CLINICAL AND PARACLINICAL CHARACTERISTICS OF LOCALLY ADVANCED DISTAL GASTRIC ADENOCARCINOMA PATIENTS UNDERWENT THE TREATMENT OF POSTOPERATIVE ADJUVANT CHEMORADIOTHERAPY AT HUE CENTRAL HOSPITAL

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ABSTRACT

Background: Stomach cancer is the most common malignancy of the gastrointestinal tract and the fourth most commonly occurring cancer worldwide. The incidence shows a wide geographical variation and Vietnam is considered a relatively high prevalence population [3]. Surgical resection including total gastrectomy and nodal dissection is the principal therapy for gastric cancer [4],[6]. However, only a few patients with early stage and localized disease are eligible for curative resection, accounting for 70% - 80%. Most of the patients are diagnosed at a late stage and therefore have a higher risk of recurrence and metastasis after resection [9],[11].

Objective: To describe clinical and paraclinical features of locally advanced distal gastric adenocarcinoma patients underwent the treatment of postoperative adjuvant chemoradiotherapy at Hue central hospital.

Methods: Fifty-four patients with locally distal advanced gastric adenocarcinoma were enrolled in the analysis. All patients underwent distal gastrectomy and postoperative adjuvant radiochemotherapy at Hue Central Hospital from January 2013 to December 2015. Patients were followed-up until August 2018.

Results: Epigastric pain was the most common chief complaint (81.4%). The mean time from symptoms onset to admission was 8.9 ± 10.3 months (range, 1 - 36 months). Anemia (defined as hemoglobin < 10g/dL) 18.5%, decreased proteinemia (3.7%), and decreased albuminemia (37.5%). Blood type: type O was the most prevalent (42.5%), followed by type A (31.5%), type B (20.4%) and type AB (5.6%). Gastric lesions and/ or regional lymphadenopathy was evident on ultrasound in 51.2% cases. All individuals (n = 54) underwent gastric and biopsy prior to operation. The most common site of the tumor was antrum (57.3%). Postoperative histopathological results confirmed adenocarcinoma. On endoscopic gross view, the ulcerative type was the most common (48.2%), followed by an infiltrative type. On CT: 74% of the tumor was seen at the pyloric antrum. The sensitivity of CT was 49/54 (90.7%). Wall thickening and focal wall infiltration were the most common findings (100% and 91.8%, respectively). Postoperative histopathological findings: 83.3% of the tumor was classified T3, 92.6% was tubular adenocarcinoma, in which 75.9% was intermediate to poor differentiation. All patients had ≥ 15 dissected lymph nodes, mean 17.02 ± 1.64 (range, 15 - 21 nodes), the highest number of positive node was 7. Staging: 87.0% stage II, 13.0% stage III.

Conclusions: The mean age was 58.56 ± 10.28 years; the age group of 51 -70 years was the most common (7.0%), the male/female ratio was 2.6/1. Epigastric pain was the most common clinical

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manifestation (94.4%). The diagnostic accuracy of gastric endoscopic biopsy was 69.2%. The sensitivity of CT scan in the detection of the gastric tumor was 90.7%; in which wall thickened was seen in all cases (100%) and wall infiltration was seen in the majority of cases (91.8%). Tubular adenocarcinoma was the most common histological type (92.6%). A majority of tumor invaded to the serosa (83.3%). The average number of dissected lymph node was 17.03 ± 1.61 nodes. Most of the tumor was at stage II (87.0%), stage III (13.0%).

Keywords: locally advanced distal gastric adenocarcinoma.

I. INTRODUCTION

Clinical manifestations of gastric cancer are often poor, atypical and overlapped with other conditions. Symptoms include weight loss, epigastric pain, nausea, vomiting, hematemesis, hematochezia. Esophagogastroduodenoscopy and biopsy have excellent diagnostic accuracy and are the most popular diagnostic tool today. Advantages of this modality are direct visualization of the lesion and tissue sampling for histological examination. Tumor markers such as CEA, CA 19-9, CA 72-4 are not typical for gastric cancer, however, the elevation of serum levels is suggestive of disease recurrence during follow-up. Laparotomy is another diagnostic tool not only to determine gastric lesion but also to evaluate adjacent organ infiltration, local metastasis or peritoneal metastasis. Abdominal ultrasound is a routine examination in the workup of gastric cancer. This technique is feasible, cost saving, available which allows the visualization of the stomach wall layers, wall thickening, luminal stenosis or obstruction, infiltration, fat stranding, local lymphadenopathy, organ metastasis or ascites.

Computed tomography (CT) has been indicated more frequently in the diagnosis and staging of gastric cancer. Improvements of multidetector CT scanner with virtual endoscopy, thin slice, multiplanar reconstruction (MPR) and 3D reconstruction technique optimizes the evaluation of gastric wall invasion and peripheral infiltration as well as early detection of subtle lesions (stage T1, T2) and lymphadenopathy ≥ 5mm.

Endoscopic ultrasound (EUS) is a valuable tool for a more precise preoperative assessment of the tumor staging, gastric wall penetration, and perigastric lymphadenopathy. EUS provides both intra- and extraluminal visualization of the GI tract and allows detection of subtle lesions in a minimally invasive fashion. However, this procedure requires designated equipment and well-trained operators.

PET/CT has a critical role in tumor staging, detection of recurrence and subtle metastases which are negative on other imaging modalities. Dasen et al (2009) reported the sensitivity and specificity of PET/CT are 81% and 78-100%, respectively.

WHO classification recognized 4 main types of gastric adenocarcinoma (papillary, tubular, mucinous, signet-ring cell type) as well as specific types of carcinoma (adenosquamous, squamous cell, small cell and undifferentiated carcinomas) and rare entities. Pathologists also classify gastric cancer into well-differentiated, intermediately differentiated and poorly-differentiated types with worsening prognosis, respectively.

II. PATIENTS AND METHOD

2.1. Patients

Fifty-four patients with locally distal advanced gastric adenocarcinoma were enrolled in the analysis. All patients underwent distal gastrectomy and postoperative adjuvant radiochemotherapy at Hue Central Hospital from January 2013 to December 2015. Patients were followed-up until August 2018. Inclusion criteria:

+ Patients diagnosed with locally advanced distal gastric adenocarcinoma (1/3 middle and 1/3 lo lower part), defined as T3-T4 (any N) or any T plus

N+ (nodal positive) underwent distal gastrectomy and lymphadenectomy, confirmed by postoperative histopathological findings.

+ No evidence of tumor on 2 resected margin of stomach and duodenum (R0).

+ Excision of a minimum of 15 lymph nodes.

+ Postoperative radiochemotherapy according to the practice guideline of NCCN 2012 [10].

2.2. Method

An observational prospective study with follow-up was conducted. Data were collected using a standard questionnaire and analyzed using SPSS 20.

III. RESULTS

3.2.1. Demographic

- Mean age: 58.56 ± 10.28. The age group of 51-60 was the most populous (46.2%).

- Sex: Male 39 (72.2%), female: 15 (27.8%), male/female: 2.6/1.

- 74.1% lived in rural area.

- 57.4% were farmer.

3.2.2. Clinical characteristics

- Past history of medically treated gastric ulcer: 15 patients, (27.8%), alcohol consumption or smoking: 36 patients (66.7%).

- Epigastric pain was the most common chief complaint (81.4%).

- The mean time from symptoms onset to admission was 8.9 ± 10.3 months (range, 1 - 36 months).

- Weight loss: 27.8%.

- Presentation on admission: epigastric pain (94.9%), vomiting with or without hematemesis (16.7%), hematochezia (11.1%).

3.2.3. Paraclinical characteristics

- Anemia (defined as hemoglobin < 10g/dL) 18.5%, decreased proteinemia (3.7%), and decreasedalbuminemia (37.5%). All of these patients received blood and albumin transfusion up to normal range prior to operation.

- Blood type: type O was the most prevalent (42.5%), followed by type A (31.5%), type B (20.4%) and type AB (5.6%).

- Elevated CEA (> 5ng/ml), CA 19-9 and CA 72-4 were observed in 12 (22.2%), 3 (5.6%) and 8 (14.8%) patients, respectively.

- Forty-one patients underwent preoperative abdominal ultrasound while 13 did not (yet CT were available). Gastric lesions and/or regional lymphadenopathy was evident on ultrasound in 51.2% cases.

- All individuals (n = 54) underwent gastric and biopsy prior to operation. The most common site of the tumor was antrum (57.3%). A preoperative endoscopic biopsy was not available in 2 patients due to uncooperative state. These patients were diagnosed with gastric cancer based on typical clinical and imaging findings. Postoperative histopathological results confirmed adenocarcinoma.

- On endoscopic gross view, the ulcerative type was the most common (48.2%), followed by an infiltrative type.

- On CT: 74% of the tumor was seen at the pyloric antrum. The sensitivity of CT was 49/54 (90.7%). Wall thickening and focal wall infiltration were the most common findings (100% and 91.8%, respectively).

- Postoperative histopathological findings:

+ Antrum was the most common site (48.1%). The ulcerative type was the most prevalent (59.3%), polypoid and infiltrative types were less common. Regarding tumor size, 75.9% of the tumor was ≤ 3cm. Two patients had tumor size > 7cm (3.7%).

+ Resection margin: all individuals had negative evidence of malignancy at 2 resection margins.

+ 83.3% of the tumor was classified T3, 92.6% was tubular adenocarcinoma, in which 75.9% was intermediate to poor differentiation.

+ All patients had ≥ 15 dissected lymph nodes, mean 17.02 ± 1.64 (range, 15 - 21 nodes), the highest number of positive node was 7.

+ 68.4% N0, 24.1% N1 (1-2 positive nodes),

5.6% N2 (3-6 positive nodes), 1.9% N3 (≥ 7 positive nodes).

+ Staging: 87.0% stage II, 13.0% stage III.

IV. DISCUSSION

4.1. Clinical characteristics

In this series, mean age was 58.56 ± 10.28 years (range, 32 – 78 years), in which the age group 51 - 60 years was the most prevalent (46.2%). Thirty-nine patients were male (72.2%) and 15 were female (27.8%), male/female ratio was 2.6/1. These findings were in keeping with domestic and international published data. Majority of patients in this study was farmer (57.4%) which was in concordant with domestic reports.

Epigastric pain was the most common chief complaint of gastric cancer patients, however, when symptomatic, the disease is usually diagnosed at a late stage with a large tumor burden.

In the present study, epigastric pain was the chief complaint in 75.8%, the patients had the mean time from onset was 8.9 ± 10.3 months. Our results were similar with those of domestic data since the study population was mostly patients at locally advanced stage (II, III).

4.2. Paraclinical characteristics

The presentation of gastric cancer is usually vague such as loss of appetite, bowel discomfort, weight loss, epigastric pain at a later stage, vomiting (with or without hematemesis), hematochezia, and pale skin.

In this study, 16.7% of patients presented with vomiting, 18.5% with GI bleeding. For the manifestation of gastric cancer, patients usually present at an advanced stage when symptomatic. In our series, 3 (5.1%) patients admitted with a palpable epigastric mass. Le Van Quang [7] et al studied on 89 gastric cancer patients of advanced stage (III – IV) reported 36% of a clinically palpable mass. Another study of Do Trong Quyet et al [8] (n = 105) revealed that 9.5% of patients had a palpable epigastric mass. The high incidence of a palpable mass in those series could be attributed to their study population which included mostly advanced stage gastric cancer.

Most investigators advocate the diagnostic accuracy of gastric endoscopy and biopsy was 90% - 100%. The more specimens were taken, the higher the accuracy achieved.

All of 54 patients in our analysis underwent preoperative endoscopy. There were 2 patients who did not undergo biopsy due to their uncooperative state. However, these patients were diagnosed with gastric cancer due to typical imaging findings (polypoid mass on endoscopy and wall thickening and infiltration on CT scan). The most common site of the tumor was antrum (57.3%), the ulcerative type was the most common gross endoscopic view (48.2%) whereas polypoid and infiltrative types were less common.

The ability of CT scan in detecting lesions depends on various factors in which tumor size is the most important. The rate of regional lymphadenopathy < 5mm detection on CT scan was 1.1%, increased to 72% when node size > 1cm. The sensitivity of CT scan in the detection of metastatic lymph node was 25% - 80%, specificity was 45%. CT is highly appreciated by various authors in the diagnostic ability of liver metastasis with the sensitivity of 28.6 -100% compared to 0 – 8% in the diagnosis of peritoneal seeding.

All of our patients in this study underwent preoperative baseline abdominal CT scan. The sensitivity of CT in the detection of gastric mass was 49/54 (90.7%). Wall thickening was seen on all patients (100%) and wall infiltration was observed in 91.8% of cases.

Tubular adenocarcinoma was the most common type of gastric cancer (92.6%), followed by signet ring cell carcinoma (3.7%) and adenosquamous carcinoma (3.7%). Well-differentiated carcinoma was reported in 24.1%, intermediately differentiated in 38.9% and poorly differentiated in 37.0% of cases.

Nguyen Ngoc Hung [5] et al studied on 300 gastric cancer patients found that 50.7% had tubular adenocarcinoma, 12.3% had a signet ring cell carcinoma, 14% adenosquamous carcinoma and 16.7% undifferentiated. Another research of Nguyen Van Bang [2] including 203 gastric cancer patients revealed that 64.53% of tumors were well differentiated, 19.21% were intermediately differentiated, 13.97% were poorly differentiated and 2.46% were undifferentiated. Findings of Mitsuru Sasako et al [12] (n = 1034) showed that 40.91% of tumors were differentiated and 58.8% were undifferentiated. The discrepancy in findings of these aforementioned series was attributed to the difference in sample size [1].

Most of our patients (68.4%) had negative regional lymphadenopathy (N0), 24.1% had 1 - 2 positive nodes (N1), 5.6% had 3 - 6 positive node (N2) and 1.9% had ≥ 7 positive nodes (N3). The incidence of regional lymphadenopathy in our series was lower than those of international data. This can be explained that in our study, 29.6% of patients underwent D1 nodal dissection and 70.4% underwent D2 nodal dissection whereas the rate of D2 nodal dissection in other researches was much higher or exclusive.

V. CONCLUSION

The mean age was 58.56 ± 10.28 years; the age group of 51 -70 years was the most common (7.0%), the male/female ratio was 2.6/1. Epigastric pain was the most common clinical manifestation (94.4%).

The diagnostic accuracy of gastric endoscopic biopsy was 69.2%. The sensitivity of CT scan in the detection of the gastric tumor was 90.7%; in which wall thickened was seen in all cases (100%) and wall infiltration was seen in the majority of cases (91.8%).

Tubular adenocarcinoma was the most common histological type (92.6%). A majority of tumor invaded to the serosa (83.3%). The average number of dissected lymph node was 17.03 ± 1.61 nodes. Most of the tumor was at stage II (87.0%), stage III (13.0%).

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