Short Report

Nuclear DNA Pattern of the Gallbladder Cancer

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KOYAMA, K., GOTO, H., OUCHI, K. and SATO, T. Nuclear DNA Pattern of the Gallbladder Cancer. Tohoku J. exp. Med., 1984, 143(1), 125-126 —— Nuclear DNA of the gallbladder cancer was stained by the Feulgen method and analyzed using a new concept of DNA score. DNA score was determined by the peak ploidy unit and decided numbers of frequency in each ploidy unit. As the result, a significant correlation between DNA score and the depth of cancer invasion was demonstrated. The depth of cancer invasion, as reported already, has close correlation to the prognosis of the patients of gallbladder cancer. These results indicate that the nuclear DNA analysis is useful for the determination of malignancy and the prediction of the prognosis of the patients.

gallbladder cancer; nuclear DNA; depth of cancer invasion; Feulgen staining

The authors have already reported that, in carcinoma of the gallbladder, the prognosis of the patients with slight depth of cancer invasion was comparatively good (Sato et al. 1981). A correlation between the depth of cancer invasion and nuclear DNA pattern of cancer cells, one of the indicators of malignancy, was investigated in cancer of the gallbladder.

Materials and methods. Twenty-six patients with gallbladder cancer resected curatively in our department from 1960 to 1983 were investigated. The depth of cancer invasion of these patients were mucosa (m) in 5 cases, proper muscle (pm) in 4, subserosa (ss) in 4 and serosa (s) in 13.

Surgical specimens of the gallbladder cancer, fixed in 10% formalin and embedded in paraffin in usual procedures, were sectioned at 6 pm and stained by the Feulgen method to demonstrate DNA (Leuchtenberger 1958). Nuclear DNA content of 100 cancer cells at the periphery of the cancer nests, verified in hematoxylin and eosin-stained sections, was measured using an OLYMPUS microspectrophotometer.

Frequency histograms were plotted from the values obtained and were expressed in ploidy unit, in which the mean value of DNA content of 20 lymphocytes in the same section was taken as the diploid value (2C, C = DNA content of a haploid chromosome set).

Results and comments. In histogram, the peak of frequency was observed in the ploidy unit of 2.0 to 2.5C in 2 cases, 2.5 to 3.0C in 21 cases and 3 to 3.5C in 3 cases.

Fig. 1 shows the histogram of average frequency of nuclear DNA of the patients with the respective depth of cancer invasion. DNA patterns can be classified according to the ploidy unit showing the peak of frequency in histogram as well as to the percent value of frequency in each ploidy unit. Since nuclei having a large ploidy unit contain a large amount of chromosome, which suggests high malignancy, the frequency value in large ploidy
To evaluate the DNA pattern of gallbladder cancer, concept of DNA scores was induced. For the ploidy unit, score of 10 was applied when the peak positioned in ploidy unit 2.0 to 2.5C, 20 when that did in 2.5 to 3.0C, 30 when that did in 3.0 to 3.5C and so on. For scoring the frequency value in each ploidy unit, following calculation was performed. When the frequency in ploidy unit \( (n \text{ to } (n+0.5)) \) was expressed as \( F_{n-(n+0.5)} \), values of \( F_{3-3.5}, F_{3.5-4.0}, F_{4.0-4.5} \) and so on were multiplied by 1, 2, 3 and so on. DNA scores were determined by summing the scores of the ploidy unit with peak of frequency and above mentioned scores of frequency in each ploidy unit.

A correlation between DNA scores estimated and the depth of cancer invasion was demonstrated in Fig. 2. DNA scores in m group were significantly lower as compared with those in ss and s groups.

DNA analysis of various cancers such as larynx, stomach, intestine and uterus has already been studied (Avtandilov 1976; Giménez and Conti 1977) and discussed from the view point of early diagnosis and determination of malignancy, but its application to the cancer of the biliary tract has been found scarcely. In addition, in the above mentioned papers, the DNA pattern has been analyzed using mean value of DNA and/or width of range of histogram. In this paper, however, for evaluation of malignancy, DNA score was adopted, which showed a close correlation to the depth of cancer invasion.

Acknowledgments

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References