CASE REPORT

Advanced Gastric Cancer in a Young Male Patient

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ABSTRACT

Gastric cancer remains the second most common GI cancer in the world, and is usually found in men, especially those over 50 years of age. Gastric cancer is a multifactorial disease resulting from the interaction between genetic and environmental factors at the stomach mucosa level. The diagnosis is made by endoscopic biopsy. The high frequency of late diagnosis or advanced stages accounts for the overall poor prognosis for this tumor. Surgery is the most frequently employed modality for both cure and palliation. However, most patients present with advanced disease that is incurable.

We reported a rare case of young male patient aged 24 years old with advanced gastric adenocarcinoma. The main clinical features were epigastric pain, vomiting, melena and weight loss. An abdominal mass was palpable on physical examination. Endoscopy showed a giant tumor mass causing gastric outlet obstruction, that appeared edematous, there were hemorrhagic lesions. The histopathologic examination revealed poorly differentiated adenocarcinoma. Palliative resection could not be performed because the tumor tightly adhered to adjacent structures. Jejunostomy or nasojejunosotmy tube were performed to allow enteral nutrition. Best supportive care is very important to improve the quality of life.

Keywords: gastric cancer, young patient

ABSTRAK


Kata kunci: kanker lambung, pasien muda
INTRODUCTION

Gastric cancer (GC) remains the second most common GI cancer in the world.\(^1\) GC is a heterogeneous, multi factorial disease. It endangers human physical and psychosocial wellbeing, causing a significant public health and economic burden both in the developed and developing countries.\(^1\) Globally, GC accounts for 989,600 new cases and 738,000 deaths annually.\(^2\) The case-fatality ratio of GC is higher than for common malignancies like colon, breast, and prostate cancers.\(^1\)\(^-\)\(^2\) Despite advances in diagnosis, the disease is usually detected after invasion of the muscularis propria, because most patients experience vague and nonspecific symptoms in the early stages and the classic triad of anemia, weight loss, and refusal of meat-based foods is seen only in advanced stages.\(^2\)

GC is distinguished into two forms, early GC and advanced GC. Early GC refers to invasion of the tumor limited to the mucosal and submucosal layers, whether or not regional lymph node metastases are present.\(^3\) The pathogenesis of GC is multi factorial, with both environmental and host factors playing a major role in its development. Among the risk factors for GC are consumption of smoked and salted food; nitrites, cigarette smoking; a lack of fiber in their diet, low socio-economic status; positive family history; A blood type; hereditary cancer syndrome (familial adenoma polyposis); Helicobacter pylori infection; and history of partial gastrectomy.\(^4\)\(^-\)\(^6\) The classic clinical symptoms and findings of GC are vague and non-specific, including epigastric pain, vomiting, nausea, bloating, early satiety, weight loss, abdominal mass, gastrointestinal bleeding, and sometimes dysphagia.\(^7\) Early GC may have no clinical symptoms. That is reason why most patients are diagnosed with GC at advanced stages of the disease. Gastroscopy is very crucial in making the diagnosis of GC.\(^8\)

Treatment of GC is mainly surgery. Other treatment modalities are chemotherapy and radiotherapy. There are two kinds of surgery: curative and non curative or palliation. Early GC can be cured by endoscopic therapy such as endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) or argon plasma coagulation (APC).\(^3\) In contrast, surgery for advanced GC is merely palliation. It has been reported that patients underwent palliative surgery had better prognoses than those who did not. Inoperable patients and those with metastatic disease have been subject to combination of chemotherapy and radiotherapy. The effectiveness of this therapeutic strategies is still controversial.\(^3\)

CASE PRESENTATION

The patient, Mr A, 24 years, was admitted to the Army Gatot Soebroto Hospital with a chief complaint of nausea and vomiting since 2 months prior to admission. At first, he usually vomited 3-4 hours after meals. He also suffered recurrent epigastric pain and discomfort. He lost his appetite and lost a lot of weight in a short period of time. Eventually, he vomited more often. He could hardly eat any food because he vomited directly after swallowing it. He usually consumed alcohol about two bottles every weekend, and his daily diet was instant noodles everyday. He reported symptoms of gastrointestinal bleeding such as melena. The patient never had symptoms like this before.

The patient was generally weak and cachectic. Physical examination revealed vital signs within normal range. The conjunctivae were pale, the sclera were jaundiced. Heart and lung examinations were within normal range. The liver were palpable. An abdominal mass was palpable, with a dimension of 8 x 6 x 4 cm. It was hard, immobile, and was non-tender. Superficial lymph nodes were not palpable. Laboratory examination results were as follows: Hemoglobin 5.8 g/dL; hematocryte 16%; leukocyte count 4580/mm; platelet count 111,000/mm; ureum level 21 mg/dL; creatinine level 2.4 mg/dL; blood glucose level 94 mg/dL; AST 61 iu/mL; ALT 57 iu/mL; total bilirubin 3.93 mg/dL; alkaline phosphatase 124 iu/mL; total protein 5.6 g/dL; albumin 4.1 mg/dL; globulin 2.0 mg/dL; cholinesterase 2473 U/L; Gama GT 104 U/L; CEA 1.1; AFP 0.70 ng/mL and CA19-9 4.5 U/mL ( normal < 37 U/mL)

Endoscopy of the upper gastrointestinal tract revealed candidosis esofagus, with giant tumor mass causing gastric outlet obstruction, that appear edematous. There was no nodular ulcerative but there were hemorrhagic lesions. Some parts of the gaster were covered with fluid and indigested food. The tumor mass was suggested to be malignancy in the antrum (Figure 1). Nevertheless, the scope could still pass through, and we were examined histopathology biopsy to confirm the diagnosis and staging. Histopathological examination demonstrated gastric was displaying tumor cells nucleated round/oval, pleomorphic, hyperchromatic, vesicular with nucleoli real partly, eosinophilic cytoplasm has a oval, pleomorphic, hyperchromatic vesicular with nuclear real partly, eosinophilic cytoplasm has a clear vacuoles partly. Mitosis is found (Figure 2). The histopathologic examination revealed poorly differentiated adenocarcinoma.

The patient was given supportive care for nutrition, fluid and electrolyte balance. We immediately consulted to the Department of Surgery and the patient was prepared for surgical intervention.
DISCUSSION

GC is rare among young patients. It is usually found in older patients of over 55 years and is more common in men, particularly in East Asian countries. In 2012, there was an estimated 1 million new cases of GC, with half of the world total occurring in Eastern Asia. The highest mortality rates are observed in Eastern Asia, occurring at 24.0 per 100,000 men and 9.8 per 100,000 women. However, prevention and screening programs for GC particularly at the national level have not yet been established in most countries. The exceptions are South Korea and Japan where GC screening programs have already been introduced. In Japan, GC screening using upper gastrointestinal series (radiographic screening) has been conducted as a national program since 1983, and it has been attributed to the decrease in GC mortality. This study had reported a worse outcome of GC in young patients compared to those who were older.

Diagnosis is usually made after the disease reaches an advanced stage because early GC produces few symptoms. Thus, early detection of the disease is very difficult. Therefore, most GC patients are diagnosed in advanced-stage disease with a poor prognosis. Common symptoms are weight loss, epigastric pain, vomiting, nausea, anorexia, dysphagia, bloating, and regurgitation. It was often initially misdiagnosed as dyspepsia syndrome. The symptoms and signs of this patient such as nausea, vomiting and abdominal mass reflected the obstruction caused by advanced GC. The main treatment option is the gastrectomy combined with chemotherapy and radiation therapy protocols. The poor understanding of the pathogenic mechanisms of GC and etiological factors, and the lack of effective treatment are reflected in the late diagnosis and high mortality of this disease. GC is a multifactorial disease resulting from the interaction between genetic and environmental factors at the stomach mucosa level.

Cutsem EV et al stated that, a genetic basis causative mutations in CDH1 has been found in only around 40% of families affected by hereditary diffuse GC. GC have been found in people with other hereditary cancer syndromes, such as gastric adenocarcinoma and proximal polyposis of the stomach syndrome, and in those with mutations in TP53 (Li-Fraumeni syndrome), APC (familial adenomatous polyposis), or STK11 (Peutz-Jeghers syndrome). Park J et al state that Several studies have been conducted to examine the association between GC, diabetes, and blood lipid profiles and instant noodle consumption. Instant noodle consumption is associated with a higher risk for GC compared with that of plain noodles (n = 105; OR = 4.76; p < 0.01). Gomez M et al concluded that GC is slightly more prevalent among young patients in their study than the prevalence that has been reported elsewhere in Columbia, the patients presented more advanced stages of cancer than did older patients,

Figure 1. Upper endoscopy shows tumor mass at the body of stomach, the mass is appear grow to the lumen of gaster, easy to bleed like cauliflower shaped mass, the size of tumor is about 8 x 6 x 4 cm

Figure 2. Histological tumor lesion was observed. A. Histological section was observed at 10 x. Showing gastric preparations with piston epithelial layer, which mostly erosive, still looks foveola gastric lamina propria accompanied by hard infiltration acute and chronic inflammatory cells. There intestinal metaplasia, with a mass of malignant tumor stroma of epithelial appears. It also seems that Bruner glands. B. Histological section was observed at 40 x. Observing malignant epithelial tumor masses composed granuler, partly infiltrative between stroma, with some hard infiltration acute and chronic inflammatory cells. C. Histological section was observed (around the tumor) at 40 x. Displaying tumor cells nucleated round/oval, pleomorphic, hyperchromatic, vesicular with nucleoli real partly, eosinophilic cytoplasm has a clear vacuoles partly. Mitosis is found. The histopathologic examination revealed poorly differentiated adenocarcinoma.
and the majority of their cancers were diffuse types (90%) which resulted in a high mortality rate. Early performance of endoscopy is mandatory for young patients. In addition preventative measures such as genetic studies for CDH1 carriers to protect family members from this terrible disease should also be mandatory. Male carriers of a mutation in the CDH1 gene have an 83% risk of developing GC while women who carry the mutation have a 67% diffuse GC risk.

Sun YQ et al concluded that, there are chromosomal maintenance (CRM1) and cyclin-dependent Kinase (CDK5) as co-expression was an independent prognostic factors for GC. Combined CRM1 and CDK5 expression had better prognostic power than their individual expression had. Chiurillo MA state that, The aberrant activation of the Wnt/β-catenin signaling pathway is involved in the development and progression of a significant proportion of GC cases. The role of key factors in Wnt/β-catenin signaling and their downstream effectors regulating processes involved in tumor initiation, tumor growth, metastasis and resistance to therapy. That constitutive Wnt signalling resulting from Helicobacter pylori infection and inactivation of Wnt inhibitors (mainly by inactivating mutations and promoter hypermethylation) play an important role in GC. Moreover, a number of recent studies confirmed CTNNB1 and Adenomatous Polyposis Coli (APC) as driver genes in GC. The identification of specific membrane, intracellular, and extracellular components of the Wnt pathway has revealed potential targets for GC therapy. High-throughput “omics” approaches will help in the search for Wnt pathway antagonist in the near future.

Endoscopic screening for GC has shown promising results, and thus deserves further evaluation to reliably establish its effectiveness and optimal use. Histopathological features of gastric tumor may also have prognostic value. In this patient, the histological lesion of GC found was displaying tumor cells nucleated round/oval, pleomorphic, hyperchromatic, vesicular with nucleoli real partly, eosinophilic cytoplasm has a clear vacuoles partly. Mitosis is found. The treatment of GC depends on the stage of the disease. Surgery is still a major treatment modality for GC and could be curative or palliative. Most patients are first diagnosed at advanced, ‘inoperable’ stages. In this case, the tumor had progressively enlarged and caused obstruction of the gastric outlet. Resection of the tumor is still recommended for palliative treatment. Studies had reported that patients underwent palliative surgery had a better prognosis than those who did not. But the tumor was not removed because it was found to closely adhere to surrounding tissue and structures. Removal of the tumor would be very difficult and carried major risks of complications such as bleeding and perforation. Surgical intervention performed to this patient was jejunostomy, to allow enteral nutrition. A nasogastric tube was also inserted to drain the physiological secretions of the upper gastrointestinal tract.

Metastasis is demonstrated to be an essential event in the prognosis of GC. Successful hematogenous metastasis cascade depends on intrinsic factors of the tumor cells and their subsequent communication with the surrounding microenvironment. During metastatic progression, tumor cells possess continuous interdependent strategies. First, tumor cells form a microenvironment, escape from primary site through surrounding extracellular matrix (ECM) and intravasate into the lumina of blood vessels. Translocation system is then formed and circulating tumor cells (CTCs) survive in the circulation and arrest at the secondary organs. Subsequently, tumor cells survive with the microenvironment of distant tissues, thereby micrometastasis and metastatic colonization emerge.

The prognosis of this patient was poor, Many GC patients are diagnosed at advanced stage with metastasis, and miss the possibility for curative resection. It has been documented that patients with advanced stage GC have a poor prognosis with a five-year survival rate less than 15%. The authors confirm no conflict of interest in this study.

REFERENCES