

Professor Kaiyo Takubo

Department of Human Tissue Research,

Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

Miwako ARIMA, MD

Department Gastroenterology, Saitama Cancer Center Hospital, Saitama-ken, Japan

Case 9

Early esophageal squamous cell carcinoma, endoscopic mucosal resection

A 72-year-old man underwent endoscopic examination during mass screening for upper GI tract cancer. He had been asymptomatic up to the time of the examination. He had drunk an equivalent of 30 mg of ethanol per day for 50 years, and his Smoking Index was 800. His medical history included arteriosclerosis obliterans of both lower extremities. At endoscopy, a slightly depressed lesion was observed in the esophageal mucosa, and a biopsy specimen from the lesion was diagnosed as a carcinoma. One month after detection of the lesion, the patient underwent endoscopic mucosal resection (EMR) of the esophageal carcinoma. Since the EMR, the patient has been well for the last 2 years. The histologic slides used for this presentation were prepared from the EMR specimen.

Pathologic Diagnosis:

Squamous cell carcinoma of the esophagus associated with squamous cell carcinoma *in situ*

Pathologic findings:

Depth of invasion: m3 = the lamina muscularis mucosae (explained later)

Lymphatic invasion: mildly positive. Venous invasion: negative

The resection margin is negative for carcinoma.

Subclassification of Depth of Invasion by Superficial Carcinoma

Mucosal carcinoma (intramucosal carcinoma)

m1 = intraepithelial non-invasive carcinoma, namely carcinoma *in situ*

m2 = carcinoma invading the lamina propria mucosae

m3 = carcinoma attached to, or invading the lamina muscularis mucosae

Submucosal carcinoma (carcinoma invading the tunica submucosa)

sm1 = carcinoma invading the upper one third of the tunica submucosa in the surgically resected specimen or carcinoma invading within 200 μ m in the submucosa in the EMR specimen

sm2 = carcinoma invading the middle one third of the tunica submucosa

sm3 = carcinoma invading the lower one third of the tunica submucosa

(Japanese Society of Esophageal Diseases, 1995.6; Takubo et al. Superficial carcinoma of the esophagus in Japan: curable lesion, Imamura ed. in Superficial Esophageal Neoplasm, Springer-Verlag Tokyo, 2002)

Indication for Endoscopic Mucosal Resection

Mucosal carcinomas that do not reach the muscularis mucosae (m1 and m2 carcinomas, n = 96) have no lymph node metastasis, and are therefore curable by endoscopic mucosal resection alone.

Early, Superficial and Advanced Carcinoma of the Esophagus

Superficial carcinoma, defined as carcinoma *in situ* or carcinoma involving the mucosa or submucosa, regardless of the presence of lymph node metastasis, can occasionally be distinguished from advanced carcinoma (invading the muscularis propria) by macroscopic observation of cut surfaces of the tumor or by determining whether or not a superficial tumor is fixed to the muscularis propria; if the tumor is not fixed, it will slide over the muscularis propria when slight force is applied parallel to the mucosa.

Early carcinoma (stage 0 carcinoma) of the esophagus was previously defined as a superficial carcinoma with no nodal or distant metastases, but this definition has now been changed. There is a high likelihood of cure. The term “early carcinoma” is widely used in Japan but is not strictly correct because the time from tumor onset is unknown. The term is mentioned in the “Guidelines for Clinical and Pathologic Studies on Carcinoma of the Esophagus” (8th edition, 1992) and, in recent years, has also apparently become accepted in the medical literature in USA and Europe. Advanced carcinoma (stage I, II, III, and IV carcinoma) of the esophagus was previously defined as a superficial carcinoma with metastasis, or a carcinoma that had invaded the muscularis propria or adventitia. This definition has now also been changed slightly, in accordance with the changes made to the definition of early carcinoma. Although the term advanced carcinoma is widely used, it is not really the true opposite of the term superficial carcinoma.

In the most recent edition of the “Guidelines for Clinical and Pathologic Studies on Carcinoma of the Esophagus” (9th edition, 2001) early carcinoma is now defined as an intramucosal carcinoma without nodal or distant metastases.

References

1. Endo M et al. Endoscopic treatment for early carcinoma of the esophagus. *Shokaki-Shinyo Practice*. Bunkodo, Tokyo, 1998
2. Japan Esophageal Society. The Comprehensive Registry of Esophageal Cancer in Japan (1988-1997, 2000), First Edition, 2000, <http://www.esophagus/>
3. Japanese Society for Esophageal Diseases. Guidelines for Clinical and Pathologic Studies on Carcinoma of the Esophagus” (9th edition, 2001, English version) Kanehara & Co. Ltd, Tokyo.
4. Makuuchi H. et al. Prognosis of early esophageal cancer: prognosis according to macroscopic and microscopic types *Rinsho-Shokakinaika* 12:1749-1756, 1997
5. Makuuchi H, et al. Treatment of mucosal and submucosal cancer in esophagus. The turning point to decide whether surgical operation or endoscopic surgery. *Jpn J Gastroenterol Surg* 26:2517-2521, 1993.
6. Takubo K. Pathology of the Esophagus. Educa, Tokyo 2000. p131-161.
7. Takubo et al. Superficial carcinoma of the esophagus in Japan: curable lesion, Imamura ed. in Superficial Esophageal Neoplasm, Springer-Verlag Tokyo, Tokyo, 2002. p21-27.

Case 10

Superficial Basaloid Squamous Carcinoma, Endoscopic Mucosal Resection

A 66-year-old man with recurrent invasive squamous cell carcinoma of the mid-pharynx was hospitalized for radical surgery. He had previously received radiation therapy for mid-pharyngeal carcinoma. He had drunk an equivalent of 36 mg of ethanol per day for 45 years, and his Smoking Index was 920. Before the radical operation, he underwent endoscopic examination of the esophagus and stomach for cancer screening, and was found to have a slightly elevated lesion in the esophagus. A biopsy specimen from the lesion was diagnosed as a carcinoma. After radical surgery for the mid-pharyngeal carcinoma, endoscopic mucosal resection (EMR) was performed twice for the esophageal carcinoma. The patient has been well with no evidence of recurrence of the pharyngeal or esophageal carcinoma for 3 years after the last EMR. The histologic slides used for this presentation were prepared from the last EMR specimen.

Pathologic Diagnosis:

Basaloid squamous carcinoma of the esophagus associated with squamous cell carcinoma *in situ*

Pathologic findings:

Depth of invasion, sm1 (carcinoma invading within 200 μ m in the tunica submucosa in the EMR specimen).

Lymphatic invasion negative, venous invasion negative.

Resection margin is negative for carcinoma.

Incidence of Basaloid Squamous Carcinoma of the Esophagus

Basaloid squamous carcinoma was observed as a minor component in 7.3% of usual squamous cell carcinomas in our Japanese series. In a review of 502 cases of esophageal malignancy in Korea, Cho et al. (2000) found 18 cases of basaloid squamous carcinoma, an incidence of 3.6%. At the time of biopsy, the incidence of basaloid squamous carcinoma is very low, suggesting that this type of carcinoma tends not to be diagnosed correctly by biopsy.

Morphological Features of Basaloid Squamous Carcinoma of the Esophagus

Macroscopically, if superficial, basaloid squamous carcinomas often have a plateau-type or predominantly subepithelial-type appearance. When advanced, they tend to have a complex ulcerated appearance.

Basaloid squamous carcinomas are characterized histologically by large cancer nests in which basaloid malignant epithelial cells are arranged in solid or trabecular patterns. Unlike basal cell carcinoma of the skin, a palisading pattern of tumor cells along basement membranes is relatively rare. The tumor cell nests may be centrally necrotic. Small keratinizing foci may be found on occasion, and a clear trabecular arrangement of cancer cells may sometimes be seen. Basaloid squamous carcinomas with a trabecular pattern may in fact resemble carcinoid tumors, and basaloid squamous carcinomas have actually been confused with primary carcinoid tumors of the esophagus in some case reports. It is common for hyaline basement membrane material, which stains PAS-positive, to be distributed within and around the tumor cell nests. With immunohistochemical stains this material is positive for laminin and type IV collagen. Staining for epithelial mucin is negative. Unlike adenoid cystic carcinoma, basaloid squamous carcinoma does not show a two-cell-type pattern of myoepithelial and ductal epithelial cells, but the distinction between these entities remains unclear. Venous invasion is often seen in advanced cases; this invasion may occur into relatively large vessels, indicating that this entity has a propensity for vascular invasion.

In cytologic preparations the tumor cells are usually cohesive and resemble the basal cells of squamous epithelium. In general they have scanty cytoplasm, which stains light green with the Papanicolaou method; some naked nuclei may also be seen. The nuclei are round or oval and irregular in size. Basement membrane material may also be seen in cytologic smears. Basaloid squamous carcinomas are somewhat similar to small cell carcinomas cytologically, but can be distinguished from them by the lack of file arrangements with nuclear molding and by the presence of thickened nuclear membranes.

Electron microscopy shows that the hyaline material consists of prominent multilayered basement membranes surrounding the tumor cells.

Prognosis of Basaloid Squamous Carcinoma

It is considered that the prognosis of this entity in the esophagus is poorer than that of usual squamous cell carcinoma, and is similar to that of basaloid squamous carcinoma of the oral cavity and upper respiratory tract. A study that reviewed 17 cases of basaloid squamous carcinoma of the esophagus documented only one patient who had survived for more than 5 years. Other reports, however, have stated that the prognosis of this tumor, if detected at an early stage, is similar to that of usual esophageal squamous cell carcinoma (Shimizu *et al.*). Yoshioka et al. (2004) reviewed 60 cases of basaloid squamous carcinoma of the esophagus; the outcome of

cases at stages I, IIa, and IIb (UICC) was similar to that of usual squamous cell carcinoma, but cases at stages III and IV had a poorer outcome than usual squamous cell carcinoma (Figure 16).

References

1. Cho K-J, et al. Basaloid squamous carcinoma of the oesophagus: a distinct neoplasm with multipotential differentiation. *Histopathology* 36:331-340, 2000.
2. Shimizu H, et al. A case of basaloid carcinoma of the esophagus. *Jpn J Gastroenterol Surg* 25:102-106, 1992.
3. Takubo K, et al. Basaloid-squamous carcinoma of the esophagus with marked deposition of basement membrane substance. *Acta Pathol Jpn* 41:59-64, 1991.
4. Takubo K, et al. Morphological heterogeneity of esophageal carcinoma. *Acta Pathol Jpn* 39:180-189, 1989.
5. Yoshioka S, et al. Progressive analysis of four cases of basaloid cell carcinoma of the esophagus and reported cases in Japan. *Jpn J Gastroenterol Surg* 37:290-295, 2004.