Superficial and Protruding Type of Esophageal Adenocarcinoma Mucocellulare and Muconodulare Confined Mostly to the Lamina Propria Mucosa and Partly in the Submucosal Layer

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We report a case with an adenocarcinoma mucocellulare and muconodulare of the esophagus which is limited to the lamina propria mucosa and the submucosal layer. The patient, a 74-year-old man had the chief complaints of hematemesis and melena. A superficial and protruding (0-1) type of lesion was found at the lower thoracic portion of the esophagus by X-ray and endoscopic examination. The surgically resected esophageal specimen showed 0-1 and predominantly subepithelial (Sep) type. The tumor is presumed to have arisen from the cardiac glands in the lamina propria mucosa of the lowermost region of the esophagus.

(Key words: esophageal cancer, histogenesis of cancer, cardiac glands of the esophagus)

Introduction

The common histologic type of esophageal carcinoma is squamous cell carcinoma; primary adenocarcinoma of the esophagus is rather infrequent in Japan. Moreover, most cases showing adenocarcinoma of the esophagus are advanced, since a diagnostic approach for early detection has not yet been established. Primary superficial adenocarcinoma of the esophagus with a depth of invasion to the submucosal (sm) layer has been rarely reported (1-3).

Here, we report a 74-year-old man with a superficial and protruding type of esophageal adenocarcinoma mucocellulare and muconodulare as documented by light microscopy. The histogenesis of adenocarcinoma mucocellulare of the esophagus is discussed and attention is given to the cells of origin of the esophageal cancer herein.

Case Report

A 74-year-old man was admitted to our hospital with hematemesis and melena on May 6, 1992. On physical examination, the patient was found to be a well-nourished male (height 156 cm, weight 72 kg) who was afebrile with a heart rate of 63/min and regular, and a blood pressure of 116/60 mmHg. No tumor mass was found just above the clavicle. No other superficial lymph nodes were palpable. Examination of the chest, abdomen and nervous system revealed no abnormal findings.

Hematological parameters were as follows: erythrocyte count, 412×10⁴/μl; hemoglobin, 10.2 g/dl; hematocrit, 31.9%; leukocyte count, 7,600/μl. Blood chemistry showed a slight decrease in total protein (5.9 g/dl). However, other biochemical and serological findings were almost completely within normal limits. Serological tumor markers were negative.

Radiological examination revealed an irregularly enlarged tumor lesion without stenosis in the lower intrathoracic portion (Ei) of the esophagus, measuring approximately 5 cm in length (Fig. 1). The initial endoscopic examination revealed an elevated tumorous lesion with a central shallow depression in the Ei esophagus (Fig. 2). The surrounding mucosa of the tumor including those of the anal side of the tumor were normal esophageal mucosa. A diagnosis of superficial and protruding type esophageal carcinoma (0-1 type) as defined by the Japanese Society of Esophageal Disease (4) was made at that time. Biopsy taken from the lesion showed adenocarcinoma mucocellulare covered with normal squamous epithelium. Computed tomography (CT) scan of the thorax and the abdomen showed an elevated tumor lesion in the Ei esophagus (data...
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Fig. 1. Double contrast esophagogram of the right anterior oblique position. A protruding type tumor, measuring approximately 5 cm in length is shown in the posterior wall of lower thoracic esophagus.

However, there was no finding of metastasis in regional lymph nodes, the lung and liver. Based on these findings, it was determined that the patient had localized superficial esophageal adenocarcinoma.

Surgical radical resection of the esophagus was planned for treatment of the adenocarcinoma, since no metastasis was found elsewhere. The patient, however, underwent a simple blunt esophageal resection on June 3, 1992, as during the beginning of surgery under anesthesia, complete atrial-ventricular block of the heart suddenly occurred. Thus, total resection of the intrathoracic esophagus through a right thoracic approach, followed by an antethoracic esophagogastrotomy could not be done.

Fresh resected material and a schematic illustration of the surgical specimen of the esophagus are shown in Fig. 3. A tumor of a superficial and protruding type (0-1), measuring 3×3.5 cm in size at the Ei esophagus was observed. The tumor showed an irregular surface that was predominantly subepithelial (Sep) and with erosion of the lesion covered with squamous epithelium. Thus, a primary lesion was macroscopically classified as 0-1 Sep type as defined by guide lines for clinical and pathologic

Fig. 2. Endoscopic picture showing superficial and protruding (0-1) type carcinoma in the posterior esophageal wall.

Fig. 3. Gross finding of primary lesion in the surgical material. a) 0-1 predominantly subepithelial (Sep) type lesion, measuring 3×3.5 cm in size was noted. b) Schematic illustration of surgical specimen of the esophagus. The overlying squamous epithelium on the tumor was focally ulcerated ( ), but otherwise ( ) normal.
studies of carcinoma of the esophagus (4). Esophageal mucosa between the lesion and the esophagogastric junction was intact. There was no evidence of the invasion of the tumor to the stomach. To perform further histological analysis, the specimen fixed in 10% formalin was cut into multiple slices parallel to the longitudinal axis (Fig. 3b). The slices were cut, routinely hematoxylin-eosin (HE) stained and examined under a microscope. A representative cut-surface of the lesion (slice #10) in the surgical material are presented in Fig. 4. Microscopically, the tumor consisted of adenocarcinoma mucocellulare and muconodulare containing abundant mucin. The tumor cells were strongly stained with periodic acid-Schiff (PAS). Coexistence of squamous cell carcinomatous component, tubular formation or papillary growth of cancer cells was not detected within the tumor in the careful and extensive histological examination. The tumor cells were mostly located in the lamina propria mucosa (m) and partly in the sm layer (Fig. 4a). However, the invasion of tumor cells did not further extend into the propria muscularis (pm) and adventitia of the esophagus. The lesion on the esophagus histologically showed a lymphatic vessel involvement of cancer cells, but no infiltration to vascular vessels. Metastasis involving the periesophageal lymph nodes was found in one of 6 examined lymph nodes. The nodal metastatic lesion also showed adenocarcinoma mucocellulare and muconodulare. Thus, histological stage of the case was stage II as defined by the guide lines for the clinical and pathological studies of carcinoma of the esophagus (4).

Figure 5a shows the presence of cardiac glands in the esophagus (slice #2) near the anal side of the tumor lesion. Deep mucous glands and their ducts were detected just under the center of the primary tumor (Fig. 5b). The glands were neither invaded nor destroyed by the tumor cells.

After surgery, the patient suffered from complications of pneumonia and mediastinal abscess due to infection of methicillin resistant staphylococcus aureus (MRSA). Drainage of the abscess with a left thoracotomy and chemotherapy was used for treatment, but the patient failed to respond to the therapy and unfortunately died on August 18, 1992.

![Fig. 4. Histological findings of the primary tumor of the esophagus.](image)

- Scanning power view of histological section (slice #10). The invasion of the tumor cells is mostly limited to the mucosal (m) and partly to the submucosal (sm) layers. The tumor was partly covered with normal squamous epithelium.
- High power view of adenocarcinoma mucocellulare and muconodulare. Mucin laden cells are easily detectable, but without any gland formation (HE stain, ×40).

![Fig. 5. Histological findings of the esophageal glands at the primary lesion.](image)

- Cardiac glands (arrow) in the esophagus between esophagogastric junction and anal edge of the tumor (slice #2) are noted (HE stain, ×20). The tumor is covered with normal squamous epithelium.
- Deep mucous glands and dilated excretory ducts are observed just under the portion of the center at the primary tumor (HE stain, ×20).
Discussion

This is a very rare case of adenocarcinoma mucocellulare and muconodulare that involves the m and sm layers of the Ei esophagus. Gross findings of the resected specimen showed a superficial and protruding type covered with noncancerous squamous epithelium.

It has been considered that primary adenocarcinoma of the esophagus occurs possibly in Barrett’s esophagus, ectopic gastric mucosa and esophageal glands. Histological analysis of the present case did not show any pathological findings (columnar epithelium) of Barrett’s esophagus. Esophageal adenocarcinoma arisen from an ectopic gastric mucosa is usually located in the middle or upper portion of the esophagus. In addition, it is generally difficult to define the islet of gastric mucosa in the esophagus. Esophageal glands consist of two kinds of glands, namely cardiac glands located in the m layer and deep mucous glands residing in the sm. Deep mucous are glands widely distributed in the esophagus, but it has been shown that the glands do not exist in the area of 2 to 4 cm from the esophagogastric junction. Embryologically, both esophageal deep mucous glands and minor salivary glands in the posterior regions of the oral cavity are of pharyngeal entodermal origin. Indeed, the adenocarcinomas arising in the deep mucous glands microscopically resemble the mucoepidermoid and adenoid cystic carcinomas originating in the salivary glands. The tumor shows a concomitant squamous element. Thus, it has been called a adenoacanthoma, mucoepidermoid carcinoma or adenoid cystic carcinoma of the esophagus, implying its origin is from the deep mucous glands. In the present case, however, squamous cell carcinomatous components were not found in adenocarcinoma tissue in the area of 2 to 4 cm from the esophagogastric junction. On the other hand, cardiac glands of the esophagus are limited to narrow zones near both ends of the esophagus, between the level of the cricoid cartilage and the fifth tracheal ring and the extreme lower portion of the esophagus including the abdominal esophagus. As shown in Figs. 1, 2 and 3, the tumor presented here occurred in the region just above the esophagogastric junction, where esophageal cardiac glands originally existed. In fact, cardiac glands were clearly shown in the normal esophagus near the anal side of the primary lesion (Fig. 5a). Although deep mucous glands could also be detected just under part of the primary lesion, the glands were intact and did not directly connect to the primary lesion (Fig. 5b). Furthermore, the tumor was histologically different from mucoepidermoid carcinoma or adenoid cystic carcinoma of the salivary gland. These results strongly suggest that adenocarcinoma mucocellulare of the esophagus in the present case possibly originates from the esophageal cardiac glands and not from the deep mucous glands. Thus, it has been considered that the adenocarcinoma cells were possibly derived mainly from the cardiac glands of the esophagus and horizontally invade to the m layer and partly extend into the sm layer (Fig. 3).

Tumor derived from esophageal cardiac glands has been histologically known as well-differentiated adenocarcinoma.