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Double Cancer of the Gallbladder-a Case Report

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The study presented the coexistence of papillary adenocarcinoma and microcellular neuroendocrine carcinoma of the gallbladder in a 56-year old female patient without cholelithiasis and developmental anomalies of the biliary-pancreatic ducts. Considering the material obtained by the authors (94 cases), the above–mentioned was diagnosed in 1,06% of gallbladder carcinomas. The authors analyzed literature data and considered pathogenetic factors, responsible for development of two gallbladder carcinomas.

Introduction

Adenocarcinomas constitute 60 to 90% of primary gallbladder carcinomas [1, 5, 6]. Primary, highly malignant neuroendocrine microcellular carcinoma is rarely diagnosed. Moskal and co-authors [6] demonstrated 41 such cases obtained from literature data, as of 1999. In 26.83% of cases the above-mentioned was connected with the presence of adenocarcinomas. Considering 12 cases of microcellular gallbladder carcinoma, Maitra and co-authors [5] demonstrated the presence of adenocarcinoma and squamous cell cancer in 50% of patients. The study presented a rare case of a patient diagnosed with microcellular gallbladder cancer and papillary adenocarcinoma.

A Case Description

B. I. 56-year old female patient complained of jaundice symptoms, which were present for the past three weeks. After excluding the inflammatory character of jaundice the patient was admitted to the Department of Surgery. Laboratory parameters were as follows: blood type- "0" Rh (-), prothrombin level – 101%, total bilirubin – 6.22mg%. Abdominal ultrasonography demonstrated a tumor of the head of the pancreas. Intraoperative cholangiograhy showed absence of contrast outflow to the duodenum. The gallbladder was small, solid, infiltrating the liver. The common bile duct was easily prepared. The patient was subjected to cholecystectomy followed by choledocho-enterostomy. Pancreatic tumor samples were not collected. After ten days the patient was discharged from the hospital in medium-severe condition. On pathological examinasion the gallbladder was solid, grey-whitish in color with thickened walls (Fig.1). The histopathological examination (B.17833–35/99) was as follows: adenocarcinoma papillare G2pT1b (Fig. 2) and carcinoma neuroendocrinale microcellulare (Fig. 3, 4). The latter was composed of small

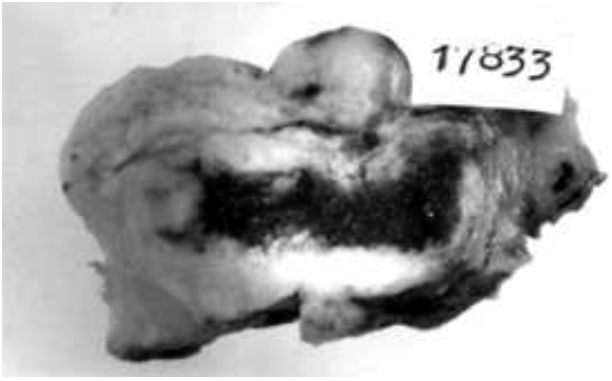

Fig. 1. Longitudinal section through the carcinomatous gallbladder (gross appearance).

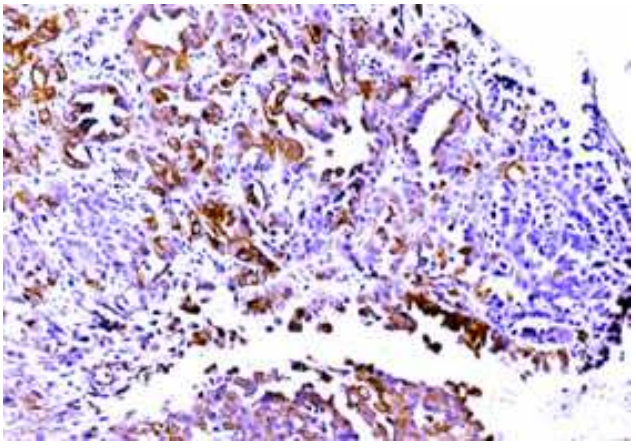

Fig. 2. EMA – positive reaction in the papillary carcinoma.

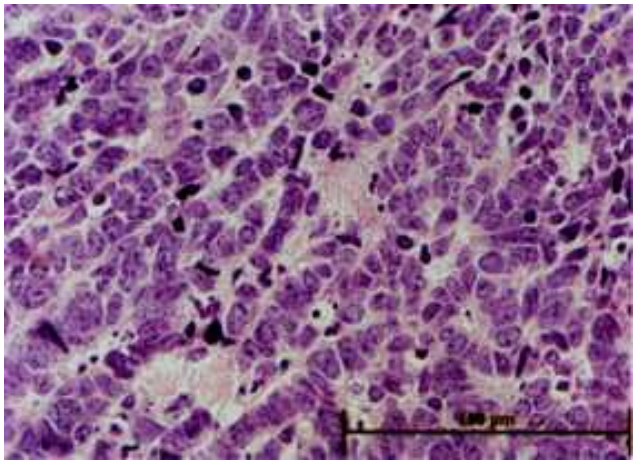

Fig. 3. Neuroendocrine carcinoma (HE).

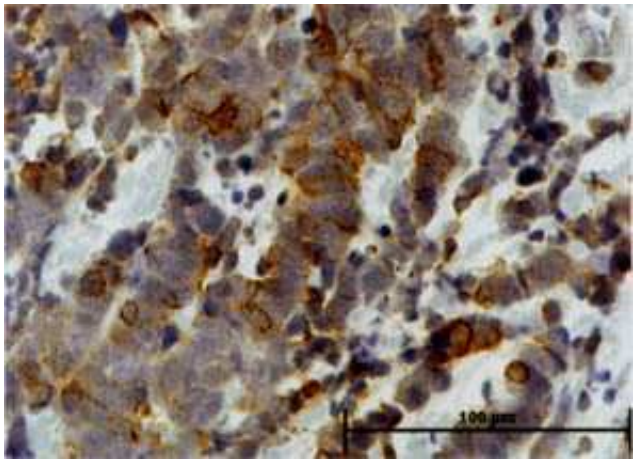

Fig.4. Chromogranin A positive reaction in the neuroendocrine part of the tumor.

polygonal, and in selected cases fusiform cells, with scant cytoplasm, homogenously staining nucleus, and invisible nucleolus. The cells were localized in solid, and in relative cases, trabecular foci. One observed in selected cases pseudo-rosettes. The adenocarcinoma proliferated exophytically into the gallbladder lumen, as well as infiltrated the muscular layer of its wall. On the other hand, the neuroendocrine microcellular carcinoma infiltrated the subserous connective tissue (which was fibro-inflammatorically changed), the serous membrane and liver parenchyma. Glandular cancer ducts as well as vascular cross-sections with adenocarinoma emboli were observed on the border of the muscular and subserous tissues. In selected cases the vascular cross-sections were filled with both types of cancer cells. Hematoxylin and eosine, PAS, mucycarmin and alcian blue staining demonstrated poor adenocarcinoma mucogenous ability. Immunohistochemical examinations revealed a positive reaction towards the epithelial-membranous antigen (EMA) in case of adenocarcinoma, and chromogranin A in case of the neuroendocrine microcellular carcinoma. NSE and neurofilament reactions proved negative. Ki-67 reaction was positive in 2% of the papillary carcinoma part and in 30% of the neuroendocrine one (Prof. hab. M. Jeleń).

Discussion

Small-cell carcinoma of the gallbladder concerned female patients in 76% of cases [6], with the average age ranging between 65–69 years [5, 6]. During clinical diagnosis the neoplasm infiltrated the liver in 75% of cases [1]. The presented case is typical of the above-mentioned. Considering our material of 94 gallbladder carcinomas, the above-mentioned was diagnosed in one patient, which amounted to 1.06%. Additionally, the neoplasm coexisted with a primary adenocarcinoma. Moskal and co-authors [6] demonstrated microcellular gallbladder carcinoma presence in 3.5% of cases. Half of the above-mentioned were additionally diagnosed with adenocarcinoma or squamous cell carcinoma [5]. Albores-Saavedra and co-authors [1] revealed diffuse squamous cell foci in 6% of microcellular gallbladder carcinomas, and in 30% of cases differentiated glandular cancer ducts. Regardless the above-mentioned the cited authors considered these lesions as a product of small- cell carcinoma, and not another primary adenocarcinoma. The presented case demonstrated two separate neoplasms, with the adenocarcinoma infiltrating the mucous membrane, and the neuroendocrine lesion, the subserous connective tissue and serosa. Unfortunately, we do not possess histological samples collected from the pancreas tumor, but in our opinion, neither of the two tumors were metastases from the pancreas one. A similar case of gallbladder small-cell carcinoma combined with small-cell carcinoma of the rectum was reported by Duan and co-authors [2], the latter being considered as metastasis from the gallbladder tumor.

In case of gallbladder carcinoid, Dirschmid [3] observed dysplastic lesions and carcinoma “in situ”, inside the glandular epithelium of the covering mucosa. The author considered this phenomenon, as a consequence of the paracrine activity of the carcinoid. Some investigations [5, 8] revealed the direct transformation of small-cell cancer into adenocarcinoma, while others observed no such change. Since the normal gallbladder mucous membrane is free of neuroendocrine cells [6] the following hypothesis was proposed: the microcellular carcinoma might be derived from the primitive pre-neuroendocrine cell capable of multi-directional differentiation [2, 6, 8]. In the presented case chromogranin A staining proved positive. One must not forget that immunohistochemical staining towards neuroendocrinity [1, 5] prove positive only in different percentage, and thus diagnosis of the above-mentioned neoplasm should be based on traditional staining methods. In some cases final diagnosis might be obtained following ultrastructural exam-

inations [2]. Maitra and co-authors [5] showed 12 cases of microcellular carcinomas without clinical neuroendocrine disturbances, similarly to the presented study patient. Cholelithiasis was absent in the presented case, similarly to data obtained by other authors [2]. Thus, when evaluating gallbladder carcinoma pathology one should consider possible biliary-pancreatic ducts developmental disturbances, in addition to retrograde pancreatic juice outflow and the damaging effect of tripsin, elastase 1 and phospholipase A2. Publications concerning the occurrence of cholangiocarcinoma and biliary ducts neoplasms, considering such developmental disturbances have been well documented [4, 7]. The presented case was clinically advanced, and intraoperative cholangiogaphy demonstrated no anomalous junction of pancreaticobiliary ductal system.

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