Morphometrical analysis of gall-bladder adenoma and adenocarcinoma with reference to histogenesis and adenoma-carcinoma sequence

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Summary. In order to examine whether our subdivision of gall-bladder adenoma and adenocarcinoma into non-metaplastic and metaplastic types is reasonable from the viewpoint of their cytological features, a morphometrical analysis was conducted on 17 adenomas and 59 adenocarcinomas. The morphometrical parameters used were nucleo-cytoplasmic ratio (N/C ratio) and nuclear areas (NA). N/C ratio in the metaplastic type of both adenoma and adenocarcinoma was significantly larger than that in the non-metaplastic. This result shows that the different tumour types are associated with a different N/C ratio. Continuous measurement of N/C ratio and NA in progressing from non-cancerous mucosa to the lesion was made and the data obtained were analysed by the Lowess method. In some adenomas the total area of polypoid lesions was serially measured and these data were also analysed by the Lowess method. The results showed different processes in non-metaplastic and metaplastic types of adenoma and adenocarcinoma from the standpoint of nuclear changes of N/C ratio and NA. These results indicate that our histogenetic classification of adenocarcinoma is reasonable in morphometrical nuclear analysis. We also investigated the adenoma-carcinoma sequence as a possible histogenesis for gall-bladder carcinoma.

Key words: Morphometry – Gall-bladder – Adenoma – Adenocarcinoma – Histogenesis – Adenoma-carcinoma sequence

Introduction

Our recent study has shown that there are two histogenetically different types of adenomas and adenocarcinomas of the gall-bladder, one being a non-metaplastic type derived from ordinary epithelium of the gall-bladder and the other being derived from metaplastic epithelium. This classification is based on the presence or absence of metaplastic changes in tumour tissue (Yamamoto et al. 1986, 1988, 1989a) and on the presence or absence of endocrine cells and/or lysozyme immunoreactivity. We have already examined the incidence of endocrine cells and lysozyme immunoreactivity and that of goblet cells, Paneth cells and pseudo-pyloric glands in the gall-bladder of the fetus, normal adult and patients with cholecystitis, and have found that these two markers are the most useful indicators of gastrointestinal metaplasia of the gall-bladder mucosa (Yamamoto et al. 1986). The metaplastic type was considered to be present in cases which contained at least one marker of endocrine cells or lysozyme immunoreactivity and that of goblet cells, Paneth cells and pseudo-pyloric glands in the gall-bladder of the fetus, normal adult and patients with cholecystitis, and have found that these two markers are the most useful indicators of gastrointestinal metaplasia of the gall-bladder mucosa (Yamamoto et al. 1986). The metaplastic type was considered to be present in cases which contained at least one marker of endocrine cells or lysozyme immunoreactivity and that of non-metaplastic type in cases which showed no markers. We have also shown that metaplastic carcinoma has a better prognosis than non-metaplastic carcinoma (Yamamoto et al. 1989b). Recently, we have made a morphometrical analysis of various gall-bladder lesions by using two parameters of nucleo-cytoplasmic ratio (N/C ratio) and nuclear areas (NA) and obtained a discriminant function.
Fig. 1a-f. Photomicrographs of two types of gall-bladder adenoma.

a Metaplastic adenoma without atypical glands. Glandular proliferation of mucous cells with oval to round nuclei. H & E, x 188.
b Metaplastic adenoma. Mucous glands contain argyrophil cells (arrows). Grimelius stain, x 375.
c Metaplastic adenoma. Mucous glands show lysozyme immunoreactivity. PAP method, x 375.
d Atypical lesion with structural and cellular atypia observed within a metaplastic adenoma, which is discriminated as carcinoma. H & E, x 188.
e Non-metaplastic adenoma without atypical glands. The glands consist of a layer of columnar cells with oval to round nuclei resembling normal gall-bladder epithelium. H & E, x 188.
f Atypical lesion observed within an non-metaplastic adenoma, which is discriminated as carcinoma. H & E, x 188.