We report a case of papillary adenocarcinoma of the sigmoid colon with psammoma bodies and intracytoplasmic hyaline globules. The patient was a 59-year-old woman. The tumor showed central ulceration with smooth elevated ridges. Histologically, the tumor was composed of numerous large irregular tubular structures accompanying infolded papillary growth. The tumor cells showed cytoplasmic basophilia and prominent nuclear atypia. Psammomatous-type calcification was scattered in the tumor stroma as well as in the glandular lumina. In addition, intracytoplasmic hyaline globules of various sizes were seen in the neoplastic cells. We propose the name papillary adenocarcinoma associated with psammoma bodies and hyaline globules for this tumor. Accumulation of further cases is needed to clarify the clinical significance of this type of tumor.

Key words: papillary adenocarcinoma – colon – hyaline globules – psammoma bodies

INTRODUCTION

Psammoma bodies are round calcific concretions exhibiting concentric lamination that occur in about 50% of papillary carcinomas of the thyroid gland (1). Other than in thyroid papillary carcinoma, psammoma bodies are frequently observed in serous papillary adenocarcinomas of the ovary (2), adenocarcinomas of the endometrium (3) and meningiomas (4). Adenocarcinomas of the lung infrequently contain psammoma bodies (5).

On the other hand, intracytoplasmic hyaline globules (HGs), spherical intracytoplasmic eosinophilic droplets, have been associated with a variety of malignancies, including hepatocellular carcinoma (6,7), undifferentiated liver sarcoma (8), pulmonary adenocarcinoma (7,9), yolk sac tumor (10), breast carcinoma (7), cartilaginous neoplasm (11) and Kaposi’s sarcoma (12).

The present report describes one case of papillary adenocarcinoma of the sigmoid colon associated with psammoma bodies and HGs, and discusses these characteristic features.

CASE REPORT

A 59-year-old woman was admitted to Yoshijima Hospital, Hiroshima, for treatment of a sigmoid colon tumor, on July 10, 1995. Her family practitioner had found occult blood in her feces. A barium enema of the colorectum revealed a tumor in the sigmoid colon. Endoscopic examination of the colorectum demonstrated a sigmoid colon tumor showing ulceration with elevated ridges. The tumor was categorized as a type 2 or well circumscribed fungated tumor with central ulceration (Fig. 1). The cut surface had a well defined margin and showed subserosal invasion.

We fixed and processed the tumor with formalin and paraffin-embedded sections for histological examination. Hematoxylin and eosin (HE) staining was performed on all paraffin-embedded sections. The sigmoid colon cancer was composed of numerous large irregular tubular structures showing infolded papillary growth, mostly without a fibrovascular core (Fig. 2a). The tumor cells possessed large, pleomorphic, hyperchromatic or pale-stained nuclei, small nucleoli...
Colonic papillary adenocarcinoma

Figure 1. Macroscopic appearance of the present tumor, measuring $3 \times 2.5 \times 0.5$ cm. It is a well circumscribed fungated tumor with central ulceration.

and basophilic cytoplasm (Fig. 2b). Not only ordinary calcium deposits at the growing edge, but also psammoma bodies were scattered adjacent to viable neoplastic cells (Fig. 3a) as well as in the glandular lumen (Fig. 3b). Intracytoplasmic hyaline globules (HGs) of various sizes (3–30 µm in diameter) were seen in the tumor cells at the tip of the papillary structure and in the superficial area of the tumor (Fig. 4). The HGs were stained by the periodic acid-Schiff method, which was resistant to diastase digestion, and with phosphotungstic acid-hematoxylin but were not stained by mucicarmine or alcian blue. To elucidate the nature of the HGs in the present tumor, we used four kinds of rabbit polyclonal antibodies against alpha-1-antitrypsin, alpha-1-antichymotrypsin, lysozyme and human chorionic gonadotropin and one mouse monoclonal antibody against AFP. The first four were from DAKO Japan, Kyoto, and the last was from Nichirei, Tokyo, Japan. The HGs were not reactive with any of these antibodies.

DISCUSSION

Among various gastrointestinal tumors, psammoma bodies are found almost exclusively in the glandular lumina of duodenal carcinoid tumors associated with somatostatin production and prominent areas of glandular differentiation, possibly leading to an incorrect diagnosis of well differentiated adenocarcinoma (13) and in the glandular lumina and stroma of gastric adenocarcinoma (14,15). In colorectal cancers, calcifications of the psammomatous

Figure 2. General features of neoplastic cells in the present tumor. (a) Low-power view of the tumor showing infolded papillary growth in the large irregularly arranged glands with or without an associated thin fibrovascular core. (b) High-power view of the tumor. The neoplastic cells have basophilic cytoplasm, large, pleomorphic, hyperchromatic and pale-stained nuclei, and small nucleoli.
type are rarely seen, except in clear cell adenocarcinoma with some resemblance to carcinoma of the kidney (16). On the other hand, psammoma bodies are found commonly in certain human neoplasms, most often in those of thyroid, ovarian or meningeal origin (1,2,4). The mechanism of psammoma body formation is controversial, but one hypothesis is that the nidus for genesis is a single necrotic tumor cell upon which successive layers of calcium salt are deposited in the thyroid gland (17). As in ovarian serous adenocarcinomas, it is suggested that psammoma bodies arise as products of neoplastic and histiocytic cellular degeneration (18). The above findings suggest that the psammoma bodies in the present tumor originated from single necrotic tumor cells, upon which successive layers of calcium salts were deposited, and which then either exfoliated into the glandular lumina, or became trapped in the fibrous stroma adjacent to the neoplastic glands (15).

Recently, osteopontin protein produced by macrophages has been reported as playing a significant role in the development of calcifying foci of both the psammomatous and non-psammomatous types in human neoplasms (19,20). In the present tumor, the neoplastic glands contained macrophages of considerable variability in their lumina, and there were many non-psammomatous-type calcium deposits surrounded by macrophages at the growing edge. Osteopontin protein may have played an important role in calcium deposition in the present case.

On the other hand, HGs have been associated with various human neoplasms (6–12,21). HGs represent secretory glycoprotein that has accumulated in the cytoplasm of tumor cells (9). In hepatocellular carcinomas and hepatoid carcinomas of the lung, AFP can be seen as HGs (21). In pulmonary adenocarcinomas, IgG, IgA, and alpha-1-antichymotrypsin are weakly positive in HGs, and represent accumulated secretory glycoprotein in the tumor cell cytoplasm (9). In the present tumor, HGs were stained by the periodic acid-Schiff method, which was resistant to diastase digestion, and with phosphotungstic acid-hematoxylin, but were negative for alpha-1-antitrypsin, alpha-1-antichymotrypsin and lysozyme. Unlike pulmonary adenocarcinomas, the HGs in the present colonic papillary carcinoma may have been enlarged autophagosomes in the neoplastic cells. To elucidate the nature of the HGs in the present tumor more precisely, further studies including electron microscopy will be necessary.

Both psammoma bodies and HGs may represent degenerative change of neoplastic cells. However, whether or not the simultaneous presence of both psammoma bodies and HGs influences the prognosis of colon cancer is still unknown, since few cases have been documented. In serous adenocarcinoma of the ovary, a significantly higher survival rate has been found in cases with psammoma bodies than in those without (2). On the other hand, the presence and number of psammoma bodies are not

Figure 3. Psammoma bodies in the present tumor. (a) Numerous laminated psammoma bodies in the tumor tissue. (b) High-power view of psammoma bodies adjacent to viable neoplastic cells and in the tumor stroma, as well as in the glandular lumina.
Colonic papillary adenocarcinoma

Figure 4. Hyaline globules (HGs) in the present tumor. The neoplastic cells contain HGs of various sizes (3–30 mm in diameter) in their cytoplasm.

Statistically significant prognostic indicators in papillary carcinoma of the thyroid (1). To our knowledge, no reports in the English literature have discussed the relationship between the presence of HGs in human malignancies and patient prognosis. Further accumulation of cases is needed to clarify the incidence and clinical significance of this type of tumor.

Acknowledgements

We wish to thank Prof. Paul D. Andrew, Division of Physical Therapy, Institute of Health Sciences, Hiroshima University School of Medicine, for reading through the manuscript, Mr Chitoshi Hidaka, Clinical Laboratory Department, Yoshijima Hospital, and Ms Eriko Miyazaki and Mr Tadatoshi Tokaji, First Department of Pathology, Kochi Medical School, for their excellent technical assistance.

References