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Synchronous Occurrence of Carcinoma with Choriocarcinomatous Differentiation and Separated Adenocarcinoma in the Stomach: A Case Report

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Abstract

Seventy eight-years-old female Japanese having simultaneous occurrence of a carcinoma in the lower gastric body and another carcinoma in the posterior wall of the pylorus received a distal gastrectomy in our hospital. Histology of the tumor in the lower gastric body was adenocarcinoma with papillary or tubular structures in the mucosal area. However, in the submucosal area, majority of tumor cells was changed to clear cells resembling cytotrophoblasts as seen in trophoblastic neoplasms. Furthermore, solitary growth of the spindle cells resembling Syncytiotrophoblast cells was apparent in the layers of muscularis propria and subserosa. Immunohistochemically, syncytiotrophoblast type cells were positive for beta-subunit of Human Chorionic Gonadotropin (HCG). Three out of 28 regional lymph nodes had metastases of the neoplasm with adenocarcinoma as well as choriocarcinomatous components. The tumor on the posterior wall of pylorus was a tubular adenocarcinoma only recognized in the mucosal layer. The tumor did not contain any trophoblastic components.

Choriocarcinomatous differentiation of the gastric carcinoma was suggested to occur during the down growth of the neoplasm. Present gastric choriocarcinoma supports the concept that gastric choriocarcinoma arises from alternate differentiation pathway of adenocarcinoma. Such synchronous occurrence of double carcinomas in the stomach may also suggest a higher oncogenesis stage of the stomach of this woman.

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Introduction

Stomach may be a common site of origin of non-gonadal, non-gestational trophoblastic tumors, although gastric cancers with germ cell tumor components are uncommon. Choriocarcinoma, hepatoid adenocarcinoma, carcinoma with enteroblastic differentiation, and York sac tumor like carcinoma are known as special type of gastric cancer. Choriocarcinoma is a trophoblastic tumor as a rare primary miscellaneous tumor in the stomach. It is known that some of gastric cancers have choriocarcinomatous components [1-3]. Regarding the pathogenesis of gastric choriocarcinoma, retro-differentiation or dedifferentiation theory has been accepted upon the observation that gastric choriocarcinoma are found with coexistent adenocarcinomas or adenocarcinoma components [4,5]. In a few tumors, the primary gastric lesion was pure adenocarcinoma and the choriocarcinomatous differentiation only became manifest in the metastasis [6]. Certainly, it is plausible that since all cells contain the entire genetic material for the whole organism, cancers may differentiate in unusual directions, including even the formation of malignant trophoblasts. However, precise mechanisms for the trophoblastic differentiation of gastric cancers are still unknown. Presently, we report a unique case with a carcinoma exerting choriocarcinomatous differentiation and another separated adenocarcinoma in the stomach. Significance of such synchronous gastric carcinomas particularly for the point of association between tumor growth and differentiation is discussed.

Case Presentation

A 78-year-old woman was admitted to our hospital for evaluation of epigastralgia. Esophagogastroduodenoscopy revealed existence of a type 3 tumor on the greater curvature of lower gastric body and a type 0-IIa+IIc lesion on the posterior wall in pylorus. By biopsy, both lesions were diagnosed as adenocarcinomas, suggesting that the stomach had double cancers with different stages. The distal gastrectomy with D2 lymph node dissection [7,8] was performed. The

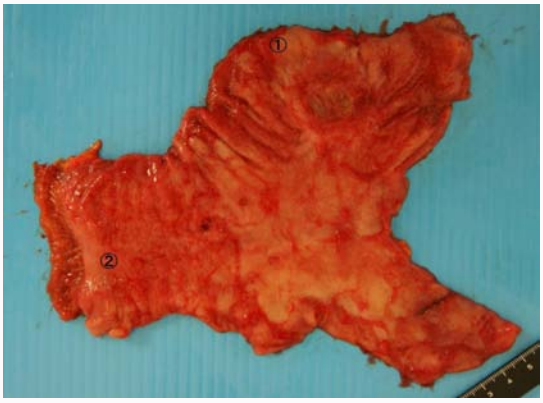

Figure 1: Resection specimen of the stomach. The type 3 tumor mass on the greater curvature of lower gastric body (1) was measured 40 mm × 40 mm. The type 0-IIa+IIc neoplastic mass on the posterior wall in pylorus (2) was measured 18 mm × 18 mm.

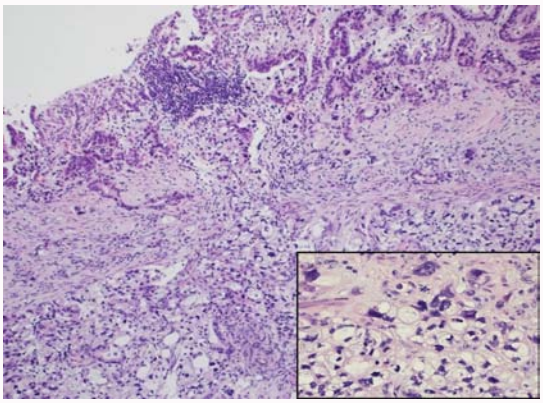

Figure 2: A low-power view of the tumor on the greater curvature of lower gastric body.
Papillary or tubular growth of the neoplastic cells are recognized in the surface area. In the submucosal area (lower half), are growing the tumor cells with clear cytoplasm. A few elongated cells with amphophilic cytoplasm are mixed in these areas (HE-stain). A high-power view of the clear cell population showing coexistence of dark cells with more pleomorphic nuclei (insert).

tumor mass on the greater curvature of lower gastric body measured 40 mm × 40 mm was a nodular, irregular, gray-pink appearance having central ulceration with a raised rolled margin. The neoplastic mass on the posterior wall in pylorus measured 18 mm × 18 mm was a polypoid lesion with surface erosions; type 0-IIa+IIc (Figure 1). On the operation, the tumors looked to be localized in the stomach wall and metastases to lymph nodes and other organs were not confirmed. On microscopy, the surface area of the neoplasm on the greater curvature of lower gastric body exhibited common features of adenocarcinoma with papillary or tubular growth. However, the main neoplastic cells infiltrating lamina propria and occupying submucosal space were changed to those composed of single nucleus, vacuolated or clear cytoplasm. They were relatively uniform population and lacked typical glandular structures. Less number of bizarre cells resembling syncytiotrophoblast cells with more pleomorphic nuclei, deeply eosinophilic to basophilic cytoplasm and less distinct cell membranes was mixed with the clear cell population (Figure 2). The tumor infiltrated through the muscularis propria into the sub serous space. In the layers of muscularis propria and subserosal area, solitary growth of syncytiotrophoblast type cells which were

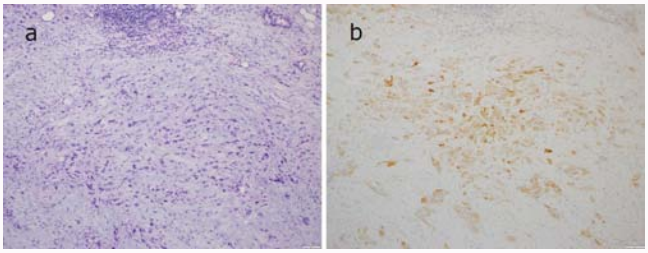

Figure 3: Invasive growth of tumor cells resembling syncytiotrophoblastic cells in the muscularis propria (a). The same area with positive reaction of beta-subunit of Human Chorionic Gonadotropin (HCG) (b).

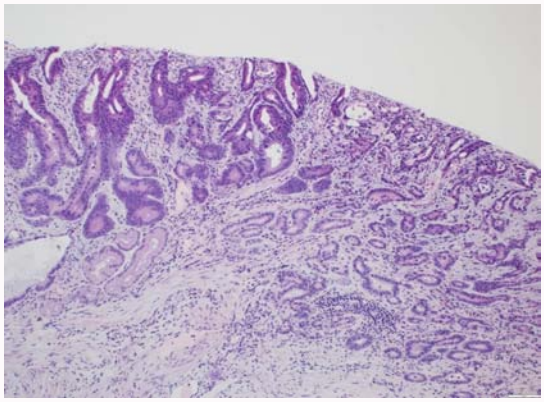

Figure 4: Histology of the tumor located on the posterior wall of pylorus. Both features of well differentiated and moderately differentiated tubular adenocarcinoma are mixed. The carcinoma is growing only in the mucosal layer.

encountered infrequently with clear cells in the submucosal area, was often recognized (Figure 3a). Immunoreaction of HCG was localized exclusively to these syncytiotrophoblast type cells (Figure 3b). Three out of 28 regional lymph nodes had metastatic lesions of the neoplasm. Interestingly, the metastatic lesions also contained adenocarcinomatous as well as choriocarcinomatous components with immunoreaction of HCG. Immunostaining of Cytokeratin (CK) 7 was strongly positive for all neoplastic cells in the all layers of the stomach. However, CK 20 was negative in any tumor cells. Furthermore, Carcinoembryonic Antigen (CEA) was clearly positive in the cells of adenocarcinomatous features. Production of Alpha-Fetoprotein (AFP) was not recognized in any tumor cells of this tumor.

Histology of the tumor located on the posterior wall of pylorus was a combined type of well differentiated and moderately differentiated tubular adenocarcinoma (Figure 4). The carcinoma was growing only in the mucosal layer. It is assumed that the tumor in the pylorus had multifocal origin, since the carcinoma was a combined type and some normal epithelium was remained among the neoplastic epithelium. The tumor did not contain any trophoblastic components. HCG, CEA and AFP were not immunoreactive. CK 7 was partially positive in the tumor tissues, although CK 20 was negative.

Postoperatively, the patient has been stable, and no evidence showing possibility of malignancy in other organs including ovary and uterus was recognized. She had taken S-1 for six months as adjuvant chemotherapy [8,9]. The recurrence and metastases of the gastric cancer have not been recognized for a year. However, the patient unfortunately died two years after the operation due to the

abdominal dissemination of the neoplasm.

Discussion

Presently, HCG positive syncytiotrophoblast type cells came into existence mainly in the layers of muscularis propria and subserosa, not in the mucosal area where was present only the cells with features of adenocarcinoma. Thus, choriocarcinomatous differentiation is suggested to occur during the down growth of the tumor. In this case, typical mix of cytotrophoblast and syncytiotrophoblastic elements as seen in representative choriocarcinomas was not apparent. However, clear cells lacking HCG activity often coexisted with syncytiotrophoblast type cells in the submucosal area. Furthermore, morphology of these cells resembles cytotrophoblasts of trophoblastic neoplasms. Accordingly, appearance of such cell population was suggested to be an evidence for the choriocarcinomatous differentiation of the adenocarcinoma.

Cytogenetic study on the gastric choriocarcinoma also supports the theory that gastric choriocarcinoma arises from alternate differentiation pathway of adenocarcinoma [10]. Although, HCG-producing cells were not confirmed in the normal antrum mucosa in this study, some authors reported presence of immunoreactive cells against beta subunit of HCG in the neck region of normal antral mucosa [11,12]. Such specific feature of the stomach might be related to the choriocarcinomatous differentiation.

In this case, synchronous development of two separated carcinomas was present in the stomach of the woman. Furthermore, the intramucosal carcinoma in the pre-pylorus was suggested to be multifocal. There is evidence that some of larger early gastric carcinomas may result from collision of smaller neoplasms [13]. Thus, existence of multiple cancers in the stomach of this woman implies a higher oncogenesis stage of this organ. The concept of field cancerization is recognized in different human organs. Regarding the mechanism of field cancerization of human stomach, genetic instability in the mucosal cells is suggested to relate [14]. Meanwhile, McDonald et al. [15] reported from the analysis using mitochondrial DNA mutations that human gastric body units are clonal and contain multiple multipotential stem cells, thereby mutated gastric stem cells spread widely within the stomach. In the present case, the patient developed two separated gastric carcinomas, one of which accompanied choriocarcinomatous differentiation. Similar case with double carcinomas of the stomach is reported by Eom et al. [16]. Recently, collision tumor of choriocarcinoma and small cell carcinoma of the stomach was reported by Fukuda et al. [17]. In the present case, the carcinoma with choriocarcinomatous differentiation showed the staining pattern of CK 7 positive and CK 20 negative. Similar staining pattern of cytokeratin is also confirmed in a gastric carcinoma with choriocarcinomatous differentiation [6]. CK 7 is evaluated as an accurate intracellular marker to assess the purity of human placental villous trophoblast [18]. Choriocarcinomatous differentiation may be concerned with function of some cytokeratin, although evidence is uncertain.

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