

Case Discussion in Medicine

Locally Advanced Gastric Cancer

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Gastric cancer is the third most common cause of cancer-related death in the world. Most cases present in advanced stage in non-endemic areas due to a lack of screening programmes. Multidisciplinary treatment (surgery along with chemotherapy with or without radiotherapy in adjuvant or neoadjuvant schedule) forms the basis of present-day management protocol for advanced non-metastatic gastric cancer. Here we discuss the diagnosis, staging work-up and treatment of locally advanced non-metastatic gastric cancer in a 55 years old patient treated with perioperative chemotherapy and surgery. Important trials that have a bearing in the management are also presented.

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Key words : Gastric cancer, staging, multidisciplinary management.

55 years, male patient presented with chief complaints of pain upper abdomen for last 1 year (usually after meals) and difficulty in swallowing solid food for last 5 months with occasional nausea but no vomiting. He complained of significant weight loss (more than 8-10 kg) over last 4-5 months. His stool colour was generally normal but occasionally blackish but not tarry. Patient was a smoker (~20 bidis a day) and an occasional drinker. There is no known co-morbidities eg. diabetes, hypertension, obstructive respiratory disease. He underwent appendectomy at age of 17 years. He had no other past history of major illnesses or hospitalisation. No significant family history relating to his symptoms.

On examination : ECOG-1 (Eastern Cooperative Oncology Group); no anaemia or oedema of the lower limbs, vitals within normal limits. Abdomen was soft, non-tender with no organomegaly or palpable lump. No ascites was detected. No significant lymph nodes were palpable in node-bearing areas.

Provisional diagnosis : Considering the patient's age, presenting symptoms (eg, dysphagia, weight loss, pain abdomen and occasional black stool) and a history of smoking and alcohol intake, esophageal/proximal stomach malignancy is the likely diagnosis. Differential diagnoses are enumerated below.

Differential diagnosis :

Benign Diseases —

- Esophagitis
- Gastritis
- Peptic Ulcer Disease
- Esophageal Varices

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Editor's Comment :

- Stomach cancer is the 5th most common cancer worldwide and third most common cause of cancer-related death.
- In early stages, when it is at the most curable state, gastric cancer has very few symptoms. Hence, clinicians should be aware to the possibility of gastric cancer, especially if risk factors are present.
- Upper GI endoscopy is diagnostic.
- CECT is the most useful imaging modality, though PET-CT has added value in non-mucinous or non-diffuse gastric cancer.
- Perioperative chemotherapy improves outcome in locally advanced gastric cancer.
- Margin free resection with an adequate lymphadenectomy (more than 15 lymph nodes) is the surgical goal.

Malignant Diseases —

- Gastric or esophageal carcinoma
- MALT (Mucosa Associated Lymphoid Tissue) lymphoma of the stomach
- Primary gastric lymphoma (non-MALT type)
- Gastro-intestinal Stromal Tumor (GIST)

Work-up :

Components —

Thorough history and physical examination, laboratory testing, diagnostic imaging and invasive tests (eg, endoscopy).

Risk assessment for gastric cancer —

Environmental factors: H pylori, smoking, alcohol
Family history suggestive of some hereditary cancers (eg, hereditary diffuse gastric cancer, Lynch Syndrome II, BRCA2 mutation and familial polyposis coli).

Physical findings :

Early stages : few significant physical findings

Locally advanced or metastatic :

Palpable upper abdominal mass (from a large primary or liver secondaries)

Lower abdominal mass (from omental or ovarian mass – Krukenberg's tumor)

Gross ascites

Enlarged left supraclavicular node (Virchow's node)

Periumbilical nodule (Sister Mary Joseph node)

Pelvic deposits on rectal examination (Blummer's shelf)

Jaundice (from obstruction of extrahepatic biliary tract or extensive liver metastasis)

Paraneoplastic syndromes associated with gastric cancer :

- Acanthosis Nigricans
- Thrombophlebitis
- Circinate erythema
- Dermatomyositis
- Pemphigoid
- Seborrhheic keratosis

Where malignancy is suspected, the aims of the workup are :

Establishment of diagnosis

Clinical staging (ie extent of disease as can be determined by clinical and radiological investigations)

Fitness of the patient regarding the proposed line of treatment.

Diagnosis: Upper gastrointestinal endoscopy is the modality of choice. It is highly accurate (~98%). Apart from tissue diagnosis, the procedure helps in determining the extent of the disease, any obstruction, and in early cases, endoscopic ultrasound can be utilised to consider suitability for endoscopic resection.

Case capsule continued :

Upper GI endoscopy (Fig 1)

Cricopharynx/Esophagus: normal

Proximal body of stomach: edematous mucosa with large ulcer with clean base

Normal antrum and pylorus

Duodenal bulb: normal

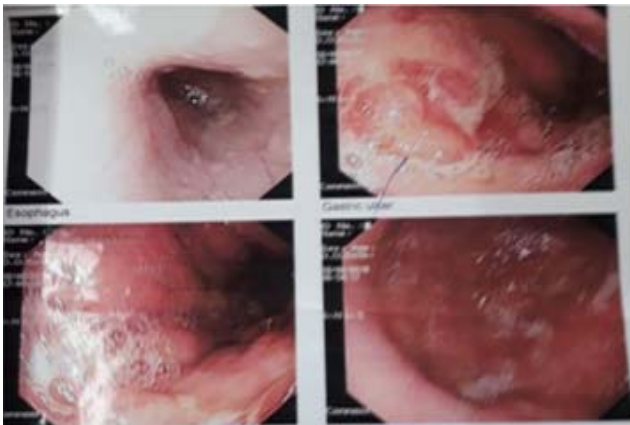


Fig 1 — Upper GI endoscopy

Biopsy report (Fig 2, H&E, x 100) : Mucin secreting adenocarcinoma

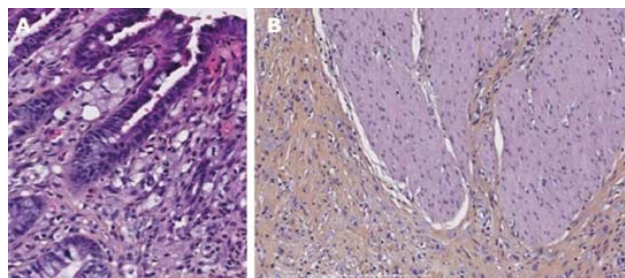


Fig 2 — Biopsy report

Clinical staging :

Evaluates

Local extent of the tumor

Resectability

Lymph node involvement

Presence of metastasis

Imaging modalities :

Contrast Enhanced Computerized Tomography (CECT) scan: most commonly used

Magnetic Resonance Imaging (MRI) : accuracy similar to CECT

Positron emission tomography-CT scan (PET-CT)

Endoscopic Ultrasound (EUS) : useful in early cases

- Value of imaging limited in detecting peritoneal deposits or small (<1 cm) liver metastases

- PET-CT : very useful in staging in advanced gastric cancer, especially in detecting distant metastases.

- Mucin secreting gastric cancer is not PET-avid, hence PET-CT does not have any added benefit over CECT in these cases.

Case capsule continued : A CECT of chest, abdomen and pelvis was performed, which showed a large proximal stomach mass with a significant lymph nodal involvement, staged as cT3N+M0 (Fig 3 & 4)

Role of diagnostic laparoscopic staging :

Currently recommended in cT3 or above, and/or cN+M0

Detects small metastases (<0.5 cm) of the peritoneum and liver, leading to upstaging in up to 40% patients

Laparoscopic peritoneal lavage, if positive for malignancy is considered as M1 and as such not operable upfront

Case capsule continued : The patient underwent diagnostic laparoscopy. No peritoneal, liver or other organ deposits were detected and the peritoneal lavage did not show the presence of malignant cells.

Multidisciplinary approach to gastric cancer: Surgery is the cornerstone of treatment of localised gastric cancer. However, multidisciplinary approach leads to a better

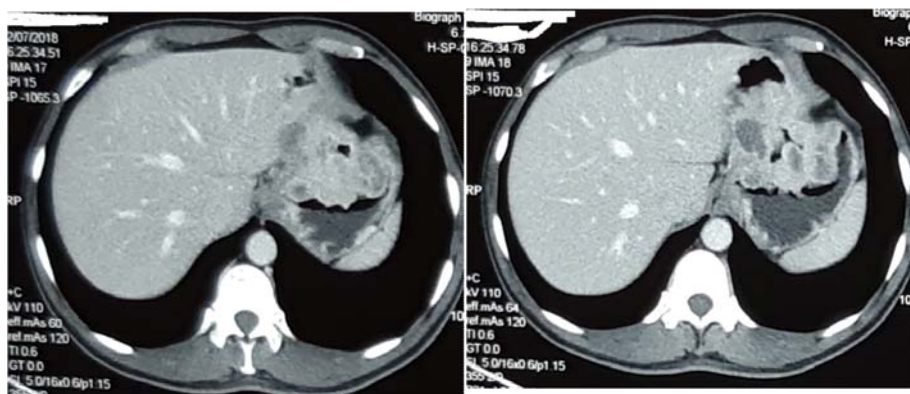


Fig 3

Fig 3 & 4 — Pre-chemotherapy CECT of abdomen

Fig 4

outcome. Standard multidisciplinary approaches are:

(1) Adjuvant Chemoradiotherapy (CRT): based on Intergroup INT-0116 trial that showed a better over all survival, as well as recurrence free survival with adjuvant chemoradiation¹. It formed the basis of acceptance of adjuvant CRT in the US and Canada. However, questions were raised regarding the quality of surgery in this trial. The South Korean ARTIST trial did not show any added benefit of adjuvant CRT over adjuvant chemotherapy alone².

(2) Adjuvant chemotherapy: Mostly used in the East. This approach is based mainly on two trials. First of these is the Japanese ACTS-GC trial that showed that S1 monotherapy for 1 year after surgery led to a better over-all survival with a low incidence of side effects³. The second one is the South Korean CLASSIC trial that reported a significant lowering of the relative risk of relapse with adjuvant capecitabine/oxaliplatin regime administered for 6 months postoperatively⁴.

(3) Perioperative chemotherapy: Used in Europe and the rest of the world. The approach is based on several trials. The first one is the British Medical Research Council's landmark MAGIC Trial that showed that perioperative chemotherapy with Epirubicin, Cisplatin and 5-fluorouracil (ECF) achieved a better over-all and progression free survival compared to surgery alone⁵. Another pivotal study recently reported is the German FLOT4-AIO Phase 3 trial that compared perioperative ECF (Epirubicin, Cisplatin and 5-Fluorouracil or ECX (EC + capecitabine) to another perioperative systemic therapy regimen, FLOT (5-Fluorouracil, Leucovorin, Oxaliplatin and docetaxel). The FLOT arm showed improved progression free and overall survival, along with more frequent pathologic complete response (ie. no viable tumour cell in resected specimen). This regimen however has a significant side effect profile compared to ECF/ECX regime⁶.

Case capsule continued :

The case was discussed in the multidisciplinary tumour board and the patient received perioperative 3 cycles of ECX regime. After 3 cycles he was restaged with CECT chest, abdomen and pelvis that showed a good response (Fig 5 & 6).

Case capsule continued: the patient underwent a total gastrectomy with Roux-en-Y reconstruction. The biopsy report revealed mucus secreting adenocarcinoma,

diffuse type, ypT2N2 status with 3/26 nodes positive, no LVI/PNI, both proximal & distal margins free. Patient received a further 3 cycles of the same chemotherapy regimen. On completion, he was put on follow up. He remains disease free at the last follow up at 4 years.



Fig 5 — Postchemotherapy CECT scan



Fig 6

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