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Comparison of the Anatomic Distribution of Stomach Cancer and Precancerous Gastric Lesions

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The anatomic distribution of precancerous gastric lesions among 3,400 residents in Linqu, Shandong Province of China, was compared with the anatomic distribution of stomach cancer (SC) among 959 patients in Tokyo, Japan. The incidence of SC is high in both areas, and locations within the stomach of the precancerous and malignant lesions were classified using similar criteria. Chronic atrophic gastritis (CAG) affected 98% of the population in Linqu, with intestinal metaplasia (IM) the most severe diagnosis in 33% and dysplasia (DYS) in 20%. Neither the SC nor precancerous lesions were uniformly distributed in the stomach. Among the DYS 3% were along the greater curvature of the body, 15% along the lesser curvature of the body, 25% in the angulus, 22% along the lesser curvature of the antrum, and 34% elsewhere in the antrum. Among the SC the corresponding percentages were 2, 16, 28, 25 and 29. The similarity to the SC distribution increased gradually from CAG to IM to DYS, providing further evidence for the multistage progression of precancerous gastric lesions.

Key words: Stomach cancer — Precancerous lesions — Anatomic distribution

Although stomach cancer (SC) death rates have decreased in many countries, this cancer remains one of the two leading forms of cancer in China and Japan.[1,2] The causes of SC are still unclear, but dietary factors including high salt and low fresh fruit and vegetable consumption and prior chronic gastritis are closely associated with increased risk.[3] SC is often preceded by a series of changes in the lining of the stomach that occur over many years,[3] a feature observed in many high risk areas including China and Japan.[4,5] This progression suggests that clues to prevention of SC may derive from studies of precancerous stomach lesions. There have been few population-based surveys of precancerous lesions, however, and due primarily to the limited number of sites biopsied in gastroscopic surveys, few comparisons have been made between the anatomic distributions of precancerous gastric lesions and SC.[6–9] Recently, we completed a screening survey to detect early SC and assess precancerous lesions in a population at high risk for this cancer in Linqu county, Shandong province, a rural area of China with one of the highest stomach cancer rates found in China and the world.[4] Multiple biopsies from standard anatomic locations for each individual enabled mapping of the distribution of precancerous lesions within the stomach. Herein, we compare the location of these lesions with the location of SC reported in a large series of Japanese patients.[9]

MATERIALS AND METHODS

The data on precancerous gastric lesions come from a study in Linqu county, a rural area in Shandong province of northeast China, described elsewhere.[4] In brief, a total of 3,433 residents were selected at random in 14 villages within four townships of Linqu county, comprising 83% of the population aged 35–64. After the names of all residents were transcribed from the village population rosters, health officials visited each person and delivered a consent form to explain the study and invite him/her to participate in a stomach cancer screening examination. If an individual was willing to participate, an appointment was made for an examination. All participants were given a brief physical examination and their medical history was recorded. The subjects received a gastroscopic examination and biopsies were taken from seven standard sites in the stomach: four from the antrum, one from the angulus, and one each from the lesser and greater curvature of the body. Pathologic diagnoses were made according to criteria proposed by the Chinese Association of Gastric Cancer. The details of the classification criteria, along with photographs of superficial gastritis (SG), chronic atrophic gastritis (CAG), intestinal metaplasia (IM) and dysplasia

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(DYS), were given in an earlier article.[4] Each slide was interpreted by three senior pathologists independently, with a sample reviewed by experts on gastric pathology in China and the United States. Each biopsy was classified according to the presence or absence of SG, CAG, IM, DYS or SC. Each biopsy was given a diagnosis based on the most severe histology found in the biopsy, and each subject was assigned a diagnosis (which will be referred to as the global diagnosis) based upon the most severe diagnosis among any of the biopsies. A total of 33 subjects were excluded because of insufficient material for histologic analysis; therefore, 3,400 subjects were included in this analysis.

Because only 13 SC cases were detected in our survey, data on the distributions of SC are cited from a study published by Yamada and Kato.[9] That study reviewed a total of 1,216 SC patients who underwent surgical resection during 1971–79 at the Cancer Institute Hospital in Tokyo, Japan. A total of 959 SCs had anatomic locations classified using the same seven biopsy sites as in the Chinese screening program. The SCs were categorized as either well-differentiated or poorly differentiated types. Comparisons between the distribution of precancerous gastric lesions and SCs were made for the seven corresponding sites in both studies.

RESULTS

CAG was detected in 98.5% of the residents in Linqu. Global diagnoses of CAG, IM, and DYS were found in 1,523 (45%), 1,123 (33%) and 683 (20%), respectively. For 63% of the subjects with DYS, the diagnosis was based on DYS appearing in one biopsy, while about 30% of those with IM had IM in 3 or more biopsies, and 84% of those with CAG had this diagnosis in 3 or more biopsies. The total numbers of biopsies across all 7 anatomic locations with DYS, IM and CAG as the most severe lesion were 1,101, 3,809 and 11,131, respectively.

The prevalence rates of the precancerous lesions and SC varied by location within the stomach. Table I shows the anatomic distribution of CAG, IM, DYS, and SC. Under a uniform distribution, about one-seventh (14%) of each lesion would be expected to occur at each of the 7 stomach locations. CAG came closest to this pattern,

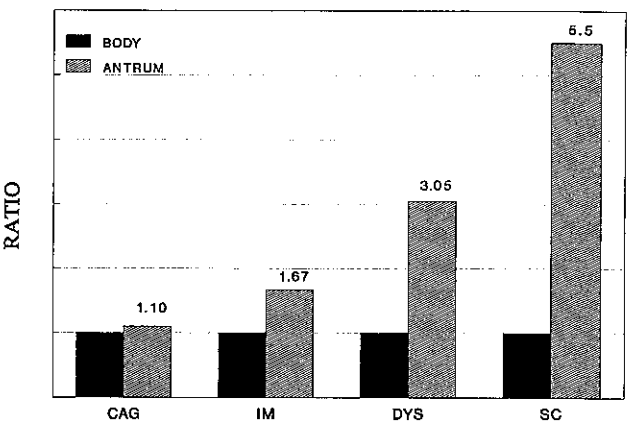

Fig. 1. Ratios of the prevalence of global diagnoses of CAG, IM, DYS and SC in the antrum compared to the body of the stomach in Linqu.

Table I. Percent Distribution of CAG, IM, DYS and GC across Anatomic Locations of the Stomach

Sites	Precancerous lesions			Stomach cancer		
	CAG	IM	DYS	Well Differentiated	Poorly Differentiated	Combined types
Body						
Lesser curvature	12	14	15	15	17	16
Greater curvature	8	5	3	1	2	2
Angulus	15	18	25	23	34	28
Antrum						
Anterior wall	16	16	12	15	9	12
Posterior wall	17	14	11	15	9	12
Lesser curvature	16	20	22	26	24	25
Greater curvature	17	13	11	5	5	5
Total	100	100	100	100	100	100
N[a]	11,131	3,809	1,101	493	466	959

a) N=Total number of biopsies with CAG, IM, or DYS as the most severe lesion, or total number of cancer cases.

although occurring signifiantly less often in the body and more often in the antrum. This tendency was progressively accentuated for IM, DYS and SC. Only 3% of DYS and 2% of SC were found along the greater curvature of the corpus, while in the angulus the frequency increased from 15% for CAG, to 18% for IM, 25% for DYS, and 28% for SC. Similarly, for the lesser curvature of the antrum the percent distribution increased from 16% for CAG, to 20% for IM, to 22% for DYS, and 25% for SC. The prevalences of CAG, IM, DYS and GC in Linqu based on the most severe diagnosis among the biopsies from the antrum and angulus were respectively 48.4%, 31.2%, 18.0% and 0.3%, compared to 43.8%, 18.6%, 5.9% and 0.06% from biopsies in the body. Figure 1 shows the ratio of the prevalence of each lesion in the antrum/angulus relative to the body of the stomach. The ratio was close to 1.0 for CAG, but increased with more advanced gastric lesions to 1.67 for IM, 3.05 for DYS, and 5.5 for SC.

DISCUSSION

China and Japan are both high-risk areas of SC, sharing similar characteristics such as a predominance of intestinal-type tumors, a male excess, and death rates increasing with age.[4, 9, 10] Our comparative pathology showed that the anatomic distributions of precancerous stomach lesions in China and of SC in Japan were also similar. The highest frequencies of IM, DYS and SC were in the antrum, especially at the angulus and along the lesser curvature of the stomach. Although the data on SC locations were obtained from a Japanese population, the results are in agreement with those in an earlier survey in Linqu, China showing that 63% of SC was located in the antrum.[10] Furthermore, among the 13 SC cases detected during the gastroscopic screening survey in Linqu, 11 were in the antrum and only 2 in the body.

Lauren classified SC according to intestinal and diffuse types,[11] with intestinal-type adenocarcinomas believed to arise from metaplastic epithelium.[12, 13] Correa[3, 14] noted that CAG tended to concentrate along the lesser curvature of the proximal portion of the antrum in young persons. As age increased, new independent foci of atrophy appeared elsewhere along the lesser curvature, eventually spreading to the lesser curvature of the body and to the anterior and posterior walls, suggesting a progression from normal to atrophic to neoplastic epithelia that takes place over an interval of many years. In another study, the sites of SC tended to correlate with IM in the antrum, especially severe IM.[15] In an earlier paper, we showed that the prevalences of IM, and particularly DYS, increased with age, with DYS affecting 14% of those age 35–39 but 34% of those age 60–64.[4]

The reasons for high frequency of precancerous gastric lesions and SC in the angulus and antrum are unknown. In animal studies the localization of precancerous gastric lesions resembles that seen in humans. Wistar rats whose stomachs were X-irradiated daily with 500 rad produced intestinal metaplasia in the pyloric region.[16] When N-methyl-N′-nitro-N-nitrosoguanidine (MNNG) was administered to four dogs, adenocarcinomas developed in the antral region of the stomach.[17] In MNNG-exposed Wistar rats, mucosal atrophy was more severe in the antrum than fundus, while 75% of carcinomas later developed in the antrum.[18] In humans, pyloric and the body mucosa are composed histologically of different glands, and in one study of SC patients, the mitotic rate of cells was significantly higher in the pyloric area than in the body of the stomach.[19]

Recent studies suggest that *Helicobacter pylori* infection may play an important role in the development of atrophic gastritis and progression to SC.[20] A differential effect of infection at different biopsy sites is under study in Linqu. Salt is also suspected to cause gastritis by irritation of the gastric mucosa, and in animal studies high concentrations of salt solution can produce acute gastritis, loss of normal glands and proliferation of intestinal glandular cells in the whole mucosal layer.[21, 22] The vigorous peristaltic movement toward the lesser curvature and prolonged contact with food during digestion also may tend to produce lesions in this area, but earlier and with greater frequency than in other sites.

In summary, the consistency of anatomic distribution between precancerous gastric lesions in the population-based survey in China and the case series of SC in Japan adds to the evidence that IM and DYS are clearly linked with the development of gastric cancer. Further research into the determinants of precancerous lesions should lead to a better understanding of the origins of SC and means of prevention of this common cancer.

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