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Cutaneous metastasis from esophageal basaloid squamous cell carcinoma: A case report

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ABSTRACT

INTRODUCTION AND IMPORTANCE: Basaloid squamous cell carcinoma (BSCC) of the esophagus is a relatively rare histologic variant of squamous cell carcinoma. Here, we reported a case of solitary cutaneous metastasis as the first symptom of esophageal BSCC and was successfully treated with multidisciplinary treatment.

CASE PRESENTATION: A 67-year-old man visited a local hospital with symptoms of dysphagia and cutaneous nodules on his left shoulder. Fluorine-18 fluorodeoxyglucose positron emission tomography revealed hypermetabolic accumulations in the middle thoracic esophagus, right recurrent laryngeal nerve lymph node, and epidermis of the left shoulder. Esophagogastroscopy revealed an ulcerative and infiltrating type tumor in the middle thoracic esophagus. Based on histopathologic examination of the endoscopic biopsy and the resected cutaneous tumor, the patient was diagnosed as esophageal BSCC with cutaneous metastasis. The patient was treated with chemotherapy followed by chemoradiotherapy. The therapeutic effect was a complete response, which was sustained for 39 months.

CLINICAL DISCUSSION: Review of previous literature in the PubMed database revealed only been two case reports on cutaneous metastasis of BSCC. Advanced BSCC of the esophagus with distant metastasis has a poor prognosis. Therefore, in our case, future careful follow-up is required.

CONCLUSION: Esophageal BSCC with cutaneous metastasis can be successfully managed by multidisciplinary treatment, including local resection of the cutaneous metastasis, systemic chemotherapy, and chemoradiotherapy.

1. Introduction

Cutaneous metastasis from esophageal cancer is rare, with a reported incidence of less than 1% [1]. Although cutaneous metastases are usually recognized as the end-stage of advanced cancer, cutaneous lesions might herald the discovery of primary cancer [1,2]. Basaloid squamous cell carcinoma (BSCC) of the esophagus is a relatively rare histologic variant of squamous cell carcinoma (SCC) and accounts for 0.068%–4% of all esophageal carcinoma cases [3]. Here, we reported a case of solitary cutaneous metastasis as the first symptom of esophageal BSCC and was successfully managed with multidisciplinary treatment. Immunohistochemical staining was useful in differentiating between cutaneous metastasis and primary cutaneous cancer. We hope that this case will be instructive for the diagnosis and treatment of future cases. This work has been reported in line with the SCARE 2020 criteria [4].

2. Presentation of case

A 67-year-old Japanese man visited a local hospital with symptoms of dysphagia and cutaneous nodules on his left shoulder in August 2017. Skin biopsy was suspicious for basal cell carcinoma, but no definitive diagnosis was obtained. Thereafter, he was referred to the Department of Dermatology of our hospital for further examination. He had a history of type 2 diabetes mellitus, hypertension, hyperuricemia, and old myocardial infarction, for which he had been receiving medical treatment. He had no other symptoms, pertinent family history, genetic disease, and pertinent psychosocial history. He smoked 20 cigarettes a day for 50 years. He had no allergies or known adverse reactions to any medications.

On physical examination, we found the presence of a 30 × 25-mm hard, stone-like, and red mass on the left shoulder (Fig. 1). He had no other physical findings. Laboratory investigation was unre-

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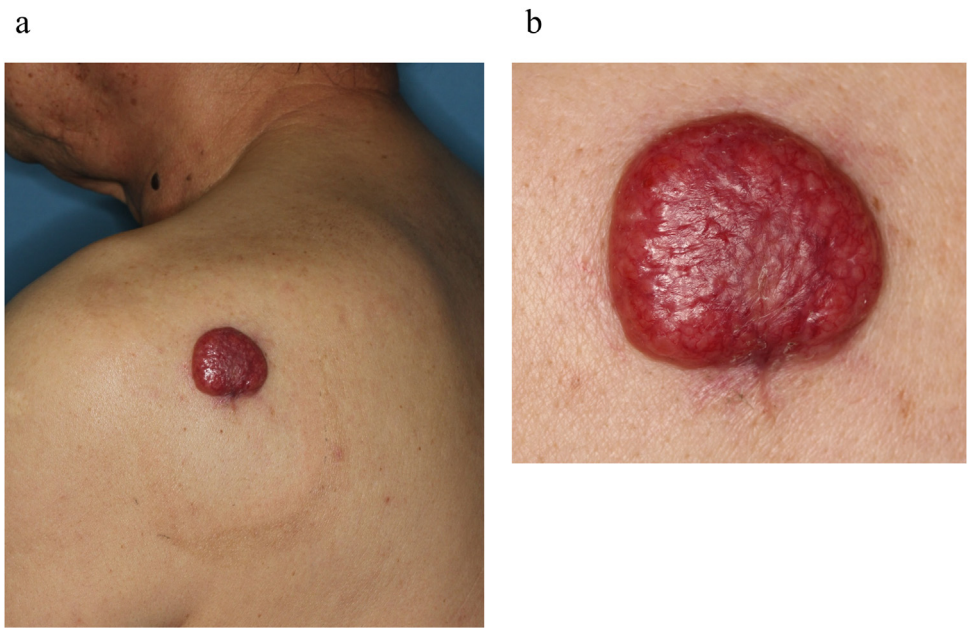

Fig. 1. Macroscopic findings of the subcutaneous lesion.
(**a**) A stone-like and red mass measuring 30 × 25 mm is seen on the left shoulder. (**b**) An enlarged view of the tumor.

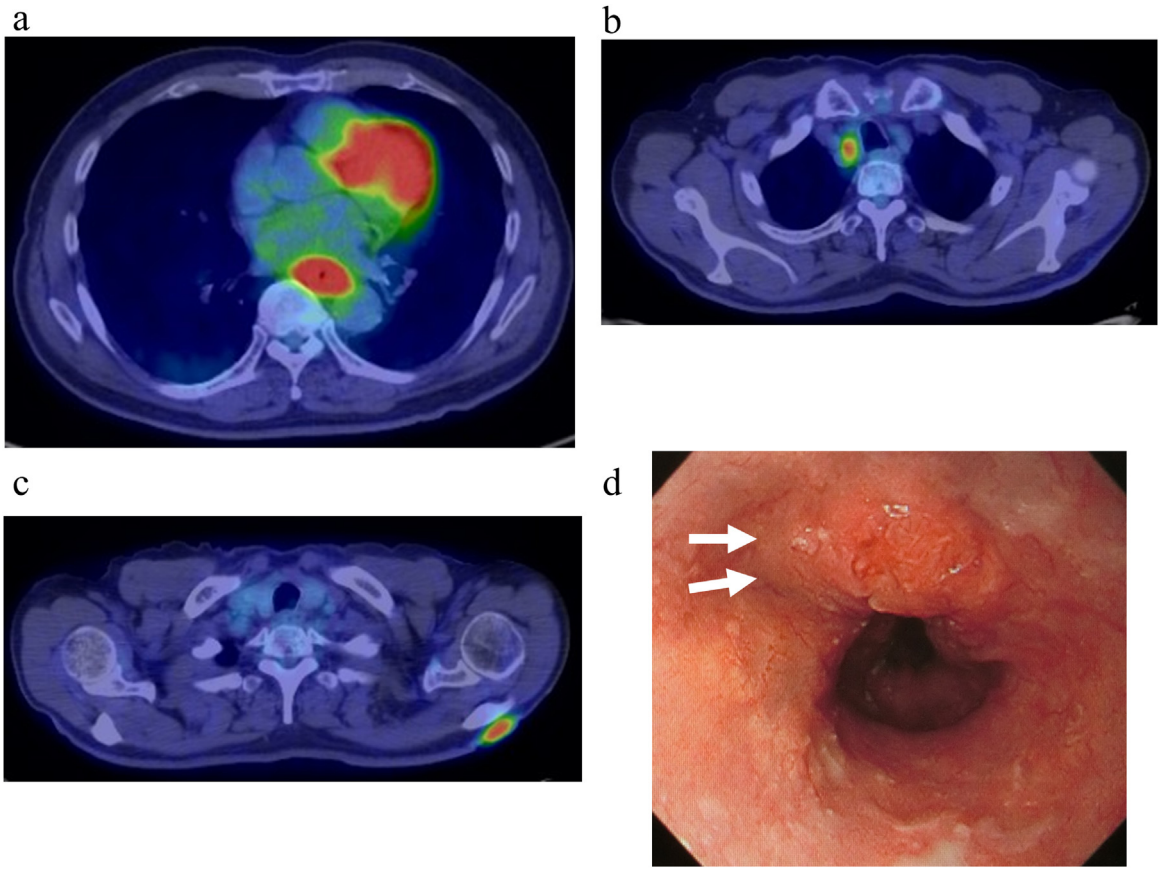

Fig. 2. Image findings of the esophageal carcinoma.
Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography reveals (**a**) hypermetabolic accumulation in the middle thoracic esophagus with an SUVmax of 11.0, (**b**) right recurrent laryngeal nerve lymph node with SUVmax of 4.4, and (**c**) the epidermis of the left shoulder with an SUVmax of 5.0. (**d**) Esophagogastroscopy reveals an ulcerative and infiltrating type tumor (white arrow) in the middle thoracic esophagus.
SUVmax: maximum standardized uptake value.

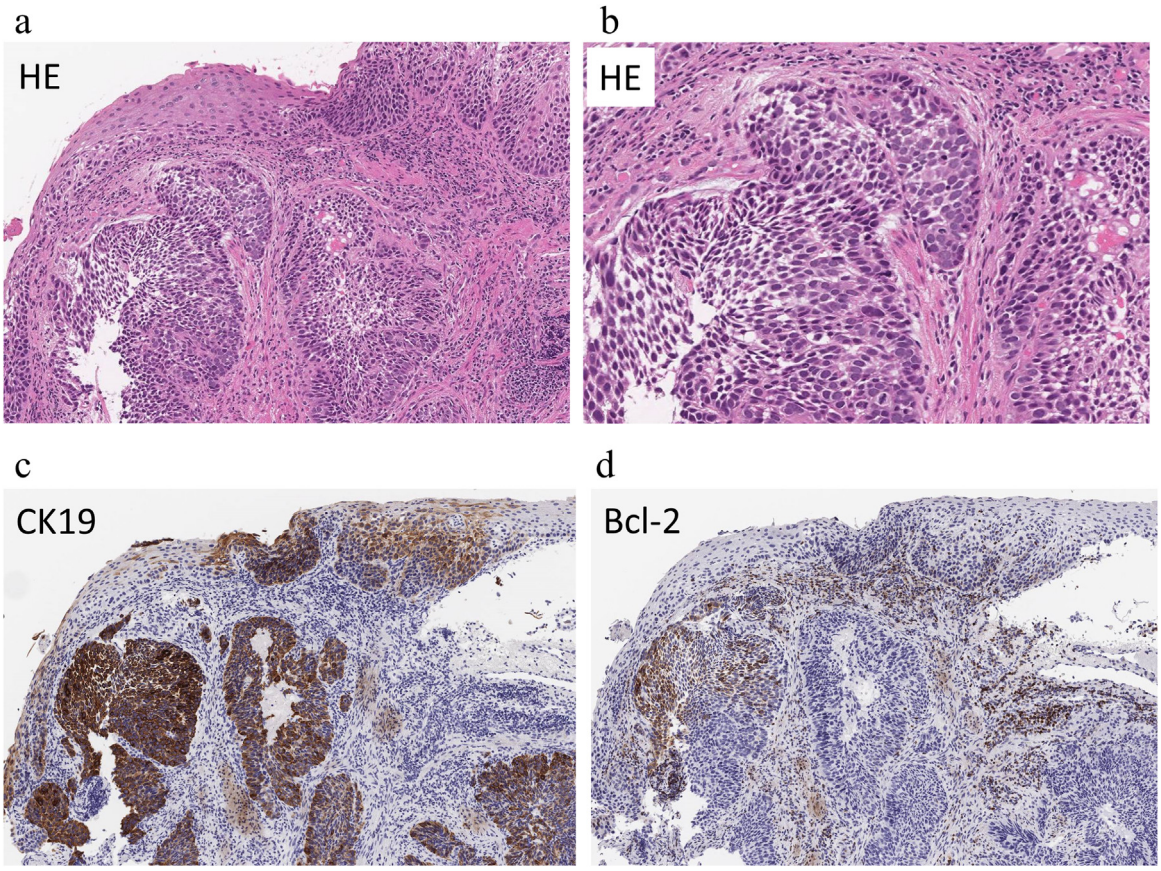

Fig. 3. Microscopic findings of the esophageal tumor biopsy.
(**a**) There is infiltration of atypical cells with solid nest (HE stain, ×100). (**b**) Tumor cells with round to oval or short spindle-shaped nuclei are observed (HE, ×200). Immunohistochemical staining is positive for (**c**) cytokeratin 19 (×100) and (**d**) Bcl-2 (×100).
HE: hematoxylin–eosin.

markable. For the tumor markers, carcinoembryonic antigen was slightly increased (5.4 ng/mL), and squamous cell cancer antigen was within normal limits (1.2 ng/mL). Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (CT) revealed hypermetabolic accumulations in the middle thoracic esophagus with a standardized uptake value (SUV)max of 11.0, right recurrent laryngeal nerve lymph node with an SUVmax of 4.4, and epidermis of the left shoulder with an SUVmax of 5.0 (Fig. 2a–c). Esophagogastroscopy revealed an ulcerative and infiltrating type tumor in the middle thoracic esophagus (Fig. 2d). Histopathologic examination of the endoscopic biopsy (Fig. 3) revealed infiltration of atypical cells with solid nest and round to oval or short spindle-shaped nuclei and chromatin-stained nuclei, similar to basal cells. There was a poor tendency for keratinization. Immunohistochemical staining for cytokeratin 19 and Bcl-2 was positive, thereby, pointing to a diagnosis of BSCC rather than SCC. Therefore, the esophageal tumor was diagnosed as BSCC.

The cutaneous tumor on the left shoulder was resected with a 5-mm margin for a definitive diagnosis by the dermatologist who had sufficient experience at our university hospital. Histopathologic examination of the resected tumor (Fig. 4) showed growth of tumor cells with solid nest and round or short spindle-shaped nuclei and the absence of continuity with the epidermis. There were no findings consistent with basal cell carcinoma. Immunohistochemical staining was positive for cytokeratin 19 and Bcl-2. Based on the similar histopathologic and immunohistochemical findings between the cutaneous tumor and the esophageal biopsy, the patient was diagnosed as clinical T3N1M1 stage IVB esophageal BSCC with cutaneous metastasis, according to the 8th edition of the Union for International Cancer Control classification [5] and was referred to our department for the treatment of esophageal BSCC.

From October 2017, the patient was initially administered with triple chemotherapy with bi-weekly docetaxel, cisplatin, and 5-fluorouracil. The patient received docetaxel (30 mg/m^2) on days 1 and 15, cisplatin (80 mg/m^2) on day 1, and 5-fluorouracil (800 mg/m^2) on days 1–5 every four weeks. After four courses of chemotherapy, the therapeutic effect evaluated by CT was partial response (Fig. 5a–c). Distant metastasis was not seen on CT. Next, chemoradiotherapy (CRT) was given for BSCC in March 2018. The CRT regimen comprised cisplatin (70 mg/m^2) on days 1 and 29, 5-fluorouracil (700 mg/m^2) on days 1–4 and 29–32, and a total of 60 Gy radiotherapy in 30 fractions. The therapeutic effect after CRT was a complete response (Fig. 5d–f). Histopathologic examination of the biopsy from the scar in the primary tumor showed no evidence of cancer. The patient was continued on oral administration of S-1 (tegafur/gimeracil/oteracil), for one year as adjuvant chemotherapy. No serious treatment-related adverse events were observed. During the course of treatment, the patient was fully convinced and agreed with the treatment plan. There were no changes to the planned treatment during the course of chemotherapy and CRT. During a meticulous follow-up with blood tests and CT every three months at our university hospital, he has remained alive and disease-free at 39 months after diagnosis.

3. Discussion

BSCC of the esophagus is a variant of SCC and is characterized by the following histologic features: (1) solid growth of cells with

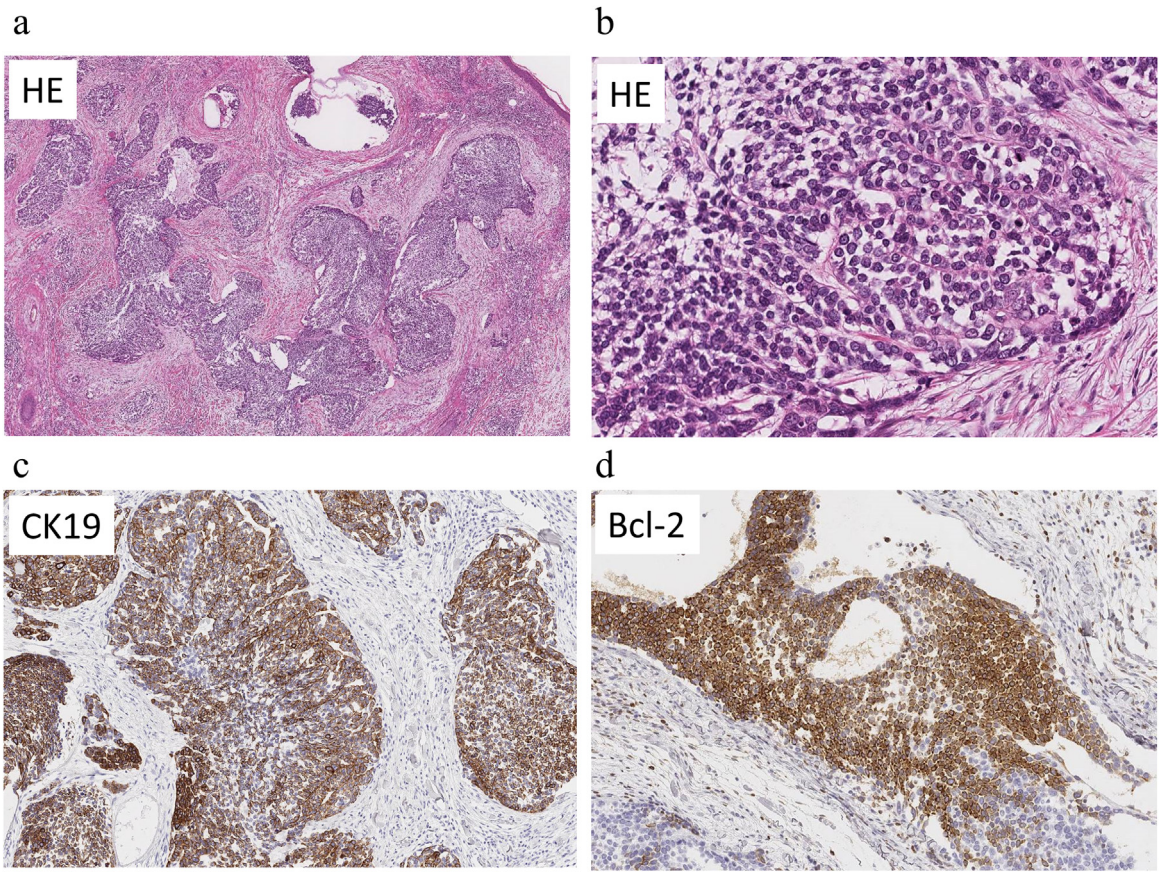

Fig. 4. Microscopic findings of the resected cutaneous tumor.
(**a**) There is growth of tumor cells with solid nest and without continuity with the epidermis (HE, ×40). (**b**) The tumor cells have round or short spindle-shaped nuclei (HE, ×200). Immunohistochemical staining is positive for (**c**) cytokeratin 19 (×100) and (**d**) Bcl-2 (×100).
HE: hematoxylin–eosin.

nesting, lobular, or trabecular arrangement; (2) small crowded cells with scant cytoplasm; (3) hyperchromatic nuclei; (4) small cystic spaces containing materials that resemble mucus and stain positively with Alcian blue PAS; (5) comedo-like necrosis in the center of the basaloid cell nests; and (6) intimately associated dysplastic squamous cell epithelium, *in situ* SCC, invasive SCC, or islands of SCC among the basaloid cells [6]. However, accurate diagnosis of BSCC is difficult on an endoscopic biopsy specimen, because endoscopic biopsy could only reach the superficial and small parts of the tumor [7].

In our case, although the specific histopathologic findings of BSCC were not observed on hematoxylin–eosin staining, the positive immunohistochemical staining for cytokeratin 19 and Bcl-2 was useful for differential diagnosis. The immunoreactivity of cytokeratin 19 and Bcl-2 is high in BSCC but low in SCC [8–10]. Therefore, the patient was diagnosed as esophageal BSCC. On the other hand, the cutaneous tumor required differentiation from a primary cutaneous cancer. Histopathologic study of the resected cutaneous tumor, including immunohistochemical staining, showed features that were similar with those of the specimen from the esophagus. Therefore, the cutaneous tumor was diagnosed as metastasis from esophageal BSCC.

Esophageal BSCC with simultaneous solitary cutaneous metastasis is rare. On review of previous literature in the PubMed database, there had only been two case reports on cutaneous metastasis of BSCC [11,12]. Houston and Telepak reported a patient who had metastasis on the tip of the left finger, which appeared seven months after the diagnosis of BSCC [11]. Puri et al. reported subcutaneous recurrence of BSCC as a nodule on the nape of the neck, approximately two years after completing CRT. The patient had nodules on the abdominal wall and left index finger, with multiple simultaneous metastases to the lung, liver, and brain, and died eight months after the diagnosis of metastatic disease despite chemotherapy and radiation therapy [12].

A worse prognosis of esophageal BSCC than of SCC remains controversial [3]. Recently, some reports revealed that the survival time of patients with BSCC was lower, compared with that of patients with well-differentiated SCC, but was not different, compared with that of patients with moderately or poorly differentiated SCC [6,9]. In any case, advanced BSCC of the esophagus with distant metastasis has a poor prognosis. Zhang et al. reported that distant metastasis was the most frequent failure pattern, with a median recurrence time of 10 months [7]. In our case, the patient was treated with chemotherapy first, because he had stage IV BSCC with cutaneous metastasis. After chemotherapy, we confirmed the absence of new metastatic lesions, including cutaneous metastasis. Although radical esophagectomy was an option for esophageal BSCC at that point, the patient did not consent to undergo surgery because of the past history of myocardial infarction and the risk for heart disease. Therefore, he was treated with CRT. In this case, complete response was obtained after multidisciplinary treatment with local resection of the cutaneous metastasis, systemic chemotherapy, and CRT. However, as mentioned above, recurrence in multiple lesions, including subcutaneous lesions after CRT had been reported [12]. Therefore, in our case, although more than two years have passed after treatment, future careful follow-up is required.

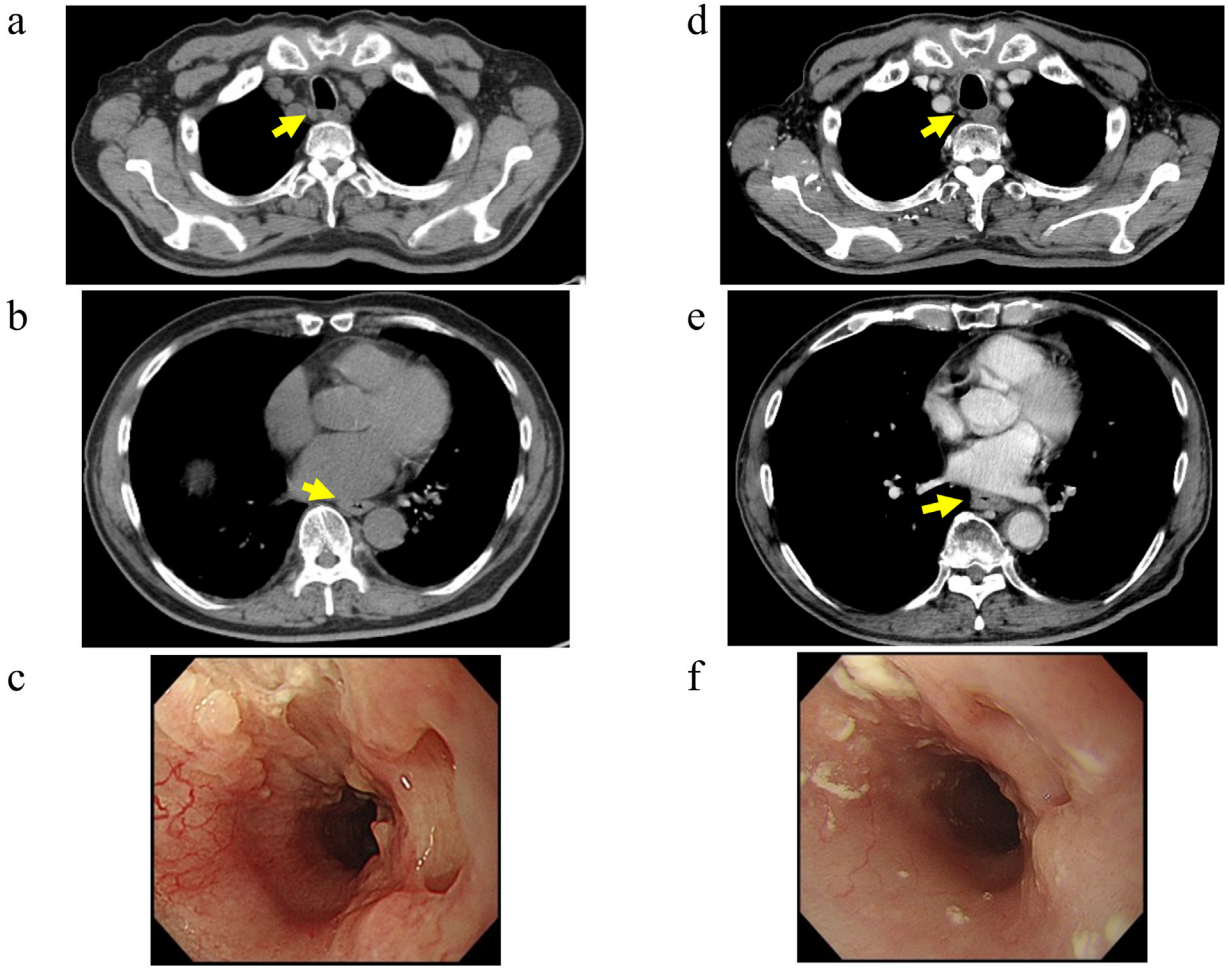

Fig. 5. Image findings after chemotherapy and chemoradiotherapy.
Computed tomography after four courses of chemotherapy reveals (**a**) decrease in the size of the right recurrent laryngeal nerve lymph node metastasis (yellow arrow) and (**b**) improvement of the wall thickness of the primary esophageal tumor (yellow arrow). (**c**) Esophagogastroscopy after chemotherapy reveals tumor shrinkage and tumor flattening of the middle thoracic esophagus. Computed tomography after chemoradiotherapy followed by chemotherapy shows (**d**) further reduction of the right recurrent laryngeal nerve lymph node metastasis (yellow arrow) and (**e**) resolution of the wall thickness in the thoracic esophagus (yellow arrow). (**f**) Esophagogastroscopy after chemoradiotherapy shows further tumor flattening in the middle thoracic esophagus.

4. Conclusions

We reported a rare case of esophageal BSCC that initially manifested as a cutaneous metastasis. The patient was successfully managed with multidisciplinary treatment, including local resection of the cutaneous metastasis, systemic chemotherapy, and CRT. Early definitive diagnosis and multidisciplinary treatment may improve the prognosis of stage IV BSCC with cutaneous metastasis.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

This case report was exempted from ethics approval by our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

FE and YA conceived this case presentation and drafted the manuscript.

MO and AS participated in the supervision of this case presentation.

NU and TS determined the pathologic diagnosis of the patient.

All authors read and approved the final manuscript.

Registration of research studies

Not applicable.

Guarantor

Yuji Akiyama.

Provenance and peer review

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