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Review Article

Gastric Carcinoma and its Common Imaging Mimickers

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Abstract

Introduction: Stomach may be affected by number of malignant pathologies like carcinoma, lymphoma, gastrointestinal stromal tumor (GIST) and metastasis. With non-specific clinical presentation and prognosis depending on histological diagnosis and stage at diagnosis necessitates the need for early imaging diagnosis **Aim:** To evaluate the imaging appearance in malignant gastric lesions and deduce narrowest differential diagnosis.

Imaging Findings: Of the various imaging modalities available Barium studies allows good mucosal details, however it provides no extragastric assessment which is necessary for disease staging. Multidetector computed tomography (MDCT) is the most commonly used technique for disease assessment allows disease diagnosis, staging and differentiation between various pathologies. Gastric adenocarcinoma and lymphoma account for majority of malignant lesions. Gastric carcinoma may presents as either polypoidal, ulcerative or as diffusely infiltrating lesion mimicking lymphoma, GIST and metastasis. Gastric lymphomatous involvement is usually secondary present as bulky non-obstructing gastric thickening with lymphadenopathy extending below renal hila. GIST is the most common mesenchymal tumor may present as submucosal, intramural or extraluminal mass. Imaging features are exophytic mass with variable enhancement, may show cystic change, hemorrhage or fistulous communication with gut. Metastasis to stomach may be either by direct extension or hematogenous dissemination. **Conclusions**: Similar pattern of gastric involvement in seen multitude of malignant etiologies, hence careful

evaluation of gastric and ancillary findings is necessary to reach definitive diagnosis.

Keywords: Gastric Carcinoma, Lymphoma, Gastrointestinal stromal tumor(GIST), Metastasis, Multidetector computed tomography.

Introduction

Stomach can be affected by multitude of both benign and malignant pathological processes which can be either epithelial, mesenchymal or neurogenic in origin. Benign causes outnumber malignant ones. Among malignant causes adenocarcinoma being the most common comprises approximately 90% of the lesions followed by lymphoma^[1].

Imaging Evaluation

Role of imaging modalities in malignant gastric lesions is tumor diagnosis, pre-operative staging

and postoperative follow-up. Imaging modalities available are upper gastrointestinal contrast radiography, endoscopic ultrasound, Multidetector Computed Tomography (MDCT), Magnetic Resonance Imaging (MRI), positron emission tomography and computed tomography (PET-CT).

Barium Studies

Barium meal examination is the study done to evaluate stomach and duodenum. It is done after oral administration of 80 % barium for single contrast and 250% weight/volume for double contrast. Double contrast is the preferred method for evaluating mucosal details, while single contrast in used in children and debilitated patient, for evaluating extrinsic impressions, good however provide poor mucosal details compared to double contrast^[2]. On barium examination lesions present as polyp, focal ulceration or diffuse wall infiltration. Ulcers on barium are evaluated with respect to position, size and morphological characteristics. Out of all features morphological characteristics are the most important to differentiate benign from malignant ulcers^[3]. Barium examination allows good evaluation of mucosal details with no or limited extra-gastric disease assessment, however cannot be performed done in cases with perforation as barium causes chemical peritonitis with high mortality.

Multidetector computed tomography (MDCT)

Multidetector computed tomography (MDCT) is the workhorse of gastric imaging. It provides good noninvasive disease diagnosis and loco-regional as well as distant staging. Thin collimation and multiplanar image reconstruction allows adequate evaluation. MDCT scans are acquired after intravenous and oral contrast administration. Optimal intraluminal distension is needed to differentiate pathological wall thickening from collapsed gastric and is achieved with the use of neutral intraluminal contrast agents, further helped by gastric hypotonia inducing drugs. Scans are acquired in the porto-venous phase at 60-70s from the start of intravenous injection of 100-150 ml of iodinated contrast at 3-4 ml/s^[4]. On CECT normal gastric wall shows multilayered appearance with innermost enhancing layer corresponds to mucosa, intermediate hypoattenuating layer is submucosa or outermost slightly enhancing layer is muscularis propria and serosa. Imaging finding in malignant gastric lesions is disruption of normal multilayered pattern, polypoidal or ulcerative wall thickening with variable enhancement of the gastric wall^[5]. Diagnostic accuracy varies from 77% to 89% for T staging, 69-92% for N staging and 72% for M stage is^[5,6,7]. Sensitivity and specificity of MDCT for peritoneal nodules varies with lower sensitivity for size $< 5 \text{mm}^{[7]}$.

Magnetic Resonance Imaging (MRI)

MRI has better soft tissue contrast compared to MDCT. Sohn KM et al.^[8] found no statistically significant difference between fast MRI sequences and helical CT regarding accuracy of gastric cancer staging and tumor detectability, however long acquisition time, susceptibility to motion artifacts, limits routine use for GI tract imaging. Current indications are in patients allergic to iodinated contrast media or where there is concern about radiation exposure.

¹⁸Fluorodeoxyglucose- Positron Emission Tomography (FDG PET)

¹⁸FDG PET has limited role in loco regional disease assessment, however plays important role in evaluation of distant metastases. It allows early detection of treatment response with reduced uptake [9]. Mucinous carcinoma, signet ring cell carcinoma and poorly differentiated adenocarcinoma show significantly lower FDG uptake compared to other histologic types^[10,11].

Gastric carcinoma (GC)

Gastric carcinoma (GC) is the fourth most common cancer worldwide and second most of cancer-related death $^{[12]}$. common cause Incidence varies across the globe with highest incidence rates are observed in East Asia, East America^[12]. South Both Europe. and environmental and genetic factors contribute to the etiopathogenesis. Environmental risk factors can be divided into modifiable as tobacco

smoking, radiation, intake of aspirin and statins, dietary factors. helicobacter pylori gastritis, atrophic gastritis, pernicious anemia, adenomatous gastric polyps and non-modifiable are old age, male sex^[13]. Anatomically gastric carcinomas are divided into cardia or non-cardiac each with different etiologies. Non-cardia carcinomas are show decreasing trend with decrease in H pylori infection rate, whereas cardia carcinoma are increasing with the increased prevalence of obesity and gastroesophageal reflux^[14,15,16]. GC occurs in equal proportion throughout the stomach 10% lesions are diffusely infiltrating and lesions^[4].

Clinical Features

Majority of patients are initially asymptomatic, or presents with vague complaints like abdominal pain, anorexia, weight loss. All this leads to delayed diagnosis Obstruction occur late during the disease course as stomach is distensible.

Prognosis like any other malignancy depends upon tumor size, depth of tumor invasion, lymph involvement, distant metastasis, nodal histopathologic type, and surgery performed, hence form basis of staging^[17]. GC is an aggressive disease with rapidly declining 5-year survival rates with increasing stage of the disease that is 85-90% in stage I tumors while 3% for stage IV tumors^[18,19,20]. Curative treatment is complete surgical resection of a tumor and involved loco- regional lymph nodes^[21] guided by early detection, followed by accurate tumor staging.

Gastric cancer can present as either polyp, ulceroproliferative growth or asymmetrical wall thickening. Polyps are focal protruded growth from mucosal surface, can be either sessile or pedunculated. It can have smooth, nodular, or lobulated surface^[22]. Malignant ulcers are due to necrosis and sloughing of tissues and have irregular nodular margins. Tumoral infilteration into surrounding gastric mucosal folds give rise to lobulated, penciled coarsed, clubbed, or appearance^[3]. Asymmetrical focal or diffuse wall thickening can present with narrowed, non distensible lumen.

Imaging Evaluation

Barium Evaluation

Barium studies provide good mucosal details with little extragastric assessment. Benign ulcers show smooth outline with no nodularity, whereas malignant ulcer are due to focal necrosis and sloughing of wall and often irregular nodular, show mass effect and project outside luminal contour^[3].

MDCT

Gastric carcinoma shows disruption of normal multilayered appearance with variable enhancing abnormal wall thickening. Imaging appearance is determined by disease extent. T staging shows the depth of tumor infiltration along the layers of the stomach with T1 is disease extension to submucosa, T2 to the muscularis propria or serosa with smooth outer, T3 tumor is transmural extension with indistinct outer serosal contour and perigastric fat stranding and T4 is tumor extension surrounding organs through peritoneal to ligaments^[9]. Peritoneal folds extending from stomach to surrounding viscera provides conduit direct tumor extension to liver from for esophagogastric junction tumors, lesser curvature, and antrum tumors infilterate into liver through lesser omentum whereas tumors along proximal part of greater curvature can spread to splenic hilum, spleen through gastrosplenic ligament, or transverse colon through supracolic omentum^[23]. CT has got poor diagnostic accuracy in T1 and T2 staging, however has an accuracy of 89% to 98% in pathological T3 and T4 stages. Yu T et al.^[24] reported accuracy of spiral CT 92.31% in pathological T3 and T4 stages.

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Figure-1 Non-contrast axial image show wall thickening in antropyloric region with gastric outlet obstruction. Peritoneal deposits noted in the form of ascitis, fat stranding.

Loco-regional lymph nodal staging is on the basis of number of involved lymph nodes is another important prognostic factor. Features suggestive of metastatic nodes are short axis diameter > 8necrosis mm, round shape. central or enhancement^[9,25,26]. However heterogeneous micrometastasis may be present in a node without changes in imaging appearance, thereby limiting diagnostic accuracy. Meta-analysis by Kwee et al.^[27] showed sensitivity and specificity of MDCT N-staging varies between 62.5% and 91.9% and 50% and 87.9% respectively. Distant metastasis can be lymphatic, hematogenous and peritoneal .Involvement of retropancreatic, para-aortic and retroperitoneal is classified as distant metastasis. Solid organ metastasis uncommon at initial presentation, however has important bearing on treatment strategy and prognosis. Most common site is liver followed by lungs, adrenal and ovary. Deep tumoral infilteration into surrounding tissues, presence of multiple metastatic lymph nodes and distant metastasis limits respectability, hence important function of pre-operative is to detect these features^[28]. Pan et al^[29] reported more than 96.6% accuracy in M-staging using MDCT while poor accuracy to detect peritoneal carcinomatosis 50.9% with16 channel MDCT and 96.2% with 64 channel MDCT^[30]



Figure-2 Axial post-contrast image shows heterogeneously enhancing antropyloric thickening with loss of mural stratification and peritoneal dissemination in the form of ascitis, plaque like peritoneal thickening and mural nodules.

FDG PET with poor spatial resolution cannot discriminate between primary and regional lymphadenopathy, however this doesn't affect outcome as they are removed along with primary tumor^[9]. It has good diagnostic accuracy in detecting distant metastasis.

Imaging differential diagnosis of gastric carcinoma include lymphoma, sarcoidosis, corrosive gastritis, amyloidosis, Crohn's disease gastric metastases from lung, and breast carcinoma.

Gastrointestinal Lymphoma

Gastrointestinal tract is rich in lymphoid tissue and may be involved by lymphomatous neoplasm. It can be either primary with origin itself in gastric lymphoid tissue or secondary involvement from metastatic disease. Secondary involvement is far more common than primary. And secondary involvement tend to be multifocal involvement while primary lesion is limited to only one site and shows its loco-regional lymphadenopathy^[31].

Diagnostic criterias for diagnosing primary gastrointestinal lymphoma as stated by Dawson et al.^[32] are isolated focal alimentary tract lesion and its loco-regional lymphadenopathy. No evidence of any other lymphadenopathy or systemic disease with normal chest radiographic findings and blood counts. Gastrointestinal (GI) lymphoma is the most common extranodal lymphoma^[33]. Stomach is the most common site of GI lymphoma, followed by small intestine, then ileocaecal lymphomas^[34].

Risk factors include congenital or acquired immunodeficiency, *Helicobacter pylori infection*, *Campylobacter jejuni*, Epstein-Barr virus, hepatitis B virus, human T-cell lymphotropic virus-1 infection, inflammatory conditions like celiac disease, inflammatory bowel disease, atrophic gastritis and parasitic infection^[35,36].

Clinical features- Most common age of presentation is sixth decade. Patient presents with non specific clinical symptoms like nausea, vomiting, weight loss leading to delay in diagnosis.GI bleed, mass or perforation are late presenting features.

Imaging Evaluation

Barium Meal Examination

May present as either ulcerative, polypoid, or infiltrative lesions making gastric carcinomas a close differential diagnosis. Imaging appearance that has been described for lymphoma are multiple polypoid lesions, tumor with central ulceration ("bull's eye" appearance), giant cavitating lesions, or extensive gastric fold thickening. Diffuse wall thickening in lymphoma show preserved gastric distensibility feature differentiating from linitis plastic^[31,37].

MDCT Examination

Lymphomatous gastric wall involvement can be either focal or diffuse infiltration or polypoidal form. Gastric wall thickening is circumferential, bulky with thickness more than 4 cm. Lymphoma tends to spread laterally within the submucosal plane and spares the muscular coats until late in its course^[38]. Lymphomatous gastric thickening poor and homogeneous shows contrast enhancement due to lack of desmoplastic response in lymphoma, contrast to that of adenocarcinoma ^[39]. Gastric distensibility and lumen is preserved till late in the course of disease, hence gastric outlet obstruction is uncommon feature^[40]. Perigastric fat planes are maintained even in large tumors^[41]. Transpyloric spread is more common in gastric lymphoma than in carcinoma, since gastric carcinoma is more common than lymphoma, it is more frequently seen with adenocarcinoma^[42]. Lymph nodes involvement extends below renal hila and more bulky^[41,43]. Complications like obstruction, perforation, or fistulization can occur as a result of the disease itself or of treatment. Advanced cases of lymphoma can show diffuse peritoneal involvement with ascites, omental infiltration, and peritoneal implants, mimicking carcinomatosis. The differential diagnosis includes adenocarcinoma, metastasis or gastrointestinal stromal tumor.



Figure- 3 Axial contrast enhanced image show imaging features of gastrointestinal lymphoma, large heterogeneously enhancing mass lesion showing aneurismal dilation.

Gastrointestinal Stromal Tumors (GIST)

GISTs are most common non-epithelial tumors arising from muscularis propria initially classified as smooth muscle tumors along with leiomyoma^[44]. Now with the introduction of immunohistochemistry there is renewed classification of theses tumors. Interstitial cells of Cajal, expressing KIT protein-CD117 is the cell of origin^[45]. These can arise anywhere along the gastrointestinal tract (GIT), including the stomach, small bowel, large bowel, mesentery, and omentum^[44,46,47]. As their location is submucosal large size is reached without causing bowel obstruction^[48].

Clinical features are non-specific includes early satiety, indigestion, bloating, vague abdominal pain, or palpable mass or gastrointestinal bleed in the form of hematemesis, melena or occult blood in the stool.

70-80% GISTs are benign^[49], however on imaging no GISTs can be labeled benign, as even smaller lesion show risk of recurrence albeit very low necessitating early detection and monitoring for therapeutic response or tumor recurrence. On barium as GISTs arise from submucosa have a smooth mucosal surface. On profile view, forms right angles or slightly obtuse angles with the gastric wall. Central ulceration due to ischaemia and necrosis seen in approximately 50% of submucosal masses. An ulcerated submucosal mass gives characteristic "target" or "bull's-eye" appearance^[2].

CT is the primary imaging modality for evaluation. Imaging appearance depends on the location, size, and mitotic frequency and can give ranging imaging appearances from benign to malignant. Approximately 80% of the tumors show exophytic growth, however intraluminal or mixed (dumbbell-shaped) pattern are also noted. Small tumors show homogeneous density whereas large tumors show heterogeneous density and enhancement, irregular lobulated margins, mucosal ulceration, central necrosis, hemorrhage, cavitation. Ulceration and fistulization to the gastrointestinal lumen are common presenting with gastrointestinal bleeding and on imaging can be demonstrated by the presence of air or an oral contrast agent in the lesion^[50]. Calcification is uncommon with stromal tumors. It displaces

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adjacent organs and vessels, but direct invasion of the adjacent structures is seen with advanced disease .Bowel obstruction is rare. Gastric GIST show better prognosis compared to small intestinal GIST^[51]. Large size, hepatic metastasis and wall invasion suggest a high-grade GIST and poor outcome^[52]. Malignant GIST commonly metastasizes to the liver or peritoneum, while loco-regional metastases to the lymph nodes and extra-abdominal origins is rare^[53,54]. Atypical imaging features like aneurysmal dilatation of the bowel, "satellite tumor" in the surrounding soft tissues either due to local invasion or multiple tumors growing synchronously can also be seen with GIST^[55]. Due to intralesional hemorrhage fluid-fluid level can be seen within the mass. Histopathological diagnosis of malignancy is based on mitotic counts and size of the tumor. Tumors less than 5 cm, fewer than 5 mitoses per 10 high-power fields (HPF) suggest low-grade malignancy. Whereas size more than 5 cm with higher than 5 mitoses/10HPF are suggestive of high-grade malignancy. Imaging features suggestive of malignancy are tumor size larger than 5 cm, ulceration, heterogeneous enhancement with areas of necrosis or hemorrhage, and distant metastases^[56].

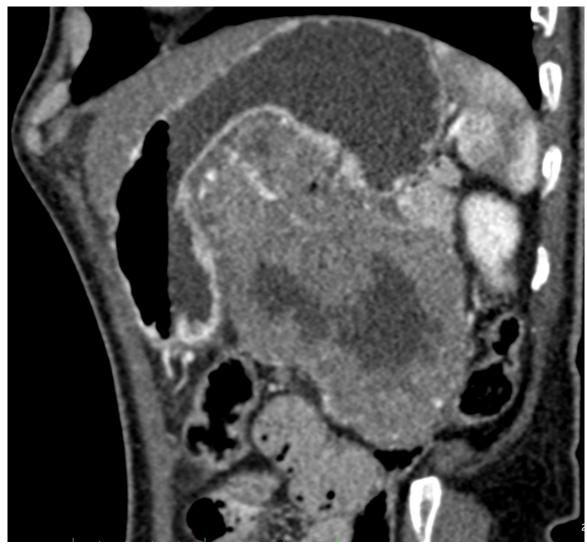


Fig-4 Saggital multiplaner reformated image shows large heterogeneously enhancing predominantly exophytic mass lesion showing central necrotic areas with normal overlying mucosa. No evidence of any calcification. It displaces surrounding tissues without any direct invasion.

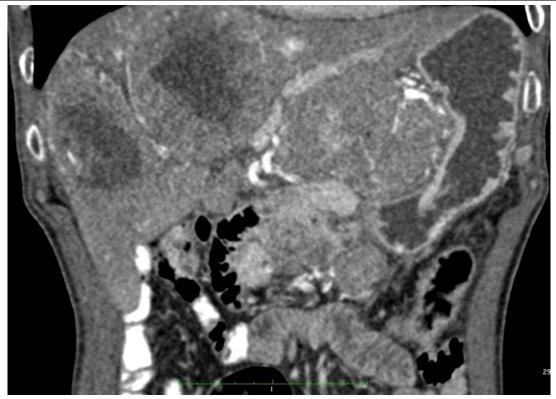


Fig -5 Coronal multiplaner refomated contrast enhanced image shows imaging features of malignant GIST that is large sized exophytic lesion with multiple hepatic metastasis.

Response evaluation on treatment is done by Choi's criterias^[57]. Partial response is more than 10 5% decrease in tumor size ans more than 15% decrease in density. Therapeutic response is decrease in tumor size, transition from a heterogeneously hyperattenuating pattern to a homogeneously hypoattenuating pattern, resolution of the enhancing tumor nodules, and decreased intratumoral vessels. Whereas development of an new enhancing nodule within the treated tumor suggests tumor recurrence regardless of changes in tumor size^[58]. Rare associations with extraadrenal paraganglioma and pulmonary chondroma (Carney triad). adrenocortical adenoma and esophageal leiomyoma are noted^[59].

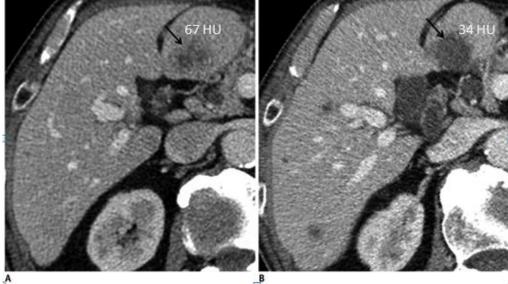


Figure -6 Metastatic GIST pre and post chemotheraphy-size in both cases remains same, however chemotheraphy shows significant decrease in enhancement suggestive of response.

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Metastatic Tumor

Stomach may be involved by either direct tumor extension from carcinomas of the transverse colon and tail of the pancreas through the gastrocolic and splenorenal-gastrosplenic ligaments, respectively or by haematogenous route. Malignant melanoma and breast and lung carcinoma are the most common primaries giving rise to haematogenous gastric metastasis^[60].



Fig- 7 Contrast enhanced axial image of the abdomen of patient with breast carcinoma shows multiple omental, mesenteric and serosal deposits.

Omenta Presenting clinical features may be that of primary disease or metastatic stomach involvement.

Imaging Evaluation

On barium and CT metstatic lesions may present as either polyp, malignant ulcer or long-segment narrowing similar to that of primary gastric malignancies.

Conclusion

Of all the malignant pathologies affecting stomach, adenocarcinoma followed by lymphoma account of majority of the cases. MDCT forms the workhorse of imaging with diagnosis, staging and post-operative follow-up. Lymphoma, GIST and metastasis are close imaging differentials of adenocarcinoma necessitating adequate examination of lesion and associated findings.

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