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• BRIEF REPORTS •

Sentinel lymph node concept in gastric cancer with solitary lymph node metastasis

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Abstract

AIM: To study the localization of the solitary metastases in relation to the primary gastric cancers and the feasibility of sentinel lymph node (SLN) concept in gastric cancer.

METHODS: Eighty-six patients with gastric cancer, who had only one lymph node involved, were regarded retrospectively as patients with a possible sentinel node metastasis, and the distribution of these nodes were assessed. Thirteen cases with jumping metastases were further studied and followed up.

RESULTS: The single nodal metastasis was found in the nearest perigastric nodal area in 65.1% (56/86) of the cases and in 19.8% (17/86) of the cases in a fairly remote perigastric area. Out of 19 middle-third gastric cancers, 3 tumors at the lesser or greater curvatures had transverse metastases. There were also 15.1% (13/86) of patients with a jumping metastasis to N2-N3 nodes without N1 involved. Among them, the depth of invasion was mucosal (M) in 1 patient, submucosal (SM) in 2, proper-muscular (MP) in 4, subserosal (SS) in 5, and serosa-exposed (SE) in 1. Five of these patients died of gastric cancer recurrence at the time of this report within 3 years after surgery.

CONCLUSION: These results suggest that nodal metastases occur in a random and multidirectional process in gastric cancer and that not every first metastatic node is located in the perigastric region near the primary tumor. The rate of "jumping metastasis" in gastric cancer is much higher than expected, which suggests that the blind examination of the nodal area close to the primary tumor can not be a reliable method to detect the SLN and that a extended lymph node dissection (ELND) should be performed if the preoperative examination indicates submucosal invasion.

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INTRODUCTION

The sentinel lymph node (SLN) which refers to the first lymph node to receive drainage from the primary tumor has been successfully introduced in the patients with breast cancer[1] and malignant melanoma[2] to assess tumor involvement in regional lymph nodes with less morbidity but equal accuracy to complete lymphadenectomy. But the feasibility of sentinel node mapping of gastric carcinoma is still unclear and controversial. To explore the applicability of sentinel node concept to gastric cancer and provide useful information for establishing a novel method to detect sentinel nodes during operation, we retrospectively investigated solitary lymph node metastases that hypothesized to represent sentinel lymph node.

MATERIALS AND METHODS

Patients

Between January 1997 and December 2003, 1 698 patients with gastric cancer underwent gastrectomy with lymph node dissection (more than D1) at the Department of General Surgery, Guangzhou General Hospital of PLA, Nanfang and Zhujiang Hospitals of First Military Medical University. Among them, 86 (5.1%) patients were rolled in this study by the following criteria: (1) the lesion was solitary and limited to one part of the stomach; (2) a curative gastrectomy with ELND was performed; and (3) the histological examination of all resected lymph nodes revealed only one lymph node involved. These patients were subdivided according to the primary site of gastric cancer: 16 upper-third (U) tumors; 19 middle-third (M) tumors; and 51 lower-third (L) tumors. According to the depth of wall invasion, mucosal (M) lesions, submucosal (SM) lesions, proper-muscular (MP) lesions, and subserosal (SS) lesions were observed in 2, 7, 47, and 30 patients, respectively. Regarding their histologic grades, 23 of high-differentiated cases, 55 of middle- differentiated cases, 7 of low- differentiated cases, and 1 of non-differentiated case were proven to have only one lymph node involved. Total gastrectomy, proximal subtotal gastrectomy and distal subtotal gastrectomy were carried out in 29, 6 and 51 cases, respectively.

Methods

The resected specimens and the lymph nodes were stained conventionally with hematoxylin and eosin (HE) and examined by pathologists. The clinicopathological data were evaluated according to the General Rules by the Japanese Research Society for Gastric Cancer[3]. In the present study, to express the group and station number of each lymph node, No. and N were inserted in front of the number, i.e., No. 4 means group 4 lymph node and N1 means station 1 lymph node. If patients were histologically verified to have distant lymph nodes (N2 or N3) involved without perigastric node metastasis (N1), they were defined to have either jumping or skip metastases. If the tumors at the lesser or greater curvatures had metastasized to the lymph nodes located in the opposite curvatures, they were then defined to have transverse metastases. Ten of 13 patients with skip metastases were followed up for 1-5 years until December 2003.

RESULTS

Upper-third (U) tumors

In 13 out of 16 U tumors, the solitary node metastasis was found in perigastric area close to the tumor (N1). In 3 cases, the metastasis was found in N2 area. Among them, 2 nodes were along the left gastric artery (LGA) (No.7), the other 1 along common hepatic artery (CHA) (No.8a).

Middle-third (M) tumors

In 9 out of 19 M tumors, the single node metastasis was found either in the lesser (No.3) or greater curvature (No.4) perigastric area close to the primary tumor. Among them, 2 tumors at the lesser curvature and 1 tumor at the greater curvature had transverse metastases. In 6 cases, the metastasis was found in the remote perigatric area (No.1, 5 and 6), and another 4 cases in the N2 or N3 area (No.7, 8a and 12) were without N1 involvement.

Lower-third (L) tumors

Of 51 patients with L tumors, 34 had the single metastasis in the perigastric node close to the tumor (No.3 and 4), 11 had metastasized to the surprapyloric (No.5) or infrapyloric (No.6), both of which were N1 but somewhat remote from the primary tumor. In the other 6 cases, the metastasis was found in the N2 or N3 area (No.1, 4 s, 7 and 11 p) without N1 involvement.

Invasion and survival of patients with jumping metastasis

Among 13 cases with jumping metastasis, the depth of invasion was M in 1, SM in 2, MP in 4, SS in 5, and SE in 1. Among 6 out of 10 patients who received a follow-up, 5 died of tumor recurrence and 1 of other disease within 3 years after operation. The other 4 were alive at the time of this report for more than 3-5 years after surgery.

Metastasis of tumors

A total of 1376 lymph nodes were harvested in this group of 86 patients with D2-D3 lymphadenectomy. The average number of lymph nodes dissected was 16 in each case. The distribution of the single positive node is shown in Table 1 according to the location of the primary tumor. In total, the single nodal metastasis was found in 65.1% of cases in the nearest perigastric node area, in 19.8% of cases in a fairly remote perigastric area, and in 15.1% of cases in the N2 or N3 area without N1 involvement.

Table 1 Distribution of solitary lymph node metastasis

Location of positive node	Location of primary tumor		
	Upper	Middle	Lower
Right cardial (No1)	2(N1)	1(N1)	1(N2)
Lesser curvature (No3)	7(N1)	7(N1)	20(N1)
Greater curvature (No4d)		2(N1)	14(N1)
Greater curvature (No4s)	2(N1)		1(N3)
Surprapyloric (No5)		2(N1)	5(N1)
Infrapyloric (No6)	2(N1)	3(N1)	6(N1)
Left gastric artery (No7)	2(N2)	2(N2)	3(N2)
Common hepatic artery (No8a)	1(N2)	1(N2)	
Splenic artery (No11p)			1(N2)
Proper hepatic artery (No12)		1(N3)	

No4d and 4 s represent nodes on right and left half of greater curvature respectively; No8a represents nodes on the anterior or upper of CHA; No11p represents nodes on proximal splenic artery.

DISCUSSION

Gastric cancer is generally thought to spread to N1 nodes first, followed by involvement of distant nodes (N2-N3) just as other carcinomas. However, more recent studies have reported that lymph node involvement was noted not only in N1 but also in N2-N3 and that the rate of N2 lymph node metastases in patients with advanced gastric cancers was higher than expected[4,5]. Lymphatic drainage route must be patient-specific and lesion-specific in gastric cancer due to complicated lymphatic streams from the stomach. Our results suggested that although most of the single nodal metastasis was found in the nearest perigastric node area, approximately one quarter of the patients had the first metastasis in a fairly remote perigastric area and up to 15% of patients demonstrated skip metastasis without N1 involvement. To date, to the authors knowledge, there are only 5 retrospective studies on gastric cancer patients with only one lymph node metastasis[6-10]. In these studies, the single nodal metastases were distributed beyond the perigasric area in 12.6-29% of gastric cancer patients, which suggested that the conventional lymphatic routes in stomach that have long been generally accepted should be clarified further. Our present data confirm these results. Among 13 cases with skip metastasis in the current study, most (10/13) of the solitary node metastases were found in No.7, 8, or 12. This result seems to be comparable with other reports, where No.7, 8, 9 and 12 nodes were most commonly involved in patients with skip metastasis[6-10], and suggests that No.7, 8, and 12 to be the most important stations as well as N1[4,5]. In our study, 3 out of 19 mol/L tumors had transverse metastases, which indicates that gastric lymph channels are multidirectional and form complex networks. The survival and depth of invasion in gastric cancer patients with skip metastases presented in this report suggest that if the preoperative examination diagnosed submucosal invasion, then a ELND should be conducted.

Results from these retrospective studies not only demonstrated the feasibility of SLN concept to gastric cancer but also provided useful information for intraoperative sentinel node mapping. That the perigastric nodal area close to the primary tumor is the first site of metastasis in 65.1% of gastric cancers in the present study indicates that the so-called shine-through effect should be considered in sentinel node mapping by radioisotope (RI) method[11]. The high incidence of skip metastasis to N2-N3 nodes suggests that blind examination of the nodal area close to the primary tumor can not be a reliable method to detect the first metastasis[6]. Visualization of dye is useful for real-time observation of lymphatic vessels, but it is difficult to detect multiple sentinel nodes and SLNs in the second or third compartments because vital dye tends to diffuse rapidly from nodal tissue. A probe-guided approach is essential to cover the widespread distribution of SLNs in gastric cancer and is very useful to detect residual SLNs in unexpected areas[12]. Therefore, a combination of the dye and radioguided methods for systemic lymphatic mapping of gastric cancers may be recommended to improve the detection rate and diagnostic accuracy[13,14].

It remains unclear why jumping metastases occurred in these cases. The following reasons could all play some role: (1) N1 involved nodes and occult metastases to N1 nodes may have been missed during the dissection and the routine histopathologic examination, which result in a false skip metastasis. The possible sentinel nodes detected by conventional means might not always be primary portions of any metastasis and true skip metastasis in gastric cancer may be rare[10]; (2) There may have been some aberrant lymphatic drainage patterns in patients with gastric cancer, through which metastasis bypasses lymphatic vessels[7,8,15]; (3) Direct lymphatic flows to distant affected nodes from primary gastric lesions have been found in SLN mapping intraoperatively[16]; (4) Lymphatic flows to the N1 nodes may have been blocked with cancer tissue; (5) The microenvironment in the N1 nodes is sometimes unfit for the

development of metastasis[17]. Free cancer cells may diffuse through regional nodes to distant nodes. In addition, the risk factors associated with skip nodal metastasis may include the stage, depth of invasion, macroscopic classification and pathological type of gastric cancer.

Most surgeons are skeptical about the application of the SLN concept for gastric cancer because of the high incidence of skip metastases and the random process occurring in nodal metastases. However, Kitagawa *et al*.[18,19] have pointed out that the sentinel node for gastrointestinal cancer is not the node necessarily located anatomically closest to the primary lesion and is not necessarily the only one. In those cases with a jumping metastasis to N2-N3 nodes, sentinel nodes in the second or third compartment are considered to be functionally first compartments. Bilchik *et al*.[20] proposed the potential for universal application of sentinel node mapping in solid tumors. Cases with one or two lymph node metastasis examined in these retrospective studies only occupy a little part of patients with gastric carcinoma in which one or more SLNs can be detected in every case theoretically. Then the results from these studies can not represent the real characteristic as to the occurrence of SLN in all gastric cancers. Actual data from sentinel node mapping for gastric cancers, rather than a retrospective analysis of metastatic patterns, are needed to explore the feasibility and validity of sentinel node biopsy in gastric cancer.

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