Gastric Carcinoma in Young Adults

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Of 720 patients with gastric carcinoma treated over a 6-year period, 37 (5%) were 35 years of age or younger. They differed from older patients in that the usual sex ratio was altered (18 men: 19 women), and in certain histologic features. Poorly differentiated or undifferentiated lesions predominated (34 patients), and the distribution of histologic types was unusual; two thirds each were of the diffuse type (Lauren classification) or signet ring type (World Health Organization classification), and over three quarters were infiltrative (Ming classification). Intestinal metaplasia was absent in the majority of patients, and gastritis was less commonly seen than in older patients. Although most patients had long histories of disease and advanced disease, the TNM stages and the proportion undergoing curative resection (8%) were similar to those seen in older patients. Except for one who has survived 5 years, all patients in this study have died.

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WHETHER GASTRIC CARCINOMA in the young differs in any way from that seen in older patients has been a controversial issue. It has been suggested that there is a higher proportion of women[1–4] and of undifferentiated tumors[2,4–6] in young patients. Both a late presentation with a poor outcome,[4,6] as well as a presentation and outcome similar to that of older patients[1–3,5] have been reported. We have studied those patients at our institution who are 35 years or younger to establish whether they differed in any way from older patients.

Patients and Methods

We reviewed the records of all patients 35 years of age or younger with gastric carcinoma who were managed at our institution from 1980 to 1985. Over this period, all cases of gastric carcinoma were registered prospectively with the recording of clinical findings, pre- and intraoperative staging, pathologic categorization, management, and follow-up. All patients had chest radiographs, a double contrast barium meal, endoscopy with biopsy, biochemical screen, routine hematologic indices, abdominal ultrasonography, and, in selected cases, computed tomography (CT) scanning of the upper abdomen. The Union Internationale Centre le Cancer (UICC) TNM[7] system was used for clinical and pathologic staging. Patients not undergoing laparotomy had the T stage assessed from the barium meal and the M stage from the presence of ascites or evidence of hepatic metastases on ultrasonography.

All histologic material was reviewed. When sufficient information was available, the histologic material was classified according to the Lauren[8] System (35 patients), World Health Organization (WHO) System[9] (35 patients), and Ming System[10] (28 patients). Twenty-two cases were assessed for intestinal metaplasia, which was classified as either complete or incomplete.[11] Gastritis was assessed on the lesser curvature in the distal stomach in pyloric-type mucosa (14 patients) and in the proximal stomach in body-type mucosa (15 patients). The frequency distribution of histologic features was compared with the reviewed material from our previous experience with patients of all ages.[12]

Results

During the 6-year period of this study, 720 new patients with gastric carcinoma were registered, 37 of whom (5%) were 35 years old or younger, and 14 of whom (2%) were 30 years old or younger, with the youngest patient being 21 years old. There were 18 men and 19 women. Thirty-two patients (87%) were of mixed ethnic background; four (10%) were black, and one (3%) was white. During the

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TABLE 1. *A Comparison of Histological Features in Young Patients* and Patients of all Ages*

	Young	Unselected
Lauren classification	(n = 35)	(n = 86)
Diffuse	23 (66%)	26 (30%)
Intestinal	6 (17%)	48 (56%)
Undifferentiated	6 (17%)	9 (10%)
Mixed intestinal/diffuse	0	3 (4%)
WHO classification	(n = 35)	(n = 86)
Tubulo-papillary	5 (20%)	47 (55%)
Signet ring	23 (66%)	21 (24%)
Undifferentiated	7 (14%)	15 (17%)
Mixed tubulo-papillary/signet ring	0	3 (4%)
Ming classification	(n = 28)	(n = 57)
Expansile	4 (23%)	26 (46%)
Infiltrative	14 (77%)	31 (54%)
Intestinal metaplasia	(n = 22)	(n = 55)
Complete	7 (32%)	42 (76%)
Incomplete	1 (5%)	27 (49%)
None	15 (68%)	10 (18%)
Pyloric gastritis	(n = 14)	(n = 42)
Absent	1 (8%)	0
Superficial	1 (8%)	1 (2%)
Atrophic	12 (86%)	41 (98%)
Body gastritis	(n = 15)	(n = 44)
Absent	2 (13%)	2 (4%)
Superficial	6 (40%)	6 (14%)
Atrophic	7 (47%)	36 (82%)

* Patients 21–35 years of age.

period of the study, 50% of all hospital inpatients were of mixed ethnic background, 22% were black, and 24% were white. Two patients had a family history of gastric carcinoma, with the disease having developed in at least one near relative.

The duration of symptoms ranged from 1 to 96 weeks, with a mean of 27 weeks. In seven patients, the length of history exceeded 1 year. The most common symptom was dyspepsia, reported by 16 patients, most of whom had been treated with several peptic ulcer drugs. The second most common presentation was insidious, involving weight loss, anemia, jaundice, and ascites. Nine patients presented with complications; six had gastric outlet obstruction, and the remaining three patients had esophageal obstruction, perforation, and haemorrhage, respectively.

Seven patients (9%) showed no physical signs of gastric carcinoma. There was a palpable abdominal mass in 20 of the patients (54%) and ascites in five (14%). Liver metastases were diagnosed by the biochemical, ultrasonographic and CT findings of three patients who did not undergo laparotomy, and by biopsy in seven patients who did. Most lesions were located in either the antrum (20 patients) or body (13 patients) of the stomach, with two patients having diffuse involvement, and two patients having, respectively, a tumor in the fundus and at the esophagogastric junction.

The histologic diagnosis of gastric carcinoma was made for all 37 patients (Table 1). In 34 cases, the tumor was poorly differentiated or undifferentiated, and in three cases, moderately to well-differentiated. When we applied the Lauren classification, we found that two thirds of the patients had diffuse carcinomas, and when applying the WHO classification, we found the same proportion had signet ring lesions. Using the Ming classification, we categorized over three quarters of the histologic types as being infiltrative. Most of the patients reviewed had no intestinal metaplasia, and intestinal metaplasia of the incomplete type was seen in only case. And although most of the patients examined had atrophic gastritis in the pyloric mucosa, it was present in the body mucosa in less than half the patients.

Nine patients (24%) were believed to have lesions too advanced for surgical treatment, with two having ascites, one having Virchow-Troisier node, three having liver metastasis, and two having linitis plastica. These patients had a median survival time from the time of diagnosis of 32 days (range of 2–169 days). An additional seven patients (19%) had a laparotomy with no further procedure being possible, and a median survival time of 40 days (range of 6–132 days). Five patients (14%) underwent gastroenterostomy and survived for a median of 57 days (range of 10–402 days), with one being lost to follow-up. A palliative gastrectomy was performed in twelve patients (32%), with a median survival time of 344 days (range of 32–1024 days, with one patient lost to follow-up). In only three patients (8%) was a curative resection considered possible by the surgeon; one patient (T1 N2 M0) is alive and well at 5 years, and the remaining two (both T1 N0 M0) have died from recurrence after 406 and 626 days, respectively.

Discussion

In treating young patients with gastric carcinoma, two issues of interest are its frequency and whether it differs from the disease in older patients. To assess this frequency and to allow valid comparisons, we have drawn from our own analyses of patients of all ages[12–15] as well as from reports from other countries.

We found that 5% of our patients were younger 35 years of age and 2% were younger than 30 years old, a finding consistent with our earlier analysis.[13] In Western nations, the proportion of patients younger than 35 years of age has been 2.7%[4] and 2.2%,[16] whereas estimates of the proportion of patients 30 years old or younger have ranged between 0.7% and 1.4%.[1,3,6] In Japan, 1.8% of all types of gastric carcinoma[17] and 1.6% of cases of early

gastric carcinoma[17] were found in patients 30 years of age or younger.

Of the patients in our study, there were fewer men than women, accounting for a sex ratio of 1:1.05, which differed markedly from the overall ratio of 1:0.5 seen at our hospital.[13] A preponderance[1-4] or equivalence[5,6,16,17] of women among younger patients has been a widespread finding, and contrasts with the consistent preponderance of men that typically is seen in older patients. The reason for this reversal in sex ratio in the young is uncertain. The high frequency of pregnancy in young women with gastric cancer has been noted, and two of our patients presented in the puerperium. We believe, however, that pregnancy is so common at this age that this apparent association could be fortuitous. The presence of estrogen receptors and intracytoplasmic estradiol in a proportion of cases of all ages fails to explain the preponderance of females among young patients.[18]

Although the mean length of history was 6 months and most patients were treated for peptic ulcers without investigation, this delay was not different from our overall experience[13,15] nor from that reported by others.[19] Only three patients (8%) had no apparent nodal or other metastatic disease, and this was comparable to the number of similar patients (13%) of our overall experience.[13] In only three patients was an apparently curative gastrectomy possible; although at 8%, this proportion of curable cases was lower than the 13% found among our unselected patients, it was not significantly different ($chi^2 = 2.55$, $0.2 > p > 0.1$). Only two of our patients (5%) had early gastric cancer, and this proportion was comparable to our overall experience of 3.5% and to that of a study involving patients 30 years old or younger reported from Japan.[20]

We found marked differences when we compared the histologic features of our young and old patients. Ninety-two per cent of our young patients had poorly differentiated or undifferentiated tumors, compared with 62% in our overall experience. This lack of differentiation in the young has been reported by others.[5,20] Lauren has observed that, in patients of all ages, the frequency of intestinal and diffuse carcinomas is equal in nonendemic areas, but that in endemic areas, the proportion of the intestinal types increases.[8] Cape Town may well be such an endemic area, as we have previously found in patients of all ages that 56% of carcinomas were intestinal and only 30% diffuse, with the remainder mixed or undifferentiated. In our young patients, however, this ratio was reversed, with 21% of the carcinomas being intestinal and 64% diffuse, the remainder being undifferentiated. The frequency of diffuse carcinoma in the young and its associated equivalent sex ratio has been well summarized by Lehtola;[21] the association with pernicious anemia, hypogammaglobulinemia and a strong family history, however, was not found by us. The infrequency both of intestinal-type carcinomas, associated intestinal metaplasia, and atrophic gastritis in the young has been noted by Japanese authors.[17]

A predominance of signet ring neoplasms (WHO classification) and a greater proportion of infiltrative neoplasms (Ming classification) also differed from our experience with patients of all ages. There is a compelling argument linking the incomplete type of intestinal metaplasia to the intestinal form of carcinoma,[11] and the low frequency of both that we have found might support this argument. Our young patients had less associated gastritis than our older patients. In Japan, gastritis is less common in young patients, both those without gastric carcinoma[22] and those with early gastric carcinoma.[20] Correa has suggested that gastric atrophy, gastritis, and intestinal metaplasia precede gastric carcinoma.[23,24] The relative infrequency of these changes in the young may suggest that another sequence is operative.

Previous studies of young patients have reported 5-year survival rates of 6–19%.[1-3,5] The 6-month survival rate of 30% in young patients of the present study was similar to our overall experience.[15] Of the 37 patients 35 years of age or younger there was only one survivor (3%); nevertheless, this group may be too small to allow accurate comparison with the overall 5-year survival rate of 8.5%.[14,15]

Conclusion

Gastric carcinoma in patients between 21 and 35 years of age represented 5% of all patients with this disease at our institution. When we compared them with older patients, we found the only differences were the high proportion of females, the frequency of the diffuse, signet ring, and infiltrating histological types, and the infrequency of associated gastritis and intestinal metaplasia. All other features were essentially similar.

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