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Lymphatic Routes of the Stomach Demonstrated by Gastric Carcinomas with Solitary Lymph Node Metastasis

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Abstract: To clarify whether or not the lymphatic routes that have long been generally accepted are indeed correct, we retrospectively examined the clinical records of patients with solitary lymph node metastasis from gastric carcinoma. From 735 patients gastrectomized with lymph node dissection (more than D1), 51 (7%) were histologically proven to have only one lymph node involved. In 44 of these 51 patients, the involved nodes were all in the perigastric region (N1). There were also 7 patients with a jumping metastasis to the N2–N3 nodes. Three of them were found along the left gastric artery (#7 according to Japanese classification) and the other 4 were found along either the common hepatic artery (#8) or the proper hepatic artery (#12). The depth of invasion was submucosal in 2, proper-muscular in 2, subserosal in 1, and serosa-exposed in 2, and the conclusive stage was II in 2, IIIa in 3, and IIIb in 2. However, 1 of these patients died of liver cirrhosis and 2 died of pneumonia, while the other 4 were still alive at the time of this report more than 5 years after surgery. These results suggest that not every sentinel node is located in the perigastric region near the primary tumor and that, if the preoperative examination indicates submucosal invasion, then a systematic regional lymph node dissection should therefore be carried out.

Key Words: gastric cancer, metastatic lymph node, lymphatic route, lymph node dissection, limited gastrectomy

Introduction

A radical resection with a lymphadenectomy has been reported to improve the survival rate of patients with advanced gastric carcinoma.[1–6] However, several studies have shown high morbidity and mortality rates after such an aggressive gastrectomy shortly after surgery.[7–11] It is generally accepted that additional extensive lymph node dissection is unnecessary in cases without lymph node metastases. In these circumstances, we can save both organs and the lymph nodes by performing a partial resection with a D0 or D1 dissection. Therefore an accurate diagnosis of lymph node metastasis is essential in selecting patients for whom an extended lymph node dissection is appropriate. It is extremely useful to know before surgery which lymph nodes should be examined during the operation. We conducted our study to clarify whether or not the lymphatic routes that have long been generally accepted are indeed correct, by retrospectively reviewing the clinical records of patients with solitary lymph node metastasis from gastric carcinoma.

Patients and Methods

Between 1984 and 1997, 735 patients with gastric cancer underwent a gastrectomy with lymph node dissection (more than D1)[12] at the Department of Surgery II, Kanazawa Medical University. Among them, 51 (7%) patients were histologically proven to have only one lymph node involved. The resected specimens and the nodes were sent to the pathologists of our hospital for a histopathologic examination. The clinicopathological data were evaluated according to the General Rules for Gastric Cancer Staging in Surgery and Pathology established by the Japanese Research Society for Gastric Cancer.[12] In the current study, to express the station number of each lymph node, # was inserted in front of the number, i.e., #1 means number 1. The patients with only one positive node were subdivided according to the primary site of gastric cancer: 11% (16/151) of the upper third (C) tumors, 9% (21/233) of the middle third (M) tumors, and 4% (14/318) of the lower third (A) tumors were proven to have only one node involved. As for the

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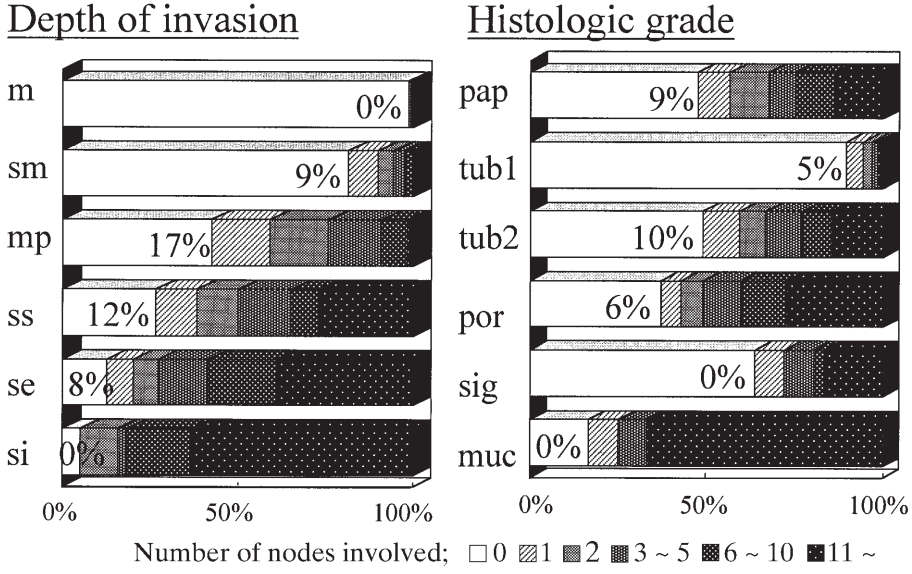

Fig. 1. Metastatic nodes distributed according to depth of wall invasion and histopathologic grade. Abbreviations: see Table 1

depth of wall invasion, 0% (0/180) of mucosal lesions (m), 9% (13/141) of submucosal lesions (sm), 13% (24/178) of t2 lesions (mp or ss), 8% (16/198) of t3 lesions (se), and 0% (0/38) of t4 (si) were proved to have only one lymph node involved. Regarding their histologic grades, 8% (35/418) of well-differentiated types (pap, tubl, or tub2) and 5% (15/306) of poorly differentiated ones (por, sig, or muc) were proven to have only one lymph node involved (Fig. 1). If patients were histologically proven to have distant lymph nodes (N2, N3, or N4) 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.

Results

Lymphatic Routes of the Stomach

The solitary metastatic nodes of C tumors were all located in the perigastric region (N1). Among them, 10 involved nodes around branches from the left gastric artery (LGA) (#1 or #3), 3 were around branches from the left inferior phrenic artery (LIPA) (#2), and 2 were around the short gastric arteries (SGA) (#4sa). In most of the patients, the metastatic node was near the original lesion. However, in 4 patients there was a relatively long distance between the primary tumor and the metastatic nodes, and no metastasis was seen in the nodes along the right gastric artery (RGA) (#5) or the right gastroepiploic artery (RGEA) (#4d or #6) in C tumors.

In 21 M cancers, the site of metastasis was the perigastric region (N1) in 18 and regional (N2 and N3) in 3. Among them, 10 nodes were along the LGA (#3 and #7), 7 along the RGEA (#4d or #6), and 4 along the RGA (#5, #8 or #12). There were 3 transverse and 3 jumping metastases in M tumors.

In 14 A tumors, 9 metastasized to the perigastric nodes (N1) and 4 to regional sites (N2). Four nodes were along the LGA (#1, #3, or #7), 5 along the RGEA (#6), and 4 along the RGA (#5 or #8). Jumping metastases involved nodes #1, #7, and #8 (Fig. 2).

Jumping Metastasis

Metastasis Along the Left Gastric Artery

There were three cases of jumping metastasis to nodes along the LGA. *Case 1.* Type 5 tumor located in the lower third, measuring 7.5 cm in size and "se" in depth. It invaded the pylorus and showed a metastasis near the trunk of the LGA (#7). *Case 2.* Type 0 (IIc) lesion located at the angle, measuring 5.5 cm in size and "se" in depth. It showed metastasis along the LGA (#7). *Case 3.* Type 3 cancer located at the minor curvature in the lower third, measuring 3 cm in size and "mp" in depth. A swollen lymph node just near the esophagogastric junction was detected during the operation and was diagnosed to be cancerous (Fig. 3).

Metastasis Around the Common and Proper Hepatic Arteries

There were four cases of jumping metastasis to nodes along the common and the proper hepatic artery (CHA and PHA). *Case 4.* Type 0 (IIa + IIc) lesion located at the lesser curvature between the upper and middle

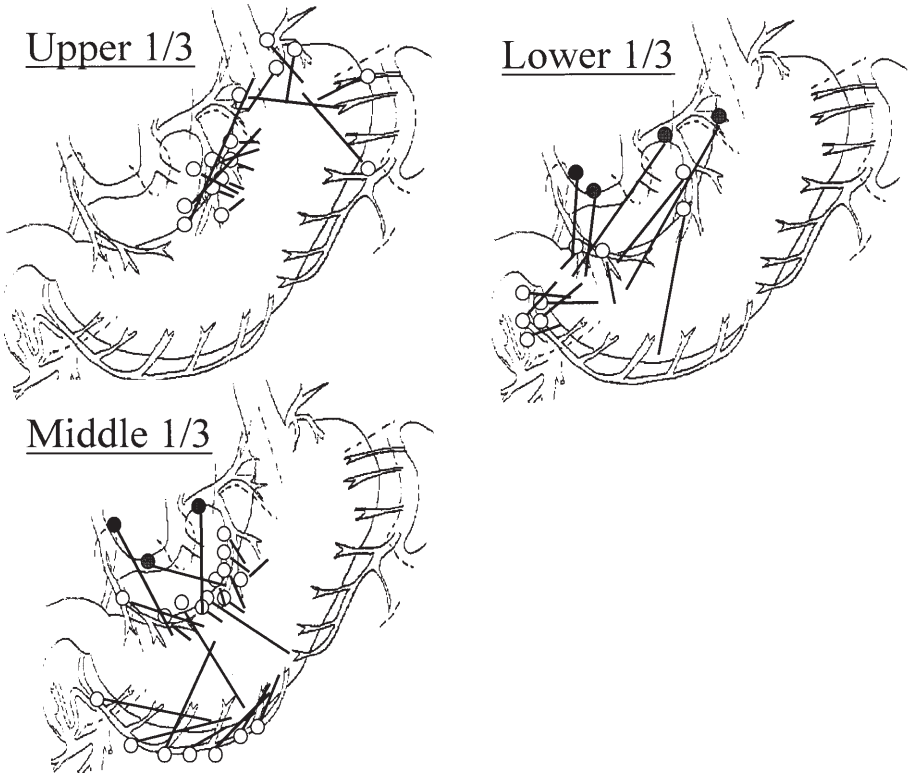

Fig. 2. Relation between the center of gastric cancer and lymph node metastasis. *Line* and *circle* show the center of a tumor and the site of the corresponding metastatic node. *Circle shading*: *white*, first group; *gray*, second group; *black*, third group

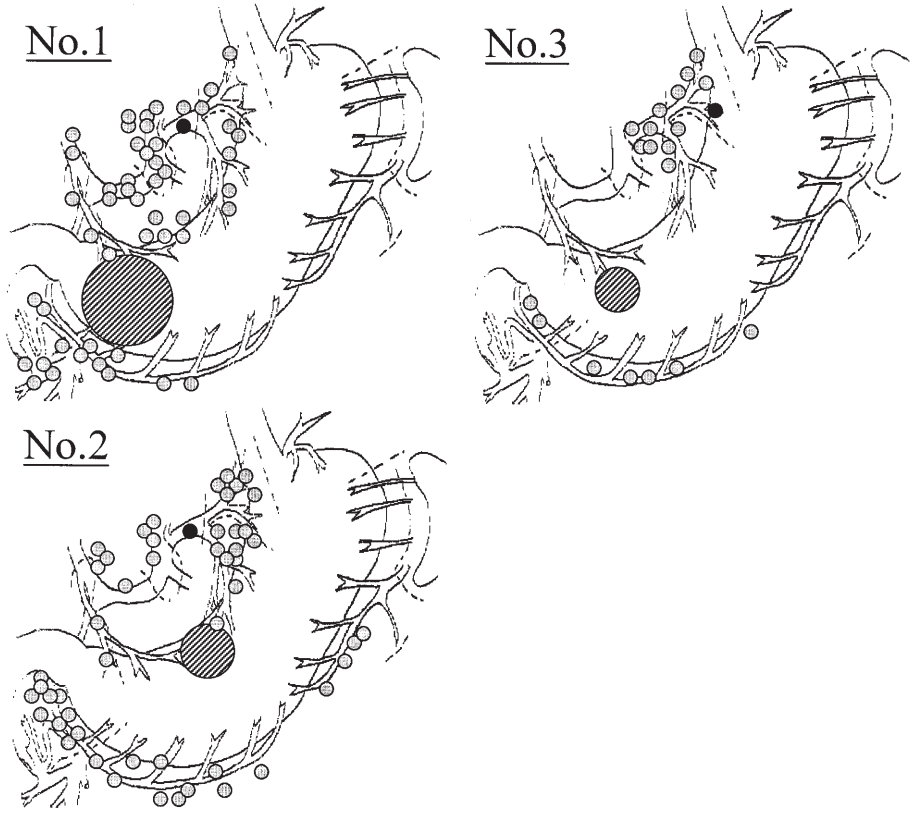

Fig. 3. Cases with jumping metastasis to the lymph nodes along the left gastric artery. *No. 1*, AD circ, type 5, 7.5 cm, se; *No. 2*, M min, type 0 (IIc), 5.5 cm, se; *No. 3*, A min, type 3, 3 cm, mp. *Circle shading*: *oblique*, primary cancer; *gray*, metastasis (−); *black*, metastasis (+). Abbreviations: see Table 1

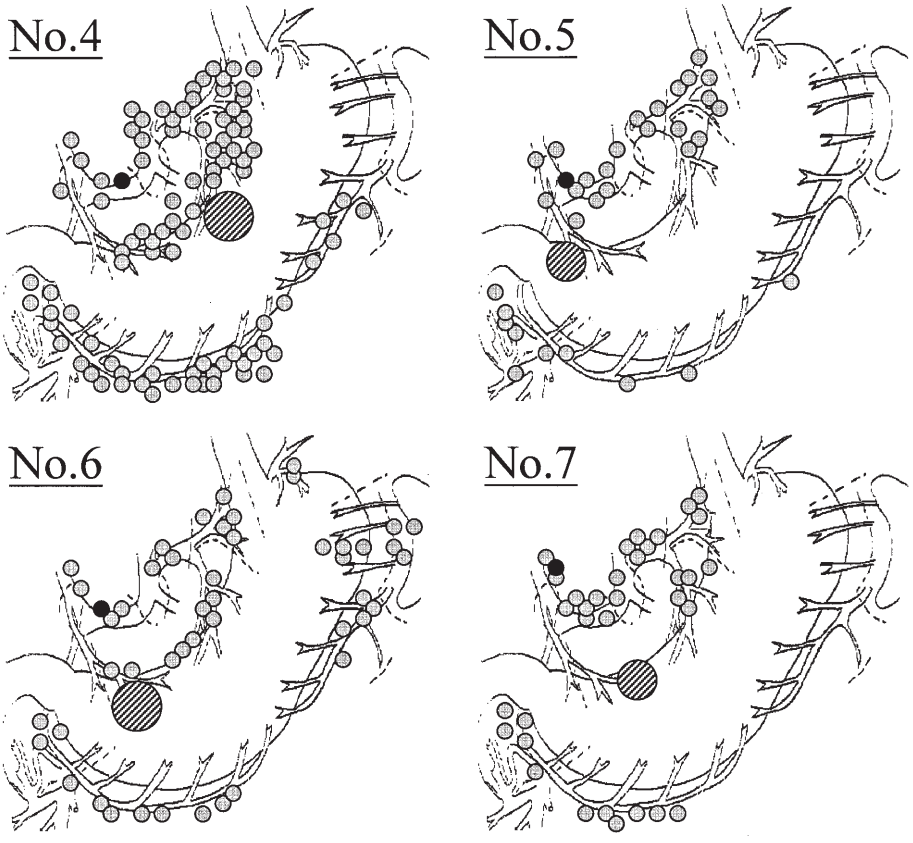

Fig. 4. Cases with jumping metastasis to the lymph nodes near the common and proper hepatic arteries. *No. 4*, MC min, type 0 (IIa + IIc), 4.5 cm, ss; *No. 5*, A circ, type 0 (IIc), 3.3 cm, mp; *No. 6*, A min, type 0 (IIc), 4.5 cm sm; *No. 7*, MA min ant, type 0 (I), 3.3 cm, sm. *Circle shading*: *oblique*, primary cancer; *gray*, metastasis (−); *black*, metastasis (+). Abbreviations: see Table 1

third, measuring 4.5 cm in size and "ss" in depth, showing metastasis along the CHA (#8). *Case 5.* Type 0 (IIc) lesion located in the antrum, measuring 3.3 cm in size and "mp" in depth; the metastasis was along the CHA (#8). *Case 6.* Type 0 (IIc) cancer located at the minor curvature in the lower third, measuring 4.5 cm in size and "sm" in depth; the metastatic node was along the CHA (#8). *Case 7.* Type 0 (I) cancer located at the angle, measuring 3.3 cm in size and "sm" in depth; the metastatic node was on the left side of the PHA (#12) (Fig. 4).

Survival of Patients with Jumping Metastasis

Three patients died — one of liver cirrhosis and two of pneumonia — without any signs of recurrence. The other four patients were alive at the time of this report for more than 5 years after surgery for stage IIIa–IIIb disease (Table 1).

Discussion

According to the Japanese Classification of Gastric Cancer, the groups of nodes in gastric cancer are classified according to the incidence of metastases subdivided by location of the tumor.[12] N1 is the group of nodes closest to the tumor, and N2–N3 are the more distant groups. Carcinoma is thought to spread to N1 nodes first, followed by involvement of distant nodes (N2–N3). In addition, the incidence of metastases to N1 is considered to be higher than that of metastases to N2–N3.

Fifty-one patients were confirmed to have a solitary lymph node metastasis in this study. There was no correlation between the degree of wall invasion and the incidence of solitary node involvement. Tumors in the upper third of the stomach were associated with a solitary metastasis in the perigastric region (N1); however, 3 of the 15 tumors in the middle third and 4 of the 14 tumors in the lower third were associated with a solitary metastasis at N2–N3 without any involvement of N1. The incidence of skip metastases was higher than expected. Two routes for the development of skip metastases have been considered: one is a route along the LGA and the other is a channel along the CHA or the PHA. Only one of them could be diagnosed during the operation based on the examination of frozen sections.

Mishima et al.[3] studied the relationship between the site of gastric cancer and lymph node metastases in patients with advanced cancer. In their cases, lymph

Table 1. Survival of patients with jumping metastasis

Case no.	Site of cancer	Depth of invasion	Histology	Node no.	Pattern of metastasis	Stage	Survival	Patient condition
1 AD	circ	se	ms	7[a]	Micro.	IIIb	8y 3m	alive
2 M	min	se	tub2	7	Micro.	IIIb	7y 5m	alive
3 A	min	mp	tub2	1	Massive	II	11m	d.o.[b]
4 MC	min	ss	tub2	8a	Micro.	IIIa	6y 1m	alive
5 A	circ	mp	por1	8a	Micro.	IIIa	5y 10m	d.o.[c]
6 A	min	sm	tub2	8a	Micro.	II	2y 3m	d.o.[d]
7 MA	min	sm	pap	12a	Micro.	IIIa	10y 9m	alive

A, lower third of stomach; M, middle third of the stomach; C, upper third of the stomach; D, duodenal invasion; circ, circular curvature; min, minor curvature; se, serosa exposed; mp, proper muscle; ss, subserosal; sm, submucosal; ms, miscellaneous type of carcinoma; tub2, moderately differentiated adenocarcinoma; porl, solid type of poorly differentiated adenocarcinoma; pap, papillary carcinoma; y, years; m, months; Micro., micrometastasis in the subcapsular sinus; Massive, replaced node by carcinoma cells 2.5 cm in size

[a] See text for explanation of node number

d.o., died of other disease: [b] liver cirrhosis, [c] pneumonia, [d] pneumonia

node involvement was noted not only in N1 but also in N2–N3. In the case of A tumors, lymph node involvement in N2–N3 was noted especially in #8 and #12, in 33% and 28% of the cases, respectively; regarding M cancers, it was seen in #7, #8, and #12 in 18%, 21%, and 15% of the cases, respectively, while as for C tumors it was seen in #7, #10, and #11, in 29%, 21%, and 21% of cases, respectively. Maruyama et al.[2] also reported a high rate of N2 lymph node metastases in patients with advanced gastric cancers. They reported the most commonly affected nodes to be the N2 nodes, #7 (23%) and #8 (25%) in case of A tumors, #7 (22%) in M tumors, and #7 (19%) in C tumors. These reports thus suggested #7, #8, and #12 to be the most important stations, as well as N1.

Iwashita et al.[13] reported lymph node metastases to be recognized in 1.3% (6/464) of the patients with intramucosal gastric cancer, while in 4 of those 6 patients the N2 nodes were involved (#7 in 3, #8 in 1 patient).They described one case of jumping metastasis to #7 without N1 involvement. Imada et al.[14] investigasted lymph node involvement in 583 patients with early gastric tumors in the M and A regions, and thus found 6 patients to have metastasis, while 3 of them had N2 (#7 in 1, #8 in 2) involvement. These results show that N2 lymph node involvement (#7 or #8) is observed in intramucosal cancers as well as in submucosal tumors.

The most common channels for metastases from the stomach, analyzed by subdividing the tumors according to their position, are thought to be as follows: the LGA channel (#1 or #3 to #7, the most common route) and the LIPA and the SGA channels (comparatively rare) in the case of C tumors; and both the LGA and the RGEA routes (equally frequent) in the case of M and A tumors. However, the RGA channel is relatively rare.[2–4] On the other hand, the most frequent location for nonperigastric node metastases in the absence of perigastric metastases were #7 (station along the LGA) and #8 (station along the CHA).

Natsugoe et al.[15] made three additional sections from the remaining half of the lymph nodes, to more precisely evaluate the incidence of lymph node metastasis in gastric cancer patients with submucosal invasion. They reported that they had initially demonstrated lymph node metastases in 19 nodes from 11 patients; however, a detailed reexamination showed cancer involvement in 9 more lymph nodes from 8 patients. This current study was constructed based on the pathologic examination of one section, and the possibility of occult metastases being missed in patients with jumping metastasis during routine examination of one section cannot be ruled out.

It remains unclear as to why jumping metastases occurred in these cases. The following reasons could all play some role: occult metastases may have been missed during the routine histopathologic examination; there may have been many lymphatic routes in the minor omentum; there may have been few perigastric nodes in those cases.

Conservative or limited gastrectomy or operation, such as a partial or transverse resection, has been reported, and some authors recommended operative examination of the perigastric nodes using frozen sections. Data from this study indicate that jumping metastases occur more frequently than previously thought and it also seems difficult to identify the sentinel nodes during the operation. Accordingly, a dissection of the regional lymph nodes should be performed at the time of surgery for patients in whom the results of a preoperative examination suggest submucosal invasion.

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