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Case Report

An Approach to Gastric Cancer in A Resource-Constrained Setting: A Case Study

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Abstract

Background: Gastric cancer is one of the top five causes of cancer-related death across the world. According to the South African Cancer Registry reported on the Cancer Association of South Africa (CANSA) in 2012 1223 gastric cancer cases were diagnosed histologically within the country. A ratio of 1.9:1 predominance for males: females, with a higher incidence in the white population followed closely by black population then coloured and Asian populations. The highest age of incidence was from the fifth to the seventh decade of life. Even with apparent localised invasion, the 5-year survival rate of patients with proximal lesions is approximately 10-15%. In a resource constrained public health care system it is, therefore, of importance to manage such cancers timeously yet appropriately and effectively.

Case presentation: aims to review how gastric cancer management may be potentially approached in the South Africa system. It involves the discussion of a 46year-old female with no medical or surgical comorbidities presenting with an upper gastrointestinal bleed. The initial oesophagogastroscopy and biopsy revealing a gastric adenocarcinoma. The challenges to access of neoadjuvant chemotherapy and the subsequent primary surgical approach, followed by adjuvant chemotherapy, thereof, in a resource constrained setting.

Conclusion: Access to evidence-based management of gastric cancer with regards to neoadjuvant therapy is particularly challenging in developing countries, therefore, various strategies may be considered in order to produce acceptable outcomes for the patient and disease process. This case discusses these difficulties and the possible considerations.

Keywords: Adjuvant therapy; Gastric malignancy; Gastrectomy; Neoplasia; Stomach cancer

Introduction

Gastric cancer is the fourth-to-fifth most common cause of cancer-related death in the world, and it remains difficult to cure primarily because most patients present with advanced disease [1]. Early gastric cancer has some associated symptoms; however, some patients with incidental complaints are subsequently diagnosed with early gastric cancer [2]. Unfortunately, most symptoms of gastric cancer reflect advanced disease. The site of gastric cancer is classified on the basis of its relationship to the long axis of the stomach with approximately 40% of cancers develop in the lower part, 40% in the middle part, 15% in the upper part; and 10% involve more than one area of the stomach [2]. These anatomic zones have distinct histologic features: the cardia contains predominantly mucin-secreting cells, the fundus contains mucoid cells, chief cells, and parietal cells, and the pylorus is composed of mucus-producing cells and endocrine cells. Gastric cancer may often be multifactorial, involving both inherited predisposition and environmental factors [3]. Environmental factors implicated in the development of gastric cancer include the following: diet, Helicobacter pylori infection, previous gastric surgery, pernicious anaemia, adenomatous polyps, chronic atrophic gastritis, radiation exposure, and smoking [4]. Ooi et al identified three oncogenic pathways that are deregulated in the majority (>70%) of gastric cancers: proliferation/stem cell, NF-kappaβ, Wnt/beta-catenin

pathways. The intestinal type of non-cardia gastric cancer is generally thought to arise from Helicobacter pylori infection, which initiates a sequence that progresses from chronic non-atrophic gastritis to atrophic gastritis, then intestinal metaplasia, and finally dysplasia, this progression is known as Correa's cascade [5]. There is a higher incidence in Asian and Black population, men affected more than women and a median age of 60 and older (if younger then represents a more aggressive variant) [6]. Early signs and symptoms may include dyspepsia, nausea or vomiting, dysphagia, postprandial fullness, loss of appetite, melena or pallor from anaemia, and Hematemesis [7]. Late signs of weight loss, palpable enlarged stomach with succussion splash, enlarged lymph nodes such as Virchow nodes (ie, left supraclavicular) and Irish node (anterior axillary), pathologic peritoneal and pleural effusions, Gastric Outlet Obstruction, gastroesophageal junction obstruction, bleeding in the stomach from oesophageal varices, intrahepatic jaundice caused by hepatomegaly, extrahepatic jaundice, and cachexia, may be seen [7].

Other differential diagnoses to be considered may be Peptic Ulcer Disease, Gastritis (Acute, Chronic or Atrophic), Gastroenteritis, Oesophagitis, Oesophageal (Stricture or Cancer), Gastroesophageal junction mass, Non-Hodgkins Lymphoma NHL. A combination of work-up investigations may be done. Performing biochemistry test in tge work-up that include Full Blood Count (FBC), liver function tests (LFT), tumour markers: CEA (Carcinoembryonic Antigen) (45-50%), Ca19-9 (Carbohydrate Antigen 19-9) (20%) may be helpful. Imaging in the form of Oesophago-gastro-duodenoscopy (gastroscopyscopy), Computed Tomography (CT) staging (Chest, Abdomen, Pelvis), and Barium Swallow/meal will allow staging of the malignancy. Biopsy of any ulcerated lesion should include at least six specimens taken from around the lesion because of variable malignant transformation. The types of malignancy that may be seen histologically are: Adenocarcinoma - 90-95%, Lymphomas - 1-5%, Gastrointestinal stromal tumours (formerly classified as either leiomyomas or leiomyosarcomas) - 2%, Carcinoids - 1%, Adenoacanthomas - 1%, and Squamous cell carcinomas - 1% [8]. The management approach of gastric cancer depends on the location, size, and locally invasive characteristics of the tumour. Surgically, a total gastrectomy may be required for negative margins, an oesophagogastrectomy for tumours of the cardia and gastroesophageal junction, a subtotal/partial gastrectomy for tumours of the distal stomach, and gastric Bypass (gastrojejunotomy) or stent placement (GOJ or pyloric) for advanced irresectable tumours [9]. Controversy exists regarding lymph node dissection and according to the National Comprehensive Cancer Network (NCCN) it is recommended that D2 dissections may be preferable over D1 dissections as pancreas- and spleen-preserving D2 lymphadenectomy provides greater staging information and may provide a survival benefit while avoiding its excess morbidity when possible [9]. Chemo-Radiation Therapy is provided for the various stages of gastric cancer as adjuvant treatment, with administration of neoadjuvant chemotherapy prior to surgery, intraoperative radiotherapy (IORT), adjuvant chemotherapy (i.e.: 5-FU), adjuvant radiotherapy, adjuvant chemoradiotherapy, and palliative radiotherapy along with Platinum-based combination chemotherapy (Trastuzumab in combination with cisplatin and capecitabine or 5-FU, Ramucirumab) for the treatment of advanced gastric cancer or Gastroesophageal (GE) junction adenocarcinoma, and Pembrolizumab for gastric or oesophago-gastric junction carcinoma.

With all this considered, in a developing country such as South Africa with a public healthcare system with severe resource constraints, adhering to management guidelines may prove to be very difficult. In the following case report, the debate of neoadjuvant chemotherapy followed by resection versus resection followed by adjuvant chemo-radiation is illustrated in a secondary hospital facility where referrals for adjuvant chemoradiation has long waiting times and delays that may extend past eight-to-ten weeks. Taking into account disease progression, access to healthcare, and the patients staging guided the ultimate decision-making in this case scenario.

Case Presentation

A 46 year-old black African female presented to the out-patient surgical clinic of a secondary level hospital in central Johannesburg with a complaint of a one-month history of malaise and persistent postprandial epigastric pain, and an episode of haematemasis (one day before presentation), No complaints of weight loss. She had no medical or surgical history of note, was of sober habits and did not smoke. She worked as a shopping-till cashier. She had no family history of malignancy.

Clinical Examination

On general examination: well-looking patient with average body habitus and weight, no generalized palpable lymph nodes, Heart Rate (HR)=76 beats per minute, Blood Pressure (BP)= 118/68mmHg, Temperature = 36.2^{o}C, respiratory rate (RR)=17 breaths per minute, Abdominal examination: soft, not distended, no palpable masses, no organomegaly. Per rectum examination: soft brown stool, no lesions, no blood. Cardiovascular and respiratory examinations were normal.

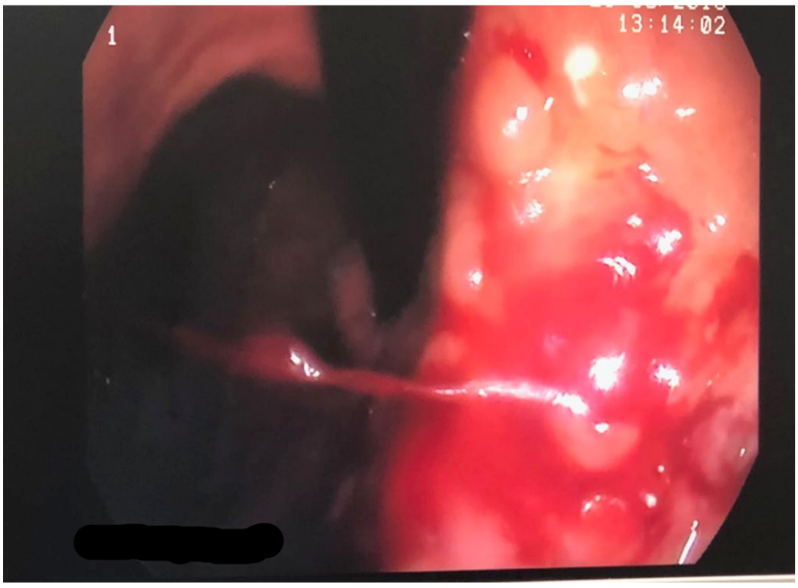
Base line bloods

(Table 1)

White Cell Count (x10^9/L)	Haemoglobin (g/dL)	Mean Corpuscular Volume (fL)	Platelet count (x10^9/L)	Urea (mmol/L)	Creatinine (micromol/L)	C-Reactive Protein (mg/L)	Albumin (U/L)
7.32	14.3	73.6	306	3.0	47	8	38

Patient subsequently booked for an oesophago-gastro-duodenoscopy (gastroscopy) as an out-patient within two-weeks time.

Gastroscopy: two-weeks post initial presentation (biopsy tissue specimens taken) (Figure 1):

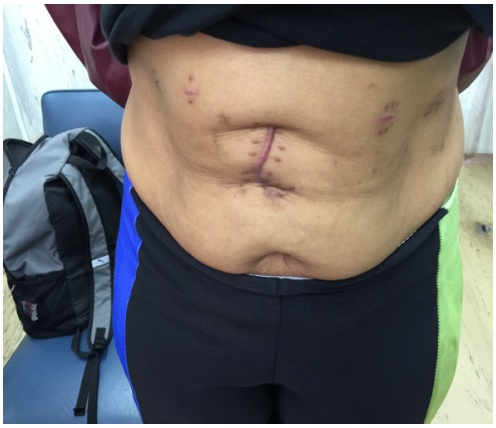


Histology result (received 3weeks post gastroscopy): Fragments of corpus-type mucosa and a single fragment of mucous secreting epithelium demonstrating neoplasia. Numerous discohesive malignant signet ring cells are noted in lamina propria. Groups of Epithelioid malignant cells demonstrating poorly formed tubular glands. Immunochemistry – Modified Hercep Test-score: 3+ (positive). Assessment: Gastric Adenocarcinoma of mixed type (focus of Barret Oesophagus)

Pre-operative management: The patient was counselled on the biopsy findings during her follow-up clinic visit. At this time options of surgical approach were detailed to her (open gastric resection versus laparoscopic gastric resection) and would be considered after her neoadjuvant treatment. Oncology referral (to the only public quaternary institution that provides this service) was submitted. The patient was to follow-up directly at the oncology department where she would receive counselling on the process on neoadjuvant treatment. A follow-up with the out-patient surgical department within one month to monitor the process of her treatment was established. However, on her follow-up visit one month later, the patient had still not received a date when her chemotherapy with start as there was a very burden of patient numbers awaiting such treatment. At this point, after thorough discussion with the surgical unit, the patient was offered the option of surgical resection first (and explained the risk of incomplete surgical margins, risk of recurrence) followed by adjuvant chemoradiation. The patient along with all the surgeons agreed on this approach of management, and booked the surgery for the following week.

Peri-operative: Patient was admitted one week later and scheduled for a total gastrectomy and a laparoscopic total gastrectomy with oesophagojejunostomy was performed successfully. The patient was admitted to Intensive Care Unit (ICU) for three days post-operatively and extubated the following day. She was kept nil per os with supplementary intravenous fluid and initiation of total parenteral nurtrition (TPN), and mobilized well within the next two days, and subsequently was discharged from ICU to the surgical ward. On transfer to the ward with continued TPN, per of feeds were introduced in a staged manner from oral sips to mixed fluids and finally full ward diet with each subsequent day. The patient was discharged home day eleven post her surgery having tolerated a full diet and passing stool and

flatus with clean surgical wounds. She had a subsequent follow-up as the out-patient clinic two-weeks after her discharge (day 25 post operative) and this was the progression of her healing surgical wounds (Figure 2):



Her following outpatient follow-up was one-month later – she had subsequently received her first cycle of adjuvant chemotherapy (Docetaxel/Cisplatin/5-Fluorouracil) the week prior. The histology on the resected specimen confirmed clear (R0) margins and correlated with the initial histology biopsy of mixed type Adenocarcinoma, one of 14 lymph nodes was deemed positive (Figure 3).

Discussion

The often poor outcome of gastric cancer within the public healthcare setting of a developing country may be due to various factors of late presentation, delayed exhibition of symptoms, natural disease progression, large volumes of patients with limited facilities of service delivery, and the challenges of resource constraints, and this makes it a difficult disease to manage at times. The need to define lesions timeously and early in the disease process may significantly improve the prognosis for the patient. As surgery and adjuvant chemoradiation remain as the cornerstone of treatment, multidisciplinary teams and approach to management of such patients is pivotal in improving patient care [9]. In our current setting and with particular reference to this case, the initiation of neoadjuvant Chemo-Radiation Therapy (CRT) was delayed and this subsequently would have delayed the patient to surgical management by approximately two or more months, and, thus, risking disease progression [10]. The immensely heavy burden of disease on a solitary oncology department that provides for a large population drainage area with limited resources and, therefore, increased waiting time to receive treatment is highlighted in this instance. Thus, disease progression is a very high risk with possible subsequent inoperability. With this all considered, this patient was prioritized with an oncological total gastrectomy and oeophago-jejunostomy first, once it had been noted that there may be an unacceptable delay to initiating neoadjuvant chemotherapy [11]. Once the patient had successfully healed from surgery, she was transferred successfully for adjuvant chemotherapy to the quaternary hospital and, subsequently, completed her six cycles of chemotherapy. She also received radiation in the following five months post surgery with her last follow-up at eight months post surgery (on completion of her radiation). The possible complication of microscopic nodal metastases and R1 resection was continually discussed and re-emphasized throughout the management of this patient. Hence, the continued follow-up appointments and persistence in receiving adjuvant chemoradiation.

Conclusion

Although literature shows good evidence for neoadjuvant therapy and its benefit when managing early gastric carcinomas with resect-ability potential, one has to be aware of barriers to access of such treatment and their implications, thereof, on the patient and the patient's disease staging particularly in a resource-constrained healthcare system. A multidisciplinary team of surgeons, dietician, oncologists and psychologists with the social worker, would need to extensively counsel and explore all options of management with the patient to settle on the most appropriate approach that is individualized. In conclusion, although the sequence of management of this patient was not typical (or as per international gold-standard) it was, however, appropriate, effective and tailored to produce the best possible outcome for this particular patient and provided an acceptable alternative treatment approach to a patient with gastric malignancy in a high-demand and low-resource setting.

Declarations

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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