Gastric neoplasms

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Abstract

There are several different types of gastric neoplasm, depending on the cell of origin. The most common gastric neoplasm is adenocarcinoma followed by lymphoma, gastrointestinal stromal tumours (GISTs), carcinoids and other rarer neoplasms. Gastric adenocarcinoma is one of the most common cancers worldwide, especially in the Far East. In the UK, the incidence is lower, but the poor prognosis of late stage disease means the impact on population health is significant. Most patients present with advanced disease at diagnosis. Therefore, primary prevention by modifying risk factors and secondary prevention with early diagnosis have the best chance of improving the grave prognosis. Diagnosis is usually made with endoscopy plus biopsies whilst staging is complex, consisting of EUS, CT, PET-CT, and staging laparoscopy. Treatment is offered in a stage-related multimodal approach that includes resection (endoscopic, laparoscopic, or open surgery) often with perioperative chemotherapy and systemic therapy depending on stage at presentation. The 5-year overall survival rate in early stage disease is over 80%, but all stage 5-year overall survival is less than 20%. GISTs arise from mesenchymal tissue in the stomach and usually have a less aggressive growth pattern, with lower rates of metastasis and direct invasion. Based on staging and pathological factors in the resected specimen, neoadjuvant or adjuvant therapy with tyrosine kinase inhibitors (imatinib) may be offered. Lymphomas and carcinoids have their own aetiology and pathophysiology with according treatments. These cancers rarely require resection.

Keywords Adenocarcinoma; chemotherapy; endoscopic resection; gastric neoplasia; GIST; lymphadenectomy; surgery

Introduction

Gastric neoplasms are defined as any new and abnormal growth of tissue within the stomach. Although they can be benign, in this article we will discuss only the most common malignant neoplasms. Adenocarcinoma is by far the most common malignant gastric neoplasm followed by lymphomas, gastrointestinal stromal tumours (GIST) and carcinoids.

Gastric adenocarcinoma

Epidemiology

Gastric adenocarcinoma (AC) is the fifth most common cancer in the world being responsible of 754,000 deaths every year. The highest incidence is reported in Asia, Latin America, and the Caribbean whilst the lowest is reported in Africa and North America. In the UK, approximately 7000 new cases are diagnosed each year, with a male preponderance (2:1) and increasing incidence after the fourth decade (peak in seventh decade).

Over the last three decades, the spatial distribution of gastric AC has shifted proximally with a higher incidence of cardia tumours. Gastric AC can be classified macroscopically using the Borrmann classification for the invasive tumours and by the Japanese classification for the early gastric cancers. Microscopically, AC can be intestinal (53%), diffuse (33%) or mixed type on the Lauren classification. Intestinal type ACs are usually sporadic, well differentiated and demarcated, found mainly in the distal stomach and are strongly associated with *Helicobacter pylori* infection. Diffuse type ACs are diffusely invasive along the proximal stomach, have a worse prognosis and can have a genetic or hereditary predisposition (e.g. E-Cadherin mutation).

Clinical presentation and risk factors

Early gastric cancer (EGC) is usually asymptomatic. More advanced disease commonly presents with new onset and persistent dyspepsia if ulceration occurs. Other frequent symptoms and signs are described in Box 1. Patients meeting these criteria are suitable for an urgent endoscopy, and direct access for primary care physicians is available via a national '2-week wait' pathway.

The most common risk factors for gastric AC are listed in Box 2. Countries with a high incidence of gastric cancer (e.g. Japan, Korea) have screening programmes for asymptomatic patients. In these countries, earlier diagnosis of gastric AC

Endoscopy referral for suspected gastric cancer

UK National Institute for Health and Care Excellence guidelines for urgent referral to endoscopy specialist

Patient of any age with dyspepsia and any of the following:

- Chronic bleeding of the gastrointestinal tract
- Dysphagia
- Weight loss
- Vomiting
- Iron deficiency anaemia
- Epigastric mass
- Suspicious barium meal

Patient without dyspepsia:

- Dysphagia
- Unexplained abdominal pain and weight loss
- Upper abdominal mass
- Jaundice
- Vomiting and weight loss
- Iron deficiency anaemia

Worsening dyspepsia:

- Barrett's oesophagus
- Known dysplasia, atrophic gastritis, intestinal metaplasia
- Peptic surgery >20 years ago
- Patient aged >55 years with unexplained and persistent recent on-set dyspepsia

Box 1

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has been achieved. In the UK, where gastric AC is less common, the main aim for primary care is modifying improvable risk factors and having a low threshold for referring symptomatic patients for endoscopy. Unfortunately, despite efforts to streamline referral of symptomatic patients, some 75% of these patients have incurable disease at diagnosis.

Diagnosis and staging

The gold standard diagnostic test for gastric adenocarcinoma is endoscopy with biopsies. The BSG guidelines for management of oesophageal and gastric cancer recommend at least six biopsies are taken from each area of abnormality on endoscopy. The endoscopist should also record accurately characteristics, size, position, and relationship of the abnormal findings with known landmarks to help plan further management. In some cases, malignancy can be difficult to confirm and further investigation is required. This may include further endoscopic procedures, imaging and diagnostic laparoscopy.

Gastric AC can progress and/or metastasize by direct invasion and lymphatic, haematogenous or transcoelomic spread. This guides the staging process which is most frequently performed in a sequential manner with MDT discussion of each case at each step.

Staging of gastric adenocarcinoma uses the TNM classification in which (T) refers to the primary tumour, (N) to the local and regional lymph nodes and (M) to metastatic disease. From January 2018, all pathology units will switch to reporting using the 8th edition of this system *(detailed in AJCC Cancer Staging Manual)*. The most relevant change for this new version is that Siewert III tumours of the gastro-oesophageal junction will be considered, for staging and treatment purposes, as gastric cancers. It is important to note that despite TNM pathological classification describing the earliest tumour stage as T*is*, for intraepithelial tumours, in the clinical setting we find it more appropriate to use the term high grade dysplasia (HGD). This avoids confusion with terms such as intramucosal carcinoma, and from a clinico-pathological view point, HGD and T*is* are synonymous.

Computed tomography (CT): chest (including neck base to assess the supraclavicular fossae), abdomen and pelvis high-resolution CT scan, with IV contrast and oral water to distend the stomach, must be performed in every patient. CT can identify T3 or T4 disease, and can classify nodes larger than 8 mm as possibly malignant. It can be used to identify peritoneal nodules over 5 mm in size and can sometimes identify subtle changes associated with peritoneal metastasis without nodules. Ascites, liver and lung metastases, as well as rarer solid organ spread can also be identified. CT cannot accurately distinguish between reactive or metastatic lymph nodes, and sub-5 mm transcoelomic spread.

Endoscopic ultrasound (EUS): the role of EUS in staging gastric AC is controversial. EUS allows accurate assessment of tumour size, depth, submucosal spread, and infiltrative disease to adjacent structures. However, as for the oesophagus, it is not possible to accurately distinguish between mucosal and submucosal disease (T1a versus T1b). Furthermore, nodal stations for gastric cancer are more widespread than for oesophageal cancer and harder to assess by EUS. EUS-guided core biopsies or fine needle aspiration (FNA) can be taken from lymph nodes if a finding of metastatic involvement would change the management (e.g. to determine if endoscopic resection should be offered or not). For some cases of suspected T1 disease or nodularity in an area of dysplasia, endoscopic mucosal resection is sometimes utilized to stage the primary lesion.

Positron emission tomography with CT image fusion (PET-CT): this test uses a radiolabelled glucose analogue (FDG) that is taken up by glucose avid malignant cells. Its main use is identifying lymphatic and metastatic disease. In cases of poorly differentiated adenocarcinomas, mucinous carcinoma, or signet ring cell carcinoma this uptake is limited and differentiating between malignant cells and normal tissue can be inaccurate. For this reason, current guidelines recommend use of PET imaging in the staging of selected histopathological types of gastric adenocarcinomas.

Staging laparoscopy: any patient with invasive disease and curative options requires a laparoscopy. Invasion to adjacent structures, ascites and small volume metastatic disease can be identified and biopsies should be taken for confirmation. Peritoneal washings can be taken for cytological examination. The optimal management of patients with micro- or macroscopic peritoneal disease is an evolving field and accurate identification of this is critical.

Risk factors for gastric adenocarcinoma

Genetic:

- Hereditary diffuse gastric cancer syndrome (E-cadherin mutation)
- Hereditary non-polyposis colorectal cancer
- Li-Fraumeni syndrome
- Familial adenomatous polyposis
- Peutz–Jeghers syndrome
- Juvenile polyposis
- Family history
- Blood group A
- Male:female

Environmental:

- *Helicobacter pylori*
- Smoking
- Obesity
- Elderly (peak age 70 years)
- Coalmining, pottery
- Food (high salt, smoked/burnt food, bacon, red meat and others)
- Vitamin A, C, E deficiencies

Premalignant conditions:

- Pernicious anaemia
- Gastric polyps: malignant transformation in 5–10% of adenomatous polyps $>$ 2 cm
- Gastric intraepithelial dysplasia
- Gastric ulcer
- Menetrier's disease
- Previous gastric surgery

Box 2

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