluation of testicular cancer; and by abdominal CT for severe acute pancreatitis.

Thirty-one of the 32 patients underwent EGD (one other patient, see Methods section). EGD is standardly performed preoperatively to characterize the anatomy and show characteristic endoscopic features of lipomas. However, EGD frequently fails to obtain diagnostic tissue due to failure of superficial mucosal biopsies to reach submucosa. Among 12 patients in whom endoscopic biopsy results were reported in the present review, only 1 (8.3%) had lipoma diagnosed pathologically by endoscopic biopsies^[18]. Pathologic findings in the other 11 reported biopsy specimens included chronic or nonspecific inflammation, gastritis, and normal or necrotic tissue. Repeated biopsies at the same site (well technique) may increase somewhat the diagnostic yield of endoscopic biopsies. Repeated or deep biopsies at EGD may expose yellow fat from the lipoma, a finding called the “naked fat” sign^[41,42]. In the tenting sign observed at EGD the superficial mucosa retracts from the submucosal mass when it is grasped with a forceps because the submucosal lipoma has a fibrous capsule and does not infiltrate into the mucosa. Submucosal lipomas tend to be smooth except for focally ulcerated areas.

CT is currently the standard imaging modality. Lipomas are identified by having an attenuation ranging from -70 to -120 Hounsfield units, characteristic of fat density^[20]. Twenty (95.2%) of 21 patients undergoing abdominal CT had CT findings highly suspicious for lipoma, and the other one had diagnostically helpful findings. CT findings consistent with a lipoma include: a well-circumscribed, submucosal, and homogeneous, mass with an attenuation characteristic of fat. Seven patients underwent upper gastrointestinal series which revealed mass size, mass location, and a smooth superficial layer, but did not show characteristic features of lipomas^[4-6,13,18,26,29]. All 7 patients undergoing UGI series were reported in publications from 1998 or before, whereas only 4 of 21 patients undergoing CT were reported in publications from 1998 or before (17 CTs reported in publications from 1999-2016) (*P* < 0.00001, OR > 3.53, Fisher's exact test). This difference is consistent with replacement of UGI series by EGD and abdominal CT which provide superior characterization. In 9 (82%) of 11 cases abdominal ultrasound showed features suspicious for lipomas of a well-demarcated, submucosal, hyperechoic lesion, but the lesion was missed in 2 cases^[4,9,11,16,19,20,22,26,27,29,30]. These results are consistent with abdominal ultrasound being a cheaper, but less definitive test than abdominal CT for giant gastric lipomas.

In 4 (80%) of 5 cases, endoscopic ultrasound (EUS) showed characteristic findings of a lipoma of a hyperechoic, well-localized, submucosal mass, but in one case the findings were atypical^[17,24,28,31,32]. EUS is useful to identify the primary wall layer of lipomas^[22,43]. The currently reported findings are consistent with EUS being an important adjunct test when abdominal CT is non-diagnostic, when a tissue diagnosis is needed preoperatively because of non-diagnostic EGD biopsies, or prior to endoscopic mucosal resection. Both patients undergoing abdominal magnetic resonance imaging (MRI) had important findings showing tumor anatomy and exhibiting signals characteristic of fat^[16,20].

Therapy was successful in all 32 patients including laparotomy with full-thickness resection of gastric wall containing tumor either *via* wedge resection, partial gastrectomy, Billroth I resection or other surgery-26; laparotomy with enucleation-2; laparoscopic transgastric resection-2; endoscopic mucosal resection-1, and successful laparotomy with polypectomy after unsuccessful, attempted endoscopic polypectomy-1. No patient suffered major postoperative or postprocedural complications. No patient died from GI bleeding from the lipoma, from the surgery, or from endoscopic therapy.

When GI bleeding or gastric obstruction are associated with a large, ulcerated gastric mass, gastric malignancy may be suspected. It is critical to preoperatively exclude liposarcomas from giant lipomas because liposarcomas require further genetic analysis of pathologic specimens, and chemotherapy after surgical resection^[44]. Lipomas have well-demarcated margins on radiologic imaging due to the presence of a fibrous capsule. They are well-differentiated, devoid of lipoblasts, and grow slowly. Liposarcomas have a densitometry close to normal submucosal tissue at abdominal CT^[20,45], and are definitively diagnosed by MDM2 and CDK4 gene amplification^[21,26]. Other tumors in the differential diagnosis of giant lipomas include GI stromal tumors, such as leiomyoma and fibroma; and rarely intramural tumors, such as neurilemoma, adenomyoma, Brunner's gland adenoma, and heterotopic pancreas^[22].

Treatment for lipomas is not standardized. They are often resected endoscopically when < 4-6 cm, and surgically when > 6 cm^[14,22], but endoscopy has been used to resect up to 9-cm-wide gastric lipomas^[25]. Lipomas may sometimes be resected by enucleation because they are encapsulated. Resection *via* subtotal gastrectomy entails much greater morbidity from potential complications of anastomotic leakage, duodenal stump rupture, obstruction, hemorrhage, decreased acid production, delayed gastric emptying,

gastroesophageal reflux, and vitamin B12, folate, iron, or calcium deficiencies^[24].

DISCUSSION

The current literature review demonstrates characteristic findings of giant gastric lipomas at EGD, abdominal CT, EUS, and immunohistochemistry, as summarized in Table 3^[3,8,14,18,20,22,36-38,40-42,47-52]. The two currently reported cases illustrate characteristic features of giant gastric lipomas: frequently presenting with acute UGI bleeding which is often severe and life-threatening, characteristic endoscopic features, characteristic CT findings, pathologic findings indicating benignity, and excellent post-operative prognosis with rare major morbidity or mortality.

The current case reports are limited by retrospective analysis, and by only reporting 2 cases due to disease rarity. The current literature review is likewise limited first, by consisting of single case reports due to syndrome rarity; and second, by retrospectively reporting of case reports. Individually reported cases may be subject to selection bias with preferential reporting of more clinically dramatic or more successful therapeutic interventions. Third, cases from different centers reported somewhat variable clinical data, such as variable follow-up and variable imaging tests (*e.g.*, abdominal CT vs MRI). Fourth, the evaluation of lipomas has evolved over time due to development of better diagnostic tests. This effect was minimized by excluding cases reported before 1980. Fifth, imaging tests were interpreted by various radiologists and pathology specimens were interpreted by various pathologists at various hospitals in the prior case reports.

In conclusion, this systematic literature review provides a comprehensive analysis to help optimize the evaluation and management of suspected giant gastric lipomas. CT and EGD are the standard tests to evaluate suspected giant gastric lipomas. When giant gastric lipomas are identified at abdominal CT by characteristic findings of a homogeneous, well-circumscribed, submucosal mass with characteristic attenuation of fat, EGD with biopsies should be performed, but the endoscopic biopsies may be non-diagnostic. EUS with deep biopsies may be performed to obtain a definitive diagnosis if biopsies from EGD are non-diagnostic. Liposarcoma should be excluded by cytogenetic analysis when necessary. If lipoma is confirmed, endoscopic resection of only the lipoma and its fibrous capsule may be feasible for small-to-moderate sized lesions, with subtotal gastrectomy reserved for especially large lipomas.

Table 3 Distinctive features of giant gastric lipomas

Test/technique/parameter	Distinctive characteristic	Pathophysiology	Ref.
Age	Average age = 54.5 ± 17.0 years old		Current Report
Gender ratio	Male-to-Female ratio approximately 2:1	Unknown (sexual hormones?)	Current Report
Lipoma size	Average maximal dimension = 7.9 cm × 4.1 cm		Current Report
Most common clinical presentation	19 of 32 presented with acute UGI bleeding	Postulated from ulcer at tip of lipoma caused by rubbing/trauma of tip against gastric wall contralateral to base of lipoma	Current Report
EGD	Smooth bulge covered by normal mucosa	Submucosal (or occasionally subserosal) location. No tumor invading mucosa due to benignity	Neto <i>et al</i> ^[22] , 2012, Thompson <i>et al</i> ^[36] , 2003
	Most commonly located in gastric antrum		Thompson <i>et al</i> ^[36] , 2003, Menon <i>et al</i> ^[40] , 2014
	Yellowish hue	Yellow color of adipose tissue in submucosa transmitted to mucosal surface	Menon <i>et al</i> ^[40] , 2014, Chen <i>et al</i> ^[41] , 2014
	Broad base	Rarely pedunculated	Singh <i>et al</i> ^[18] , 1987
	Cushion or pillow sign: easily deforms like a cushion with mild pressure applied against it by an endoscopic probe (closed biopsy forceps).	Lipoma consists of soft, compressible tissue.	De Beer <i>et al</i> ^[37] , 1975, Hwang <i>et al</i> ^[38] , 2005
	Tenting sign: Mucosa easily retracts after it is grasped and gently pulled with a forceps	Mucosa separates from submucosa when gently pulled <i>via</i> forceps because lipoma has fibrous capsule and does not infiltrate into adjacent tissue	Priyadarshi <i>et al</i> ^[14] , 2015
	Naked fat sign: repeated biopsies at same site reveals yellow fatty tissue	Multiple biopsies at same site (using well technique) exposes submucosal lipomatous tissue	Chen <i>et al</i> ^[41] , 2014, Patrick <i>et al</i> ^[42] , 2007
	Moderately frequent focal central ulceration of mucosa	Likely secondary to giant lipoma abutting and rubbing against contralateral gastric wall. Ischemia may also contribute to ulceration.	Kumar, <i>et al</i> ^[8] , 2015, Thompson <i>et al</i> ^[36] , 2003
Highly useful diagnostic test for lipomas	Typically strongly suggestive of diagnosis	Demonstrates anatomy of mass. Shows if ulcerated or intussuscepting mass. Characteristic findings: yellow hue, smooth overlying mucosa, relatively homogeneous, round margins. Exhibits pillow, tenting or naked fat signs.	Current Report
Endoscopic biopsies	Standard endoscopic biopsies usually reveal only normal mucosa and insensitive for pathologic diagnosis.	Standard endoscopic biopsies typically sample superficial mucosa and miss deeper submucosal lipoma.	Current Report, Neto <i>et al</i> ^[22] , 2012
	Techniques to increase yield of endoscopic biopsies; use jumbo forceps for endoscopic biopsies; or well technique (repeated endoscopic biopsies at same mucosal site).	Repeated biopsies at same site permits sampling of deeper (submucosal) tissue	Wang <i>et al</i> ^[47] , 2015
Abdominal CT	Submucosal mass	Typically submucosal, occasionally subserosal, and never mucosal.	Beck <i>et al</i> ^[3] , 1997
	Well-circumscribed with well-defined edges	Characteristically has a firm fibrous capsule with no invasion through capsule due to benignity	Thompson <i>et al</i> ^[36] , 2003
	Typically solitary	Multiple gastric lipomas are very rare	Park <i>et al</i> ^[48] , 1999, Skinner, <i>et al</i> ^[49] , 1983
	Homogeneous	Composed of homogeneous lipocytes	Park <i>et al</i> ^[48] , 1999, Alkhatib <i>et al</i> ^[50] , 2012
	Densitometry of -80 to -120 HU (Hounsfield units).	Characteristic of adipose tissue	Alberti <i>et al</i> ^[20] , 1999
Highly useful as diagnostic test for gastric lipomas	Demonstrates characteristic findings in about 95% of cases.	Characteristic findings: well-circumscribed, submucosal, homogeneous mass with an attenuation characteristic of fat.	Current Report
EUS	In third layer of gastric wall	Typically submucosal (rarely subserosal)	Chen <i>et al</i> ^[43] , 2011
	Hyperechoic (bright)		Alkhatib <i>et al</i> ^[50] , 2012, Eckardt <i>et al</i> ^[51] , 2012

EUS-guided needle biopsy or endoscopic mucosal resection	EUS guidance used to obtain diagnostic deep (submucosal) biopsies	Deep biopsies permit sampling of submucosal lipomas	Alkhatib <i>et al</i> ^[50] , 2012, Karaca <i>et al</i> ^[52] , 2010
Transcutaneous abdominal ultrasound	Not very useful for gastric lipomas.	Supplanted by abdominal CT or EUS for evaluating suspected gastric lipomas	Current Report
Upper gastrointestinal series	Mostly obsolete test	CT is a superior alternative	Current Report
Histopathology	Diagnostic features	Rounded, plump cells with abundant clear, homogeneous cytoplasm containing fat, eccentric nuclei, mature adipocytes with no lipoblasts, scant stroma, rare inflammatory cells.	Current Report
Immunohistochemistry	Reveals no MDM2 or CDK4 gene amplification.	Distinguishes lipoma from liposarcoma.	Shimada <i>et al</i> ^[45] , 2006, Boltze <i>et al</i> ^[46] , 2001
Immunohistochemistry	Lipoma stains positively for CD4	Indicates spindle-cell lipoma variant	Lau <i>et al</i> ^[39] , 2015

UGI: Upper gastrointestinal; EGD: Esophagogastroduodenoscopy; CT: Computerized tomography; EUS: Endoscopic ultrasound.

COMMENTS

Background

Gastric lipomas are rare, constituting < 1% of all gastric tumors, and giant gastric lipomas (≥ 4 cm) are extremely rare, with this systematic review identifying only 32 cases reported since 1980. Although small gastric lipomas are usually asymptomatic, giant gastric lipomas typically produce major, clinically important, symptoms from GI obstruction, tumor ulcers, or upper gastrointestinal bleeding. Due to its extreme rarity, all prior studies of giant gastric lipomas have comprised single case reports. The individual case reports are scattered among numerous, and sometimes obscure, journals. This work systematically reviews the literature since 1980, to comprehensively report what is known about this disease and to inform clinicians and clinical researchers what is not known or controversial about this disease.

Research frontiers

A systematic review is important to collate all the prior data presented as case reports to establish what is known about the clinical evaluation (tests) for this disease. This systematic review demonstrates that the standard clinical evaluation should include: (1) abdominopelvic computerized tomography (CT) to demonstrate the characteristic CT findings of a giant gastric lipoma of a well-circumscribed, submucosal, and homogeneous mass with attenuation of fat; and (2) esophagogastroduodenoscopy (EGD) to demonstrate the characteristic endoscopic findings of these lesions of yellowish hue, well-demarcated margins, smooth overlying mucosa, and endoscopic cushion, tenting, or naked fat signs.

This systematic review demonstrates that the following tests are nonstandard or generally obsolete tests: (1) upper gastrointestinal series has been superseded by EGD and should only be performed in highly unusual circumstances; and (2) traditional abdominal ultrasound has been largely superseded by abdominopelvic CT which is a better diagnostic test for this condition, and the traditional abdominal ultrasound should be performed only if the differential diagnosis is broad and not specifically directed at documenting a giant gastric lipoma.

This work systematically reviews several clinically important but controversial topics, including: (1) the role of endoscopic ultrasound: this work shows that conventional mucosal endoscopic biopsies frequently result in a non-diagnostic pathologic diagnosis because giant gastric lipomas are generally submucosal, and therefore endoscopic ultrasound with ultrasound-guided needle biopsies may be necessary if preoperative tissue diagnosis is not obtained by conventional mucosal endoscopic biopsies; and (2) the relative roles of the available therapies: endoscopic mucosal resection, laparoscopic transgastric resection, laparotomy with enucleation, laparotomy with full-thickness wedge resection, and laparotomy with partial gastrectomy and gastric reconstruction.

Innovations and breakthroughs

While several case reports have recently been published on giant gastric

lipomas, these case reports generally incorporate limited literature reviews. The present work differs in that it provides a systematic review of the literature. The present work also reports 2 new cases of giant gastric lipomas in a review of 117110 EGDs performed during 11 years at two large teaching hospitals.

Applications

This work provides the following highly clinically relevant conclusions: (1) standard evaluation for suspected giant gastric lipomas should include EGD to demonstrate the characteristic endoscopic findings of yellowish hue, well-demarcated margins, smooth overlying mucosa, and endoscopic cushion, tenting, or naked fat signs; (2) at EGD a submucosal mass that is a suspected lipoma should be biopsied, even though the yield of superficial endoscopic biopsies in pathologically diagnosing a gastric lipoma is relatively low. The diagnostic yield of biopsies at EGD may be increased by using jumbo forceps for the biopsies, or by repeated biopsies at the same site ("well" or biopsy-on-biopsy technique); (3) abdominopelvic CT is a standard test in the evaluation of suspected giant gastric lipomas to demonstrate the characteristic CT findings of a giant gastric lipoma of a well-circumscribed, submucosal, and homogeneous mass with characteristic attenuation of fat; (4) upper gastrointestinal (UGI) series is now generally considered an obsolete test for evaluation of suspected giant gastric lipomas and should be replaced by EGD; (5) conventional abdominal ultrasound is not the preferred test for highly suspected giant gastric lipomas, and should be replaced for this indication by abdominopelvic CT. However, abdominal ultrasound may be a very useful initial imaging test for numerous abdominal conditions in which giant gastric lipoma is in the differential diagnosis; and (6) due to scant data about this rare lesion, and absence of prospective, controlled, therapeutic trials there is no universally accepted standardization of preferred therapies for giant gastric lipomas. Reported therapies include endoscopic mucosal resection, laparoscopic transgastric resection, laparotomy with enucleation, laparotomy with full-thickness wedge resection, and laparotomy with partial gastrectomy and gastric reconstruction. All the reported therapies result in a highly favorable prognosis with no reported mortality among the 32 currently reviewed cases and rare severe morbidity because this tumor is benign, is characteristically biologically nonaggressive, and is well-encapsulated that renders it readily amenable to resection. There is recent interest on selecting less invasive techniques for lesion removal, including endoscopic mucosal resection or laparoscopic removal, as opposed to the traditional laparotomy for removal. This systematic review shows that further research is needed on the optimal therapy for giant gastric lipomas, and on individualizing the therapy according to the clinical presentation.

Terminology

The term giant gastric lipomas refers to gastric lipomas ≥ 4 cm in diameter. The distinction of size ≥ 4 cm vs size < 4 cm is clinically important because gastric lipomas ≥ 4 cm generally produce major clinical symptoms from GI obstruction, tumor ulcers, or upper gastrointestinal bleeding, whereas smaller lesions are usually asymptomatic or produce minor symptoms. Furthermore, lesion size often affects the selected therapeutic modality, with lipomas < 4 cm

in diameter often removed endoscopically and lipomas ≥ 4 cm in diameter generally removed surgically.

Peer-review

This is a very important review paper of the main characteristics of the giant gastric lipomas studied in one Hospital through 10 years of study and follow-up. The diagnosis is very well established and also the treatment and prognosis.

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