Introduction

Basaloid cell carcinoma is rare but distinct variant of squamous cell carcinoma that arises in various anatomic sites, including the upper aerodigestive tract, thymus, uterus, cervix, and anus.1,2) Esophageal basaloid cell carcinoma is a rare disease that is classified as a primary epithelial malignancy of the esophagus3-6). Histologically, this tumor should be differentiated from adenoid cystic carcinoma and small cell undifferentiated carcinoma. Compared to typical squamous cell carcinoma, this disease is associated with more severe vascular invasion, causing extensive lymph node and hematogenous metastasis, and the prognosis is generally considered to be extremely poor.5-7) Early detection and multidisciplinary therapy are essential for improved outcomes. We report our experience with a surgical case of superficial esophageal basaloid cell carcinoma.

Case presentation

A 69-year-old male patient had no chief complaint. The patient had phlebothrombus of the lower extremities and hypertension. He had been smoking 20 cigarettes daily for 49 years.

In January 2012, upper gastrointestinal series performed as a part of a health checkup revealed a protruding lesion in the esophagus. A 10-mm-diameter nodular, elevated lesion slightly dented at the center was found at 34 cm from the incisor in esophageal endoscopy. The histological examination of a biopsy specimen revealed cancer cells resembling poorly differentiated squamous cell carcinoma. cStage I esophageal cancer (Lt 0-IIa, T1bN0M0) was diagnosed and surgically removed. The patient underwent a subtotal esophagectomy with two regional lymph nodes (thoracic lymph nodes and abdominal lymph nodes) dissection via a right thoraco-laparotominal approach and reconstruction of the esophagogastric tube anastomosis at the upper mediastrium area. The histopathology of the removed sample showed squamous cell carcinoma in the superficial epithelium and non-invaded part. The tumor cells had invaded the upper submucosal layer involving basaloid cell carcinoma. Based on the findings, superficial basaloid cell carcinoma of the esophagus was diagnosed (pT1b pN0 pM0 ly0 v0 pStage I). The patient had a good postoperative course and was discharged at about 3 weeks after surgery. No adjuvant chemotherapy has been performed. Currently at about 4 years postoperation, the patient is being followed up on an outpatient basis without recurrence.

Key Words: Esophageal cancer, Superficial cancer, Basaloid cell carcinoma.
ing lesion was thick, so we diagnosed that tumor invaded the massive submucosa (Fig. 2). The histological examination of a biopsy specimen revealed cancer cells resembling poorly-differentiated squamous cell carcinoma.

Thoracoabdominal computed tomography: There was no space occupying lesion in the lung, liver, etc., and no lymphadenopathy was observed, either.

Clinical diagnosis: Surgery was performed under a diagnosis of esophageal squamous cell carcinoma, Lt 0-IIa T1b(SM2 or 3) N0 M0 cStage I.

The depth of this tumor invasion was T1b(SM2 or 3), so endoscopic submucosal dissection was not indicated. This patient chose operative treatment than chemoradiotherapy.

The patient underwent a subtotal esophagectomy with two regional lymph nodes (thoracic lymph nodes and abdominal lymph nodes) dissection via a right thoraco-laparotominal approach and reconstruction of the esophagogastric tube anastomosis at the upper mediastrium area. A thin gastric tube was constructed along the greater curvature before a subtotal esophagectomy.

Resected specimen: As with the endoscopic findings, the macroscopic findings revealed a nodular protruding lesion with a major axis of 10 mm and a slightly depressed center in the lower thoracic esophagus (Fig. 3). Histopathologic examination revealed squamous cell carcinoma in the superficial epithelium and the non-invasive area. Tumor cells invaded the superficial submucosa, where small alveolar structures were formed. A gland duct was partially involved. Moreover, myxoma-like/basal lamina-like substances were markedly deposited in the interstitium. Thus, esophageal basaloid cell carcinoma was diagnosed (pT1b pN0 pM0 ly0 v0 INFb pStage I, Fig. 4).

The postoperative course was favorable, and the patient was discharged approximately three weeks after surgery. In the clinicopathologic factor, there were few recurrence risk factors except basaloid cell carcinoma and the patient didn’t wish chemotherapy, so adjuvant chemotherapy was not administered. At present, approximately four years after surgery, the level of SCC antigen, a tumor marker, is normal, and no sign of recurrence has been detected by imaging studies. He is being followed up at the outpatient clinic.
Fig. 3 Resected specimen: It revealed a nodular protruding lesion with a major axis of 10 mm and a slightly depressed center in the lower thoracic esophagus.

Fig. 4 Histopathologic examination: It revealed squamous cell carcinoma in the superficial epithelium. Tumor cells invaded the superficial submucosa, where small alveolar structures were formed. Moreover, basaloid cell carcinoma were markedly deposited in the interstitium.
Discussion

Esophageal basaloid cell carcinoma is classified as a type of epithelial malignancy according to the guidelines for the treatment of esophageal cancer and is a rare disease found in 0.068% of patients undergoing resection of esophageal cancer. Thus, there are still many unknown aspects with respect to the histological and clinical features. In the guidelines for the treatment of esophageal cancer, basaloid cell carcinoma is described as follows: “Small cells resembling basal cells proliferate in a solid alveolar or funicular pattern and sometimes form irregular adenoid/microcyst-like structures. Furthermore, this carcinoma is characterized by deposition of basal lamina-like substances in and out of alveolar structures. It is also accompanied by duct-like differentiation in some cases. While basal cell carcinoma is often complicated by squamous cell carcinoma in the epithelium, the invasive area is also accompanied by squamous cell carcinoma in some cases.” Moreover, because many cases present the features of squamous cell carcinoma in part, basaloid cell carcinoma is also called basaloid-squamous carcinoma. In our case, the epithelial lesion was also complicated by squamous cell carcinoma.

Regarding the characteristic growth pattern, esophageal basaloid cell carcinoma is considered to progress by forming large solid cancerous alveolar structures in the esophageal submucosa as the major site of growth. Thus, it is considered that, in the majority of cases of superficial carcinoma, the macroscopic pattern is protruding submucosal tumor-like morphology covered by squamous epithelia, and that erosion or ulcer is formed on a part of the surface. Thus, the main body of the tumor is not always obtainable by conventional biopsy for histological examination, and cases of difficult differentiation from submucosal tumor have also been reported. Our case also presented a similar macroscopic pattern, and the histological examination of a biopsy specimen also yielded a diagnosis of cancer cells resembling poorly-differentiated squamous cell carcinoma.

Regarding the clinicopathologic features of esophageal basaloid cell carcinoma, 119 Japanese patients examined by Mori et al. presented a mean age of 65.2 years, are predominantly male with a male-to-female ratio of 101:18, and included 72 patients with superficial carcinoma and 47 patients with advanced carcinoma. The majority of the superficial carcinomas presented as a protruding tumor with submucosal tumor-like morphology, while many of the advanced carcinomas presented as an ulcerative tumor as is the case in typical squamous cell carcinoma. Moreover, lymph node metastasis was detected in 19.4% of the patients with superficial carcinoma and in 66.0% of the patients with advanced carcinoma. Especially in those with pN2 or greater advanced carcinoma, extensive lymph node metastasis was observed. The outcomes of the patients with superficial carcinoma were relatively favorable, whereas the majority of the patients with advanced carcinoma developed recurrence and died within two years.

Although other reports also indicate that the prognosis of esophageal basaloid cell carcinoma is generally poor, it is considered that a prognosis comparable to typical esophageal cancer (squamous cell carcinoma) can be expected for esophageal basaloid cell carcinoma at the relatively early stage. Meanwhile, there is also a report of cases of early esophageal cancer recurring in the liver/lymph nodes soon after surgery.

However, long-term survival is considered difficult in advanced carcinoma at stage III or greater. The reasons for this include that this tumor, which grows and progresses mainly in the submucosa, is more likely to have severe vascular invasion leading to extensive lymph node or hematogenous metastasis in comparison to typical esophageal cancer, and that the biological malignancy of this tumor is basically high and becomes higher as the tumor advances in stage. There are several other reports describing the reasons for the high biological malignancy of this disease.

Morita et al. report that epithelial cadherin, an intercellular adhesion molecule, had disappeared from between tumor cells. Koide et al. report that B cell leukemia 2 (Bcl-2) protein, which is considered to inhibit apoptosis and programmed cell death and to promote carcinogenesis, was more highly expressed in this disease than in typical squamous cell carcinoma. In addition, Kawaguchi et al. indicate that the epidermal growth factor receptor is expressed in this disease. Arai et al. report that recent advances in molecular pathology have demonstrated peculiar features of basaloid cell carcinoma, including aneuploidy, frequent Bcl-2 expression, and less frequent expression of p16 protein. Imamhasan et al. report that aberrations of p53 and epidermal growth factor receptor genes are possibly involved in progression of esophageal basaloid cell carcinoma. Saito et al. report that a characteristic feature of basaloid cell carcinoma is nuclear accumulation of β-catenin, without a mutation of the gene, and show that secreted frizzled-related protein 2 (sFRP-2) is a target gene of hypermethylation in esophageal basaloid cell carcinoma and suggest that sFRP-2 might contribute to basaloid cell carcinoma tumorigenesis through the Wnt/β-catenin signaling pathway. Recently, Baba et al. analyzed KRAS, BRAF, and PIK3CA mutations, p53 immunohistochemical expression, and long interspersed nucleotide element-1 methylation (LINE-1) status in basaloid cell carcinoma. Basaloid cell carcinoma tumors displayed definitive molecular alterations, including LINE-1 hypomethylation and an absence of PIK3CA mutations. That results imply that esophageal basaloid cell carcinoma and squamous
cell carcinoma retain different cellular phenotypes with distinct genetic and epigenetic alterations. There is no doubt that basaloid cell carcinoma differs from typical squamous cell carcinoma. Thus, new therapeutic strategies should be developed against basaloid cell carcinoma. We think that the molecular target treatment such as anti-EGFR antibodies is expected as new therapeutic strategies. Although our case is superficial carcinoma without lymph node metastasis, we think that it also requires closer follow-up than regular cases.

In conclusion, we experienced a surgical case of superficial esophageal basaloid cell carcinoma. This disease is considered to have high biological malignancy. New therapeutic strategies should be developed against this disease. Although our case is superficial carcinoma without lymph node metastasis, it requires close follow-up.

Reference