Consistency of DNA Ploidy between Primary and Recurrent Gastric Carcinomas

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ABSTRACT

Eleven patients with gastric carcinoma, who had undergone resection of the lesion due to recurrence in the remnant stomach, were the subjects of a cytophotometric DNA analytical study. The objective was to determine whether or not the DNA cytogenic profile of cancer cells would be consistent during the growth of the carcinoma. The DNA distribution patterns were grouped into types I, II, and III, according to the proportion of aneuploid cell population. Ten of 11 had the same DNA distribution patterns in the primary and recurrent lesions, while in the other one patient with type III in the primary lesion, type II was evident at the time of recurrence. The DNA cytogenic profile of cancer cells is thus a valid cell marker of a given tumor and should be applicable for determining the natural history of gastric carcinoma.

INTRODUCTION

The relationship between early and advanced carcinomas of the stomach has been of interest to pathologists and clinicians. There is a general agreement that early carcinoma with a rather broad proliferating form will mostly lead to the advanced carcinoma of non-Borrmann type. The non-Borrmann type advanced carcinoma means that macroscopically resembling an early stage of carcinoma, but histologically going beyond the submucosal layer (early simulating advanced carcinoma) (1, 2). On the other hand, in the case of an elevated lesion, the classical Borrmann type of advanced carcinoma will occur (3, 4) (Fig. 1). In previous studies (5), we postulated that the former carcinoma was of the superficially spreading (Super) type with a slow growth and that the latter was of the penetrating (Pen) type with a rapid growth. However, the detection rate of early carcinoma is dominant in the Super rather than in the Pen type (6), whereas that of advanced carcinoma is infrequent in the non-Borrmann type, as compared with the Borrmann type (2, 6). Such a paradox indicated that the relationship between early and advanced carcinomas had to be studied further.

The aneuploid cytogenic profile is an indicator of cells with a malignant biological behavior (7, 8). A foregoing study on cytophotometric DNA analysis of early gastric carcinoma revealed that the highly malignant type termed Pen A was closely associated with aneuploidy, and the other types were related to low ploidy (9). On the other hand, the classical Borrmann types of advanced carcinoma mostly presented an aneuploid DNA profile (9, 10). Provided that DNA ploidy remains unchanged during the growth of carcinoma, DNA analysis will be a useful guide for clarifying the relationship between early and advanced carcinomas.

The present study was done to determine the consistency of DNA ploidy during the growth of gastric carcinoma.

MATERIALS AND METHODS

Patients. The study was based on 11 cases of postoperative recurrence of carcinoma in the remnant stomach. The patients had been surgically treated in the Second Department of Surgery, Faculty of Medicine, Kyushu University, or the First Department of Surgery, Faculty of Medicine, Tottori University, during the 24 yr from 1959 to 1983. All patients underwent resection of the recurrent lesion. Postoperative intervals preceding the second operation were 7 mo to 17 yr and 4 mo with the average of 6 yr and 3 mo. All the specimens were verified histologically. The designation of various clinicopathological factors was based on the general rules proposed by the Japanese Research Society Committee on Histological Classification of Gastric Cancer (11). In the gastric stumps resected at the first operation, no residual carcinoma could be seen in 8, while cancer cells were detected in 3. Histological types were consistent in the primary and recurrent lesions in 8. Changes in histological types from well- to moderately differentiated adenocarcinoma were confirmed in 1 and that from moderately to poorly differentiated adenocarcinoma in 2 (Table 1).

DNA Measurements. For cell nuclear DNA measurements, 10-μm-thick paraffin sections were made from the portion just adjacent to the hematoxylin-eosin-stained section, and Feulgen staining was done by the method of Naora (12). Cell nuclear DNA content was measured using a microspectrophotometer (MMSP; Olympus Co., Japan) and the 2-wavelength method (13). The data were processed using a personal computer (HP-85; USA) combined with a microspectrophotometer. The mean DNA value of 25 stromal lymphocytes was used as the control of the normal diploid content (2C) in order to determine variation in the DNA content of the cancer cells. Based on the measurement of DNA content of 100 cancer cells in each lesion, the DNA distribution patterns were classified into 3, according to the frequency of aneuploid cells with over 4C and 6C (9), as illustrated in Fig. 2: type I, ≥90% of cells with <4C with scattering of cells confined to <6C; type II, >10% of cells with ≥4C and/or <10% of cells with ≥6C; and type III, ≥10% of cells with ≥6C. The DNA distribution patterns in the primary lesions were compared with those in the recurrent lesions in the remnant stomachs, in relation to the histological types and the depth of invasion.

RESULTS

The results of DNA distribution patterns in the primary and recurrent lesions are briefly summarized in Fig. 3. Among 11 cases, there were no occurrences of type 1. Three belonged to type II, and 8 to type III, in the primary lesions. These 3 patients classed as type II had the same DNA distribution pattern in the recurrent lesions in the remnant stomachs. Seven of 8 patients...
with type III in the primary lesions also had similar patterns on
the DNA histogram, while the other 1 with type III in the primary
lesion presented type II at the time of recurrence. In 3 with
change in histological evidence between the primary and recur-
rent lesions, the DNA distribution patterns were similar in both
lesions.

An example of DNA histograms in a patient with a primary
gastric carcinoma and recurrent lesion in the remnant stomach
resected 10 mo after the initial operation is shown in Fig. 4. The
primary and recurrent lesions are in close agreement with regard
to DNA distribution patterns, being classed as type II. Fig. 5
shows an example of a patient with widely scattered DNA values
on the DNA histogram (type III) in the primary and recurrent
lesions, respectively. The interval preceding the second opera-
tion is 6 yr and 3 mo, but there was a resemblance in the DNA
distribution patterns between both lesions.

The consistency of DNA distribution patterns was evident in
10 of the 11 patients, independent of changes in histological
types.

DISCUSSION

To assess the consistency of the DNA cytogenic profile of
cancer cells during the growth of gastric carcinoma, it is advisable
to study malignant tissues of recurrent lesions in the remnant
stomachs. In the current series, we treated 11 such patients, all
of whom had to undergo reresection. The DNA cytogenic profiles
showed surprising similarities between primary and recurrent
lesions, except for one in whom the DNA distribution patterns
were type III and type II in the primary and recurrent lesions,
respectively.

Frankfurt et al. (14) reported the stability of DNA ploidy by
means of comparative study in the primary and metastatic solid
tumors. Similar findings were observed by Auer et al. (15) in
cases of breast carcinoma and by Bäckdahl et al. (16) in those
with thyroid carcinoma. On the contrary, Böhmann and Sandritter
(7) found at autopsy a case in which the DNA ploidy in the
primary carcinoma of the stomach was transformed into the
more widely scattered one in the metastatic lesion of the liver,
but the change in DNA ploidy was due to the selection of one of
2 clearly different modal cell populations in the primary lesion. In

Table 1

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<th>Patients</th>
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<td>Sex (case)</td>
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<tr>
<td>Age (yr)†</td>
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<tr>
<td>Intervals‡</td>
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<td>Changes in histological types (case)§</td>
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<td>Cancer cells in the resected stump (case)∥</td>
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† At the first operation.
‡ Postoperative intervals preceding the second operation.
§ Between primary and recurrent lesions.
and recurrent gastric carcinomas, respectively. The DNA values are expressed as arbitrary units (A.U.).

In our cases, there was a modal cell population preponderance, and another difference population was absent in the primary lesions. Considering these observations, DNA ploidy may be stable between the primary and recurrent lesions when the tumor is composed of a modal cell population. The minute discrepancy in DNA ploidy observed in this series can probably be ascribed to differences in cell population between the primary and recurrent lesions, since the primary carcinoma was confined to the mucosa and was resected curatively (without a residual carcinoma) for 10 yr and 7 mo after the initial operation. This was considered to be a new carcinoma occurring in the remnant stomach, rather than a recurrence. In the light of these findings, the DNA ploidy seemed to be a fairly stable tumor cell marker inherent to a given type of carcinoma.

Our previous study showed that, among cases of early gastric carcinoma, there is a superficially spreading (Super) type with slow growth and a penetrating (Pen) type with rapid growth (5,6), the former of which was featured by low ploidy, whereas the latter, especially the highly malignant Pen A subtype, was characterized by high ploidy (8). On the other hand, most of the box and mountain types of advanced carcinoma which are of the classical Borrmann types revealed high ploidy, whereas the funnel type of advanced carcinoma which can be equated to the non-Borrmann type commonly presented low ploidy (17). From the viewpoint of consistency of DNA ploidy inherent to the characteristics of cancer cells, these findings suggest that the Pen type of early gastric carcinoma will lead to the Borrmann types of advanced carcinoma and the Super type to the non-Borrmann type.

There is a discordance in the detection rate between Pen and Borrmann types, and between Super and non-Borrmann types. It seems reasonable to consider that the rapid-growing carcinoma (Pen type) is less likely to be detected until it has reached the advanced stage, since it remains at the early stage for a short period, while the slow-growing carcinoma (Super type) is more likely to be detected at the early stage of development because it remains at the early stage for a longer period. From this aspect, the current study on DNA cytogenic profile should aid in elucidating the relationship between early and advanced carcinomas. The natural history of gastric carcinoma, in terms of the growth pattern, was thus to some extent elucidated.

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