

RESEARCH COMMUNICATION

Clinicopathologic Characteristics of Esophageal Cancer Patients in Northwest Iran - Very Low Incidence of Adenocarcinomas

Yousef Bafandeh^{1*}, Shahriar Hashemzadeh², Mohsen Sokouti², Heidar Esmaili³

Abstract

Aims: Iran is one of the known countries with a high incidence of esophageal cancer in Asia. We have recently shown that the incidence of Barrett's esophagus, a precancerous lesion for esophageal adenocarcinoma (AC) is very low in the north-west of the country. Therefore, we hypothesized that esophageal AC would also be lower than in the Western world. The aim of this study was to assess the clinicopathologic characteristics of esophageal cancer in comparison the data from western populations. **Methods:** This mixed (prospective-retrospective) study enrolled 350 consecutive patients with esophageal cancers (216 endoscopically and pathologically documented, including 134 surgically proven cases) from May 2000 to May 2006, in our referral center in Tabriz, in the north-west of Iran. We localized the tumors in esophagus and esophago-gastric junction. Type III gastric cardiac cancers were excluded. **Results:** The mean age of the patients was 61 ± 12.36 (min 16, max 83). The male to female ratio was almost equal (51.7% vs 48.3%). The lower third of the esophagus was involved in 62% of the patients and esophageal ACs accounted for 18.9% of the cases. However, distinct esophageal adenocarcinomas was only seen in two and in the remainder gastric cardia was also involved. SCC was more frequent in females, and adenocarcinoma in males ($x^2=8.89$, $df=2$, $p=0.012$). Among 134 operated cases, resection was feasible in 74.6%. **Conclusion:** In this Iranian population, the incidence of esophageal adenocarcinoma is very much lower than in Western countries.

Key Words: Esophageal cancer - esophagogastric adenocarcinoma - Iran

Asian Pacific J Cancer Prev, 7, 480-482

Introduction

Esophageal cancer, one of the least studied cancers worldwide (Enzinger and Mayer, 2003), displays unique epidemiologic features that distinguish it from all other malignancies. It shows marked geographic variation both internationally and nationally (Blot, 1994) and in the last decades, studies in Americans (Daly et al., 1996), English (Rios-Castellanos et al., 1992), and European centers (Keighley, 2003) indicated an increase in incidence of adenocarcinoma (AC) of the esophagus and / or gastric cardia. In fact, incidence rates for AC of the esophagus and gastric cardia have tripled in the US over the last several decades (Devesa et al., 1998). In contrast, in Japan and China (Blaser and Saito, 2002; Wang et al., 2003) the predominant histologic type of esophageal carcinoma is squamous cell carcinoma (SCC). Also, in a multi-ethnic study in the USA a very low incidence of esophageal ACA was found in Asian people (Kubo and Corley, 2004).

Iran is one of the known areas with a high incidence of esophageal cancer in Asia (Ghavamzadeh et al., 2001). Most of the patients have been reported from north and northeast

regions of the country. We have recently shown the lower incidence of Barrett's esophagus, a precancerous lesion of esophagogastric AC, in the north-west of Iran (Bafandeh et al., 2005). Therefore, we estimated that the incidence of esophageal AC would also be low.

In the present study the clinicopathologic data of patients with esophageal cancers admitted to our referral center in northwest of Iran were evaluated and the results were compared with those reported for Western populations.

Materials and Methods

The subjects of the prospective study were 216 consecutive patients with clinical symptoms and signs of esophageal cancer, admitted to our referral center in northwest of Iran from May 2000 to May 2006. Their cancers were documented after endoscopic and histopathologic examinations. To localize the lesions UGI series in 164 cases, chest and abdominal CT scans in 164, and palliative dilation by bogies or balloons in 75 patients (with severe stricture) were performed. Endoscopic criteria

Departments of ¹Gastroenterology, ²Thoracic Surgery, and ³Pathology, Tabriz University of Medical Sciences, Tabriz, Iran.

*For Correspondence, E-mail: Y_bafandeh@yahoo.com

for the identification of esophogastric junction (cardia) was the point at which the tubular esophagus flares to become the saclike stomach at the proximal margin of the folds (Marsman et al., 2005). The segments of the esophagus for tumor localization were as follows: upper third, up to 23 cm from incisura teeth; middle third, 24-23 cm; and lower third, 34 cm up to cardia. Of 3 types of gastroesophageal junction cancers [according to Siewert classification (Siewert et al., 2005; Stein et al., 2000)], only types I and II were selected for study.

We also reviewed medical records of 134 consecutive patients with esophageal cancer (with or without involvement of the cardia) who were operated on during the same time period by two chief surgeons. Data were analysed, retrospectively, in these cases by the same criteria as defined for endoscopically diagnosed cases. Chi-square and Pearson's coefficient correlation tests were used for comparison the frequencies and to assess correlations between the variables, respectively.

Results

A total of 350 cases (216 endoscopically diagnosed and 134 operated cases) were analysed, with a mean age of 61 ± 12 years (min 16, max 83). The male to female ratio was almost 1 to 1 (51.7% vs 48.3%). The most common age decade of the patients was 7th (32.3%). Main complaints were: dysphagia (94.2%), epigastric pain (4.4%), upper GI bleeding (1.2%) and vomiting (0.3%). Involved regions were as follows: upper third, 43 (12.3%); mid-esophagus, 90 (25.7%); lower third, 120 (34.3%), middle and lower thirds, 29(8.3%); lower third and cardia, 68 (19.4%) Histopathologic diagnosis were: SCC, 237 (80.3%); AC, 64 (18.9%), one with Barrett's epithelium in adjacent tissue; and metastatic carcinoma, 1 (0.3%). Distinct esophageal adenocarcinoma was seen in two cases, one accompanied with AC in the cardia but separated by a long normal segment. There was no significant correlation between age of the patients and topography of the lesions ($\chi^2=31.12$, $df=24$, $p=0.15$), or histopathologic findings ($\chi^2=16.30$, $df=12$, $p=0.17$). SCC was more frequent in females than males (143 vs 13.1), and AC in males than females [(43 vs 21) ($\chi^2=8.89$, $df=2$, $p=0.012$, $r=0.116$)]. Involvement of the mid-esophagus in females was more than in males (53 vs 37), in contrast to involvement of the lower third of the esophagus and cardia (45 in males vs 23 in females). The main location of the ACs was the lower third of the esophagus with cardia involvement, and SCC was commonly located in other parts of the esophagus ($\chi^2=292.11$, $df=8$, $p=0.0005$, $r=0.573$).

From the retrospective analysis of 134 patients, resection was feasible in 100 (74.4%) of them, and 34 cases (25.4%) were unresectable. There was a significant correlation between site of involvement and resectability ($\chi^2=32$, $df=8$, $p=0.0005$, $r=0.039$). Most of the upper esophageal lesions were unresectable (9 vs 3). Out of 116 operated patients with SCCs, 90 (67.4%) were found to be resectable ($\chi^2=16.52$, $df=4$, $p=0.002$, $r=0.136$).

Discussion

During the past three decades, important changes have occurred in the epidemiological pattern of esophageal cancer (Enzinger and Mayer, 2003). In 2002 and 2003 two separate reports of population based cancer registries were published from Iran (Sadjadi et al., 2005). Esophageal cancer was the second most common cancer in both males (after stomach cancer) and females (after breast cancer). Most of the patients in Iran have been reported from north and northeast regions, known to have the highest esophageal cancer in the country (16). The only prospective, endoscopic and histopathologic proven study from this region was published by Islami et al conducted in patients with upper GI cancers (Islami et al, 2004). They suggest that the proportional occurrence of upper GI cancers in this region is similar to that seen in Linxian, China. In our present study, SCCs were relatively more frequent in females and ACs in males. This pattern of sex distribution has been reported by Schouten et al, in Netherlands (1997). A study from USA showed that men were affected 8 times more than women. In a retrospective study by Semnani et al, in northeast of Iran, male predominance was reported in both histopathologic types (2005).

We in fact only found only one case (0.3%) of primary AC involving only the esophagus, and in the remaining 63 (18.6%) of patients with ACA, gastric cardia was involved concomitantly. As the esophagogastric junction forms the border between esophagus and stomach, the classification in this region is inherently complicated (Marsman et al., 2005). There are many similarities between the AC of the gastric cardia and distal esophagus, and consequently they tend to be classified as one group of tumors (Kalish et al., 1984). In 1996, esophagogastric tumors were divided into three separate subtypes (Siewert and Stein, 1996). Most institutions consider the type III subcardial cancers as true gastric cancers and therefore they were excluded from our study. The proportion of esophageal ACs in our patients (18.9%) was very much lower than the greater than 60-70% seen in Western populations (Anikin et al., 1997; Bollschweiler et al., 2002). Approximately three quarters of all ACs are found in the distal esophagus, whereas SCC are more evenly distributed the middle and lower thirds (Siewert et al., 2001).

In most parts of Asia and African countries the predominant esophageal cancers are SCCs (Blot, 1994). In Japan no increase in incidence of esophageal ACs has been reported (Yuasa et al., 2006). Linzhou, in China, has one of the highest incidence rates of esophageal carcinoma in the world and 60% of patients were diagnosed with esophageal SCCs and 40% were found to have ACs of the esophagus or gastric cardia (Wang et al., 2003). Barrett's esophagus (BE) is the predominant precursor for the development of AC and it has been suggested that almost all esophageal ACAs arise from areas of intestinal metaplasia (Theisen et al., 2006). In the study by Yuasa et al in Japan, in 44 type II Siewert esophageal ACs, BE was recognized in only 2 patients. In

our present study only one patient had BE. There are some reports of increasing of GERD in Iranian population in recent years (Sotudemanesh et al., 2001; Nasser-Moghaddam et al., 2003). With westernization of Iranian's diet, it might be expected that the pattern of lesions will change. However, for esophageal ACs, infection with *H.pylori* seems to have a protective effect (Marsman et al., 2005). In a recent study in Northwest of Iran the infection rate with *H. pylori* was 89.2% (Malekzadeh et al., 2004). The low rate of BE occurrence and high rate of HP infection, could probably explain the lower incidence of esophageal ACA in the Iranian population.

In conclusion, in this Iranian population the incidence of esophageal adenocarcinoma was lower than Western countries since primary esophageal AC, without involvement of the cardia, was exceedingly rare.

References

- Anikin VA, McManis KG, Graham AN (1997). Total thoracic esophagectomy for esophageal cancer. *J Am Coll Surg*, **185**, 525-9.
- Bafandeh Y, Esmaili H, Aharizad S (2005). Endoscopic and histologic findings in Iranian patients with heartburn. *Ind J Gastroenterol*, **24**, 236-8.
- Blaser MJ, Saito D (2002). Trends in reported adenocarcinomas of the esophagus and gastric cardia in Japan. *Eur J Gastroenterol Hepatol*, **14**, 107-13.
- Blot WJ (1994). Esophageal cancer trends and risk factors. *Semin Oncol*, **21**, 403-10.
- Bollschiweiler E, Wolfgarten E, Gutschow C, Holscher AH (2001). Demographic variations in the rising incidence of esophageal adenocarcinoma in white males. *Cancer*, **92**, 549-55.
- Daly JM, Karnell LH, Menck HR (1996). National Cancer Data Base report on esophageal carcinoma. *Cancer*, **78**, 1820-8.
- Devesa SS, Blot WJ, Fraumeni JF (1998). Changing patterns in the incidence of esophageal and gastric carcinomas in the United States. *Cancer*, **83**, 2049-53.
- El-Serag HB, Mason AC, Peterson N, Key CR (2002). Epidemiological differences between adenocarcinoma of the esophagus and adenocarcinoma of the gastric cardia in the USA. *Gut*, **50**, 368-72.
- Enzinger PC, Mayer RJ (2003). Esophageal cancer. *N Engl J Med*, **349**, 2241-52.
- Ghavamzadeh A, Moussavi A, Jahani M, Rastgarpanah M, Irvani M (2001). Esophageal cancer in Iran. *Semin Oncol*, **28**, 153-7.
- Gregory G, Ginsberg, Fleischer DE (2002). Esophageal tumors. In: Sleisenger and Fordtran's 'Gastrointestinal and liver disease'. 7th ed, Philadelphia, Saunders pp 647-71.
- Islami F, Kamanger F, Aghcheli K, et al (2004). Epidemiologic features of upper gastrointestinal tract cancers in northeastern Iran. *Br J Cancer*, **90**, 1402-6.
- Kalish RJ, Clancy PE, Orringer M (1984). Clinical, epidemiologic, and morphologic comparison between adenocarcinomas arising in Barrett's esophageal mucosa and in the gastric cardia. *Gastroenterology*, **86**, 461-7.
- Keighley MRB (2003). Gastrointestinal cancers in Europe. *Aliment Pharmacol Ther*, **181 suppl**, 7-30.
- Kubo A, Corley DA (2004). Marked multi-ethnic variation of esophageal and gastric cardia carcinomas within the United States. *Am J Gastroenterol*, **99**, 582-8.
- Malekzadeh R, Sotoudeh M, Derakhshan MH, et al (2004). Prevalence of gastric precancerous lesions in Ardabi, a high incidence province for gastric adenocarcinoma in the northwest of Iran. *J Clin Pathol*, **57**, 37-42.
- Marsman WA, Tytgat GNJ, Kate FJW, Lanschot JJB (2005). Differences and similarities of adenocarcinomas of the esophagus and esophagogastric junction. *J Surg Oncol*, **92**, 160-8.
- Nasser-Moghaddam S, Malekzadeh R, Sotoudeh M et al (2003). Lower esophagus in dyspeptic Iranian patients. *J Gastroenterol Hepatol*, **18**, 315-21.
- Pisani P, Parkin DM, Bray F, Ferlay J (1999). Estimates of the worldwide mortality from 25 cancers in 1990. *Int J Cancer*, **83**, 18-29.
- Rios-Castellanos E, Sitas F, Shepherd NA, Jewell DP (1992). Changing patterns of gastric cancer in Oxfordshire. *Gut*, **33**, 1312-17.
- Sadjadi A, Nourai M, Mohagheghi MA, et al (2005). Cancer occurrence in Iran in 2002, an international perspective. *Asian Pac J Cancer Prev*, **6**, 359-63.
- Schouten LJ, Kiemency LA (1997). Remarkable age-dependent sex differences in the incidence of adenocarcinoma of the gastric cardia and esophagus in the Netherlands. *Eur J Cancer*, **33**, 1519.
- Semmani SH, Besharat S, Abdolahi N, et al (2005). Esophageal cancer in northeastern Iran. *Ind J Gastroenterol*, **24**, 224.
- Siewert JR, Feith M, Stein HJ (2005). Biologic and clinical variations of adenocarcinoma at the esophago-gastric junction: relevance of a topographic-anatomic subclassification. *J Surg Oncol*, **90**, 139-46.
- Sotudemanesh R, Nasser-Moghaddam S, Shirazian N, et al (2001). Prevalence of endoscopic gastroesophageal reflux disease in a 6-year period. *Endoscopy*, **3**, 27.
- Stein HJ, Feith M, Siewert JR (2000). Cancer of the esophagogastric junction. *Surg Oncol*, **9**, 35-41.
- Theisen J, Stein HJ, Feith M, et al (2006). Preferred locations for the development of esophageal adenocarcinoma within a segment of intestinal metaplasia. *Surg Endoscopy*, **20**, 235-8.
- Wang LD, Zheng S, Zheng ZY, Casson AG (2003). Primary adenocarcinomas of lower esophagus, esophagogastric junction and gastric cardia: in special reference to China. *World J Gastroenterol*, **9**, 1156-64.
- Yuasa N, Hideo M, Tatsuharu Y, et al (2006). Clinicopathologic comparison of Siewert type II and III adenocarcinomas of the gastroesophageal junction. *World J Surg*, **30**, 364-71.