Early Carcinoma of the Esophagus Associated with Achalasia Treated by Endoscopic Mucosal Resection: Report of A Case

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A case of endoscopically resected early esophageal carcinoma associated with achalasia is reported. A 63-year-old woman was made diagnosis of esophageal achalasia, sigmoid type and Grade III. The patient was operated by Tokai University method, Heller’s long esophagomyectomy, Hill’s posterior cardiopyexy, fundoplication and selective proximal vagotomy using a laparotomy. Two years and six months after the operation, an early carcinoma of type 0-IIb, 1cm in size, was detected in the upper thoracic esophagus, and treated by endoscopic mucosal resection using EMR-tube method. Pathological examination revealed proliferation of squamous cell carcinoma in situ (Tis: mL). The entire esophageal mucosa around the carcinoma demonstrated hyperplastic changes of stratified squamous epithelium and foci of dysplastic changes. In the patient of achalasia, food stasis in esophagus is thought to induce chronic hyperplastic esophagitis, converting eventually to malignant transformation. Achalasia is known as a risk factor of esophageal carcinoma. Early operation or good drainage of the esophageal lumen might reduce the risk. Long-term follow-up for patients of achalasia by endoscopic screening is recommended.

Key words: Achalasia of esophagus, esophageal carcinoma, carcinogenesis, endoscopic mucosal resection

INTRODUCTION

Achalasia is an idiopathic primary esophageal motor disorder characterized by insufficient relaxation of the lower esophageal sphincter to muscle and the absence of esophageal peristalsis. Decreased and/or diminished myenteric ganglia have been reported in the lower esophagus (1, 2). Achalasia is known as a risk factor of esophageal carcinoma (3, 4, 5). Fagge first reported the relationship between achalasia and esophageal carcinoma in 1872 by their autopsy findings (6). Since this initial observation, the increased risk of developing esophageal carcinoma has been postulated in the patients with long-standing achalasia (7). The incidence of carcinoma in achalasia patients has been reported to range from 1.7 to 20% (3, 8–17). Chronic inflammatory irritation by retained food may induce carcinogenesis of the esophageal squamous epithelium. In this report, a case of endoscopically resected early esophageal carcinoma developing after the operation for achalasia is described.

CASE REPORT

A 63-year-old woman was suffering from dysphagia to solids and liquids from 1992. She had been treated conservatively, such as calcium-channel blocker and pneumatic dilatation for symptomatic achalasia in the other hospital. But, her symptom became worse progressively, and she noted a 5kg weight loss over in four months. The patient was admitted to Tokai University Hospital on November 5, 2002 for evaluation of dysphagia. Physical examination at admission did not reveal abnormalities. Laboratory data were within normal limits, including tumor makers such as SCC and CEA, except for slight anemia.

Esophagography of double contrast examination demonstrated marked dilatation of the esophagus proximal to gastroesophageal junction, measuring 7.5cm in diameter (Figure 1). The Upper GI series also showed sigmoid-type elongation and aperistalsis of the distal half of the esophagus. Conventional endoscopic examination revealed the dilated and atomic esophagus with a large amount of diet staying inside. The entire esophageal mucosa demonstrated significant hyperplastic changes of stratified squamous epithelium, but iodine-unstained lesion was not detected by chromoendoscopic examination (Figure 2A, B). The preoperative diagnosis was achalasia, sigmoid type and Grade III (18). The surgical operation by Tokai University method (19), Heller’s long esophagomyectomy, Hill’s posterior cardiopyexy, fundoplication (4/5 of circumference) and selective proximal vagotomy using a laparotomy with upper median abdominal skin incision, were performed on November 19, 2002. The postoperative course was uneventful and the patient was discharged two weeks later. She has been well without complaint of dysphagia after the operation.

Endoscopic examination with iodine staining was
performed every six months and esophagitis was well controlled without marked hyperplastic change after the operation. Two years and six months after the operation, an early carcinoma of type 0-IIb, 1cm in size, was detected at 23cm from incisor in the upper thoracic esophagus by endoscopy (Figure 3A,B). Computed tomography and echogram showed no evidence of metastasis. Endoscopic mucosal resection (EMR) using EEMR-tube method was performed on October 13, 2005 (Figure 3C, D). Pathological examination of the resected specimen revealed proliferation of squamous cell carcinoma, closely associated with dysplastic foci. The invasion of carcinoma cells was limited to the squamous epithelium (Tis: m1) (Figure 4A) (20). The entire esophageal mucosa around the carcinoma demonstrated hyperplastic changes of stratified squamous
epithelium accompanying foci of dysplastic changes (Figure 4B, C). No lymphatic or blood vessel invasion was found. She was discharged three days after EMR without complication, and has been well without recurrence of cancer for two years.

DISCUSSION

Achalasia of the esophagus is a benign disease caused by dyskinesia of the lower esophagus and cardia, and is regarded as an increased risk of squamous cell carcinoma due to persistent mucosal irritation by alimentary retention. According to the Japanese classification, the types of dilatation is divided into three grades as follows: (a) spindle type, (b) flask type, (c) sigmoid type (18). The grades of dilatation is similarly divided into three groups as follows: (a) Grade I: d (maximum diameter in lower esophagus) < 3.5 cm, (b) Grade II: 3.5 ≤ d < 6.0 cm, (c) Grade III: 6.0 cm ≤ d (18). Most patients with achalasia undergo conservative therapy and/or esophagomyectomy, and there have been few cases of surgical resection of achalasia of the esophagus. The incidence of carcinoma is reported as 1.7 to 20% among achalasia patients (3, 8–17), while that of ordinary esophageal carcinoma is approximately 0.3% (7, 21). Thus, the patients with achalasia have a risk of carcinoma. In the previous studies, the mean interval from onset of dysphagia in achalasia patients to diagnosis of esophageal squamous cell carcinoma was 17–21.5 years (3, 4, 5, 7, 17). Before treatment for carcinoma, all the patients with achalasia had been performed pneumatic dilatation and/or esophagomyectomy for their symptom. In the myectomy cases, the carcinoma was diagnosed after a mean period of 17 years of post-operative follow-up (17). The prognosis of achalasia-associated carcinoma is poor, because the symptoms of carcinoma are usually hidden by the severe dysphagia of achalasia. Radiographically, most of the patients lose peristalsis, and distal esophageal stricture, retention of barium and food material in the esophagus is observed. Endoscopically, esophageal food stasis and chronic hyperplastic esophagitis are often observed. Thus, the carcinomas associated with achalasia are mostly found and diagnosed in the advanced stages (22). In patients with achalasia the carcinoma was rarely found in its early stage, and the incidence of early carcinoma was reported only 9.1% (23). Therefore, endoscopic surveillance using iodine staining has been recommended in patients with achalasia to detect the cancer in early stage (3, 5, 11, 17). If detected, the early cancer can be treated by EMR. In this case, the type of achalasia was sigmoid type and grade III dilatation. Since persistent esophagitis of achalasia is thought as a premalignant condition (8–10, 12, 17), Heller’s esophagomyectomy or dilatate bouginage of esophagus are recommended in early stage of the disease. However, surgery in the late stage does not

Fig. 4. Microscopic findings of achalasia-associated squamous cell carcinoma. The carcinoma showed a mucosal carcinoma, closely associated with dysplastic foci and hyperplastic mucosa. A: carcinoma in situ (x10, H & E), B: dysplasia (x20, H & E), C, hyperplasia (x10, H & E).
seem to be effective for achalasia-mediated carcinogenesis.

In the previous studies, histological examination of the resected esophageal specimens demonstrated marked hyperplastic changes of stratified squamous epithelium and multiple foci of dysplastic changes. The squamous cell carcinomas were of well to moderately differentiated type with low-grade atypia, closely associated with dysplastic foci (17, 24, 25). We speculate that food stasis induces chronic hyperplastic esophagitis, leading eventually to malignant transformation of esophageal epithelial cells, in accordance with dysplasia-carcinoma sequence (8–10, 12, 17).

The previous immunohistochemical investigations regarding p53 accumulation of esophageal squamous cell carcinoma show frequent over-expression of p53 in both achalasia-associated carcinoma and dysplasia (17, 26, 27). Immunohistochemical studies of p21 and p53 expression suggest that the cell cycle might be increased in achalasia-associated carcinoma because of persistent inflammation (17, 27–30). Under these conditions of accelerated cell cycle, the achalasia-associated carcinoma may develop according to the dysplasia-carcinoma sequence.

In conclusion, we reported a case of early esophageal carcinoma associated with postoperative achalasia treated by EMR. Achalasia is known as a risk factor of esophageal carcinoma. Long-term follow-up for patients of achalasia by endoscopic screening is recommended.

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