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【 CASE REPORT 】

A Case of Superficial Primary Malignant Melanoma of the Esophagus Detected and Treated at Stage 0

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Abstract:
The patient was a 79-year-old male. At three years and eight months after his initial presentation, upper gastrointestinal endoscopy revealed a black-flattened elevated lesion in the middle third of the esophagus, which was diagnosed as malignant melanoma on biopsy. No lymph node or distant metastasis was found. A diagnosis of cT1bN0M0 Stage I was thus made. We performed a robot-assisted, minimally invasive esophagectomy and D2 dissection. The postoperative diagnosis was pT1a(MM), N0, M0, vascular invasion+, stage 0. The patient was recurrence-free for 14 months after surgery. We presume that an aggressive biopsy diagnosis is important for the early detection of malignant melanoma.

Key words: esophageal malignant melanoma, primary malignant melanoma, Stage0, esophageal melanosis

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I. Introduction

Primary malignant melanoma of the esophagus is a rare disease, accounting for from 0.3% to 0.4% of all primary malignant esophageal tumors in Japan (1). Although the prognosis has improved in recent years, it still has a poor prognosis, with a 5-year survival rate of 30.7% to 37% in surgical cases (2, 3). In this report, we describe a case of primary malignant melanoma of the esophagus that was diagnosed during the follow-up of melanosis and underwent surgical treatment at Stage 0.

II. Case Report

A 79-year-old asymptomatic man underwent an upper gastrointestinal endoscopy as part of a routine physical examination. He had a medical history of type 2 diabetes mellitus, dyslipidemia, hypertension, and benign prostatic hyperplasia. He had been a heavy smoker until the age of 63, consuming 40 cigarettes a day, but he only occasionally drank alcohol.

Current medical history: Esophageal melanosis was noted during upper gastrointestinal endoscopy at a medical checkup 3 years and 4 months prior to presentation (Fig. 1). However, a biopsy was not performed.

A second upper gastrointestinal endoscopy revealed a black, map-like flattened lesion in the middle thoracic region to the lower esophagus, where melanosis had been present, and a biopsy confirmed a diagnosis of malignant melanoma.

At the time of the initial examination, there were no subjective symptoms or pigmentation of the skin or mucous membranes. Blood tests showed no abnormality other than mild anemia with Hb 9.1 g/dL. Tumor markers, such as CEA, CA19-9, and SCC were all negative.

Close examination of the upper the gastrointestinal endoscopy findings revealed a map-like black-flattened lesion extending 27 to 34 cm from the incisor row. The black mucosa was partially interspersed with the dark brown mucosa (Fig. 2). Iodine staining showed that the lesion was not stained, and the “tatamime” sign of the lesion itself was partially irregular and thickened (Fig. 3).

Contrast-enhanced CT tomography revealed no lymph node or distant metastases. On PETCT, there was a slight accumulation of the lesion in the posterior neck region, but no skin metastasis was observed. No other abnormal accumulations were observed throughout the patient’s body.

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In the biopsy tissue specimens, HE staining showed atypical cells with melanin deposition centered on the basal portion of the stratified squamous epithelium, and junctional melanocytic activity was found. Melan-A staining also showed an increased number of positive cells in the basolateral to middle layers of the epithelium, leading to the diagnosis of malignant melanoma (Fig. 4). Based on the above, the preoperative diagnosis was primary malignant melanoma of the esophagus (cT1bN0M0 Stage I), and robot-assisted minimally invasive esophagectomy with D2 dissection was performed.

In the resected specimen, atypical cells containing melanin proliferated in an alveolar form, invaded the lamina propria, and partially reached the muscularis mucosa. EVG staining (Elastica van Gieson staining) revealed atypical cells in the vein; therefore, we diagnosed it as being positive for venous invasion (Fig. 5). The final diagnosis was primary esophageal malignant melanoma (pT1a-MM, pN0, cM 0, Stage 0, INFa, ly0 (D2-40), v1a (EVG), pIM0, pPM0 (15.6 mm), pDM0 (40 + 100 mm), and pRM0) (Fig. 6). No nodal metastases were observed. It has been 20 months since the surgery, and there has been no recurrence.

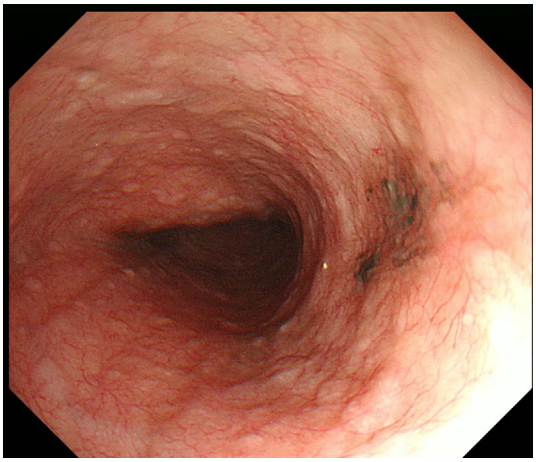

Figure 1. The lesions are flatter and lighter in color due and the vascular permeability is relatively good.

III. Discussion

In general, the incidence of primary esophageal malignant melanoma is 0.1-0.2% (2) of all esophageal malignancies. The average age of onset is 60.5 years old, which is younger than that of patients with esophageal cancer. It is more common in men than in women at a ratio of 2:1. Dysphagia is the most common symptom, accounting for 64.2-75%, followed by epigastralgia (6.2-69%) (4, 5). Regarding the lesion site, the middle to lower esophagus is the most common site in 76.2% to 90% of patients (6, 7). In addition, 85% of the patients had hyperpigmentation, while 15% were apigmented. It has also been reported that 50% of patients had already metastasized to distant locations at the time of diagnosis, thus making early detection difficult (4, 8).

The frequency of melanosis is estimated to range from 0.07% to 2.1% in the esophagus of healthy individuals, whereas 25% to 30% of patients with primary malignant melanoma of the esophagus have been reported to have melanosis. In addition, melanosis is often found in the middle and lower esophagus, a common site of malignant melanoma, and it is significantly more common in males (male: female = 1.8:1), suggesting that melanosis may be a precursor lesion of malignant melanoma (9, 10).

The gross findings of malignant melanoma on endoscopy include many lesions protruding into the lumen (3,4). In early lesions, such as in this case, superficial and flat types are also seen. It is difficult to distinguish between flat malignant melanoma and melanosis based solely on the endoscopic findings.

The key to distinguishing melanoma from melanosis is that, in malignant melanoma, the lesions are slightly thicker and darker in color, and light penetration of tumor cells is low, making it difficult to observe deep dendritic vessels.,

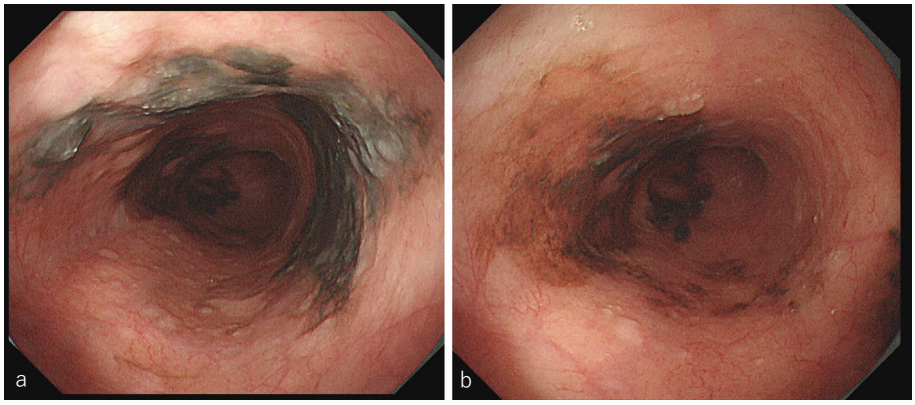

Figure 2. a: Observed from incisor row 25 cm. b: Observed from incisor row 28 cm. Close examination of the upper gastrointestinal endoscopy revealed a map-like black-flattened lesion extending 27-34 cm from the incisor row. The black mucosa was partially interspersed with the dark brown mucosa.

whereas in melanosis, the lesions are flatter and lighter in color due to low proliferative capacity, and vascular permeability is relatively good (11). In addition, although biopsy of malignant melanoma is conventionally not considered to be indicated, there have been no reports of metastasis or dissemination after biopsy, and it has been reported that the presence or absence of biopsy has no effect on the prognosis (3). Therefore, in order to obtain a definitive diagnosis, many reports suggest that a biopsy should be performed when a suspicious lesion is detected by endoscopy (12-15).

The accuracy of diagnosis using a preoperative biopsy has been reported to be low, ranging from 54% to 57.9% (16, 17). In a review of cases reported in Japan, the accuracy was 80.7%, which was higher than that reported overseas (3, 15) but still low. Factors contributing to the low diagnosis rate on preoperative biopsy include the fact that approximately 15% of primary malignant melanomas of the esophagus are anaplastic (4), and that performing a differential diagnosis from melanosis is difficult.

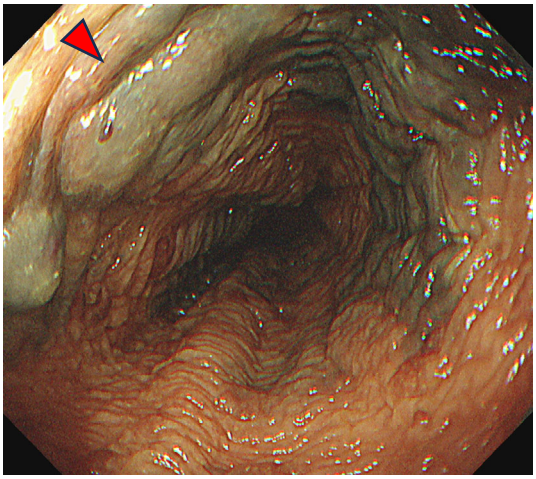

Figure 3. Iodine staining showed that the lesion was not stained, and the "tatamime" sign of the lesion itself was partially irregular and thickened (red arrow).

In 1989, Sabanathan et al. reported a mean survival of 9.8 months and a 5-year survival rate of 4.2% for 134 patients undergoing surgery (16). Subsequently, Volpin et al. reported a 5-year survival rate of 37% in 25 patients who underwent surgery between 1989 and 2000 (2). Yamaguchi et al. reported a 1-year survival rate of 74.1% and a 5-year survival rate of 30.7% for 72 cases reported in Japan from 1993 to 2003; the survival rate has improved in recent years (3). One reason for this is the increase in the number of cases detected early because of the widespread use of endoscopic examinations. Yamaguchi et al. reported that 50% of the cases were detected at stages 0, I, and II. The 5-year survival rate for each stage was 62.9% for stages 0 and I, 26.5% for stages II and III, and 8.9% for stages IVa and IVb. They reported a rapid deterioration in the prognosis as the disease progressed. Prognostic factors other than the stage classification were age (>60 years), depth (T2 or deeper), lymph node metastasis, distant metastasis, and the tumor size did not play a role in the prognosis.

Cases such as the present case, which are detected at stage 0, are rare. Of the cases reported in Japan in which malignant melanoma was discovered during the follow-up of melanosis, four cases, including the present case, were reported up to Stage I (Table); (18-20).

The mean survival was 74.5 months for Stage 0 and 14.9 months for Stage I, thus showing a large discrepancy (21). Since 14% of patients with Stage I disease relapse, adjuvant chemotherapy should be administered to patients with SM or deeper disease (22). As this case was stage 0, no additional chemotherapy was administered. Nivolumab, an immune checkpoint inhibitor, has recently become the first-line drug in the guidelines for malignant melanoma of the skin (23). In the event of recurrence, nivolumab is considered the first-line drug with the hope that it will be effective.

Compared with Stage 0 cases, the cases detected at Stage

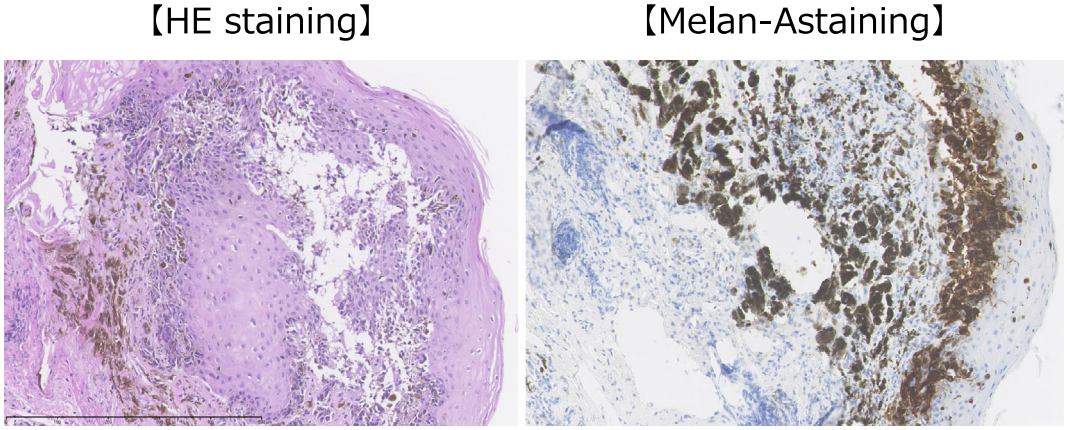

Figure 4. a: Hematoxylin and Eosin staining showed atypical cells with melanin deposition centered on the basal portion of the stratified squamous epithelium, and junctional melanocytic activity was found. b: Melan-A staining also showed increased positive cells in the basolateral to middle layers of the epithelium.

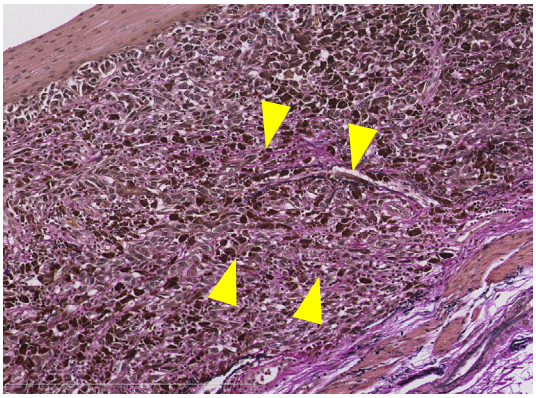

Figure 5. EVG staining (Elastica van Gieson staining) revealed atypical cells in the vein (yellow arrow).

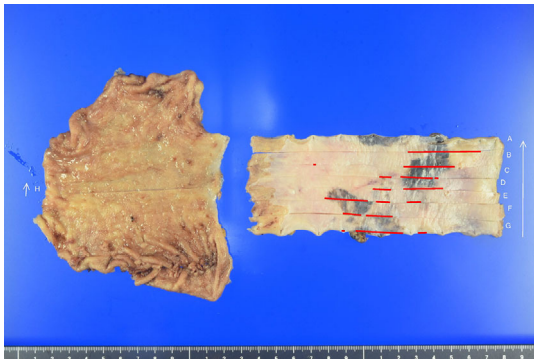

Figure 6. Primary esophageal malignant melanoma (red lines indicate lesions) [pT1a-MM, pN0, cM0, Stage0, INFa, ly0 (D2-40), v1a (EVG), pIM0, pPM0 (15.6 mm), pDM0 (40+100 mm), pRM0].

Table.

	Author	Age	SeX	Symptom	Timing of melanosis indication	Location	Endoscopic findings	Final stage	treatment	Out come
1	2013 Kato	71	M	-	2 years ago	Mt	black 0-Ip	pT1bN0M0 StageI	surgery* + Chemo**	>10M
2	2014 Osuga	70	M	-	2 years ago	Mt	black 0-IIb	pT1aN0M0 Stage0	ESD	>15M
3	2019 suzuki	70s	F	-	4 years ago	U~Mt	black 0-I+IIb	pT1bN0M0 StageI	surgery*	>5Y
4	this case	79	M	-	3years 4month ago	Mt	black 0-IIa	T1aN0M0 Stage0	RAMIE*** + D2	>20M

* Right-thoracotomy+D2

**DAC+tam

***Robot-assited minimally invasive esophagectomy

I had an interval of 2 years or more between endoscopic examinations. One of the three patients had symptoms of chest tightness. This is a rare case in which the patient was asymptomatic and at stage 0, even though the interval between endoscopic examinations was 3 years and 4 months. Although the association between melanosis and malignant melanoma has not been reported in many cases and thus requires further investigation, it is important to follow up such cases with endoscopy within a short period of time, from 6 months to at least 1 year, and to perform an aggressive biopsy if there are findings suggestive of malignant melanoma.

IV. Conclusion

We herein described a case of primary malignant melanoma of the esophagus that developed during a follow-up for melanosis, which had been treated surgically at Stage 0.

The authors state that they have no Conflict of Interest (COI).

Human/Aminal Rights: All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and in line with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent: Informed consent was obtained from all the patients included in the study.

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