Mesenchymal tumor of the esophagus is rare, and the most common mesenchymal tumor of the esophagus is leiomyoma [1-3]. The incidence of esophageal leiomyoma from autopsy cases ranges from 0.005 to 5% [2, 3]. Although detailed histopathological examination of autopsy and surgically resected case series demonstrated that its incidence is higher at 7.9% [1]. This disease is typically found in patients between 20 and 50 years of age, and more often in men by ratio of 2:1 [1]. Esophageal leiomyoma represents 10% of all gastrointestinal leiomyomas [4]. Moreover, it usually appears as a solitary tumor (97%) [5], and multiple leiomyomas of the esophagus have been extremely rarely documented [4-6]. Albeit extremely rare, coexistence of squamous cell carcinoma (SCC) of the esophagus overlying benign mesenchymal tumor has been reported [5]. Herein, we describe the fifth documented case of SCC in situ (high-grade intraepithelial neoplasia) of the esophagus overlying leiomyoma with review of the literature.

A 75-year-old Japanese female with past history of hyperglycemia and osteoporosis was detected with an esophageal tumor at health checkup, and was subsequently referred to our hospital. Endoscopic examination revealed a submucosal tumor, measuring 5 x 4 mm in diameter, 20 cm from the incision (Figure 1). Endoscopic mucosal resection of the esophageal tumor was performed.

Histopathological examination of the endoscopically-resected specimen revealed a well-circumscribed submucosal nodular lesion with continuity with the muscularis mucosae (Figure 2A). The submucosal nodule was composed of proliferation of interlacing bundles of spindle cells with eosinophilic cytoplasm and bland cigar-shaped nuclei without conspicuous nucleoli (Figure 2B). Neither mitotic figures nor necrosis was noted. A tiny intraepithelial depressed lesion, measuring 1 x 0.8 mm in diameter, was present overlying the submucosal tumor (Figure 2A). Proliferation of atypical squamous cells with large nuclei in the entire layer of the squamous epithelium was observed (Figure 2C). Mitotic figures were present in the upper region of the squamous epithelium. No invasive growth was noted (Figure 2A, 2C).

Immunohistochemical studies were performed using an autostainer (Ventana) by the same method as previously reported [7-10]. The spindle cells were diffusely positive for desmin, alpha-smooth muscle actin (Figure 3A), but negative for CD34, c-kit, and S-100 protein. Ki-67 labeling index was less than 1%. Ki-67-positive atypical squamous cells were observed in the entire layer of squamous epithelium (Figure 3B), but overexpression of p53 protein was not noted.

According to these results, an ultimate diagnosis of coexistence of esophageal SCC in situ (high-grade intraepithelial neoplasia) overlying leiomyoma was made. There have been several reports of esophageal SCC overlying benign submucosal tumor [5]. Iwaya et al. have summarized the previously reported 13 cases of esophageal SCC overlying benign submucosal tumor [5]. The most common histopathological subtype of submucosal
Esophageal SCC overlying leiomyoma

Figure 1. Endoscopic examination showing a well-circumscribed submucosal tumor in the esophagus.

Figure 2. Histopathological features. A: Squamous cell carcinoma in situ (arrows) overlying submucosal tumor. HE, x 40. B: Fascicular growth of the spindle cells with eosinophilic cytoplasm and bland cigar-shaped nuclei. HE, x 200. C: Proliferation of atypical squamous cells with large round nuclei in the entire layer of the squamous epithelium. Mitotic figures are scattered. HE, x 200.

Figure 3. Immunohistochemical features. A: Desmin is expressed in the spindle cells. x 40. B: Ki-67-positive atypical squamous cells are present in the entire layer of the squamous mucosa. x 200.

most of the SCC had invaded into the lamina propria [5]. The present case is the fifth documented case of esophageal SCC in situ overlying leiomyoma. Table 1 summarizes the clinicopathological features of the four previously reported cases as well as the present one [11-13]. All cases were middle-aged to elderly Japanese patients, and males were preferentially affected (male: female 4:1). Leiomyoma
Esophageal SCC overlying leiomyoma

Table 1. Clinicopathological features of esophageal squamous cell carcinoma in situ overlying leiomyoma

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age/Gender</th>
<th>Size of leiomyoma (mm)</th>
<th>Origin of leiomyoma</th>
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