Rare presentation of esophageal squamous cell carcinoma with rectal metastasis: A case report

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Abstract. Esophageal cancer is usually diagnosed at an advanced stage, resulting in poor survival. The common sites of distant metastasis include lung, liver and bones. The present study reports a rare case of esophageal squamous cell carcinoma (SCC) with rectal metastasis. A 65-year-old man was diagnosed with middle thoracic esophageal SCC with multiple lymph node metastasis. The patient achieved good response after chemoradiotherapy and adjuvant chemotherapy. During following up, the computed tomography and magnetic resonance scans showed a mass in front of the rectum with intact mucosa. Biopsies were performed and histopathological findings showed SCC, consistent with metastasis from primary esophageal SCC. The patient subsequently received palliative chemoradiotherapy to the rectal tumour and survived for 5 months. To the best of our knowledge, the present case is the first report of metastatic rectal SCC from the esophagus. It is important to take a biopsy of this unexpected lesion for histological analysis, which can help to discriminate metastatic from primary cancer. The goal of treatment is palliative therapy to improve quality of life and survival for this metastatic disease.

Introduction

Esophageal carcinoma (EC) is one of the leading causes of cancer-associated mortalities, and the majority of EC in China are squamous cell carcinoma (SCC) (1). The characteristics of esophageal SCC are quite different from those of esophageal adenocarcinoma (EAC). The gene expression of ESCC is most semblable to that of head and neck squamous cell carcinoma, while EAC is most semblable to gastric adenocarcinoma (2). Esophageal SCC predominate in the upper and middle third of the esophagus and are associated with nitrosamine compounds, hot food, smoking and alcohol exposure, etc.

The symptoms are usually not obvious in early stage of EC. Therefore, most patients are diagnosed with advanced disease, resulting in poor survival. The common sites of metastasis are the lymph node, lung, liver and bones. Certain unexpected sites have been reported, such as the skin, eyes, muscles and breasts (3). Metastasis to the pelvic cavity from esophageal SCC is extremely rare, and the clinical manifestations are not typical. The standards for the diagnosis of these unexpected sites are less established. The present study reports a rare case of esophageal squamous cell carcinoma (SCC) with rectal metastasis, which may help us to have a better understanding for this disease.

Case presentation

A 65-year-old man was admitted to the Department of Radiation Oncology, First Affiliated Hospital of Anhui Medical University (Hefei, China) with dysphagia for >1 month at March 2018. Esophagoscopic evaluation revealed a protruding lesion of esophageal wall located 25-cm from the incisors, precluding passage of the endoscope (Fig. 1A). Histopathological findings showed SCC after biopsy (Fig. 1B and C). The barium swallow showed irregular esophageal stricture and destruction of esophageal mucosa in the upper-middle segment (Fig. 1D). A thickened esophageal wall and an enlarged lymph node in the left supraclavicular area were found on computed tomography (CT) scans of the neck, chest and upper abdomen (Fig. 1E and F). Fine-needle aspiration biopsy of this lymph node was performed, and a diagnosis of SCC was rendered. After a systematic evaluation, the patient received definite intensity modulated radiotherapy (IMRT) with 64.0 Gy in 32 fractions and two concurrent cycles of chemotherapy with paclitaxel and platinum. In addition, 2 additional cycles of adjuvant chemotherapy using the same regimens were admitted thereafter.

The patient achieved a clinical complete response; however, 1 year later, numerous enlarged paraaortic lymph nodes with no symptoms were found by a follow-up CT scan (Fig. 1G-I). The esophageal mucosa was normal (Fig. 1J) and there were no signs of metastatic spread in other sites. The patient received IMRT with 50.0 Gy in 25 fractions to the retroperitoneal area

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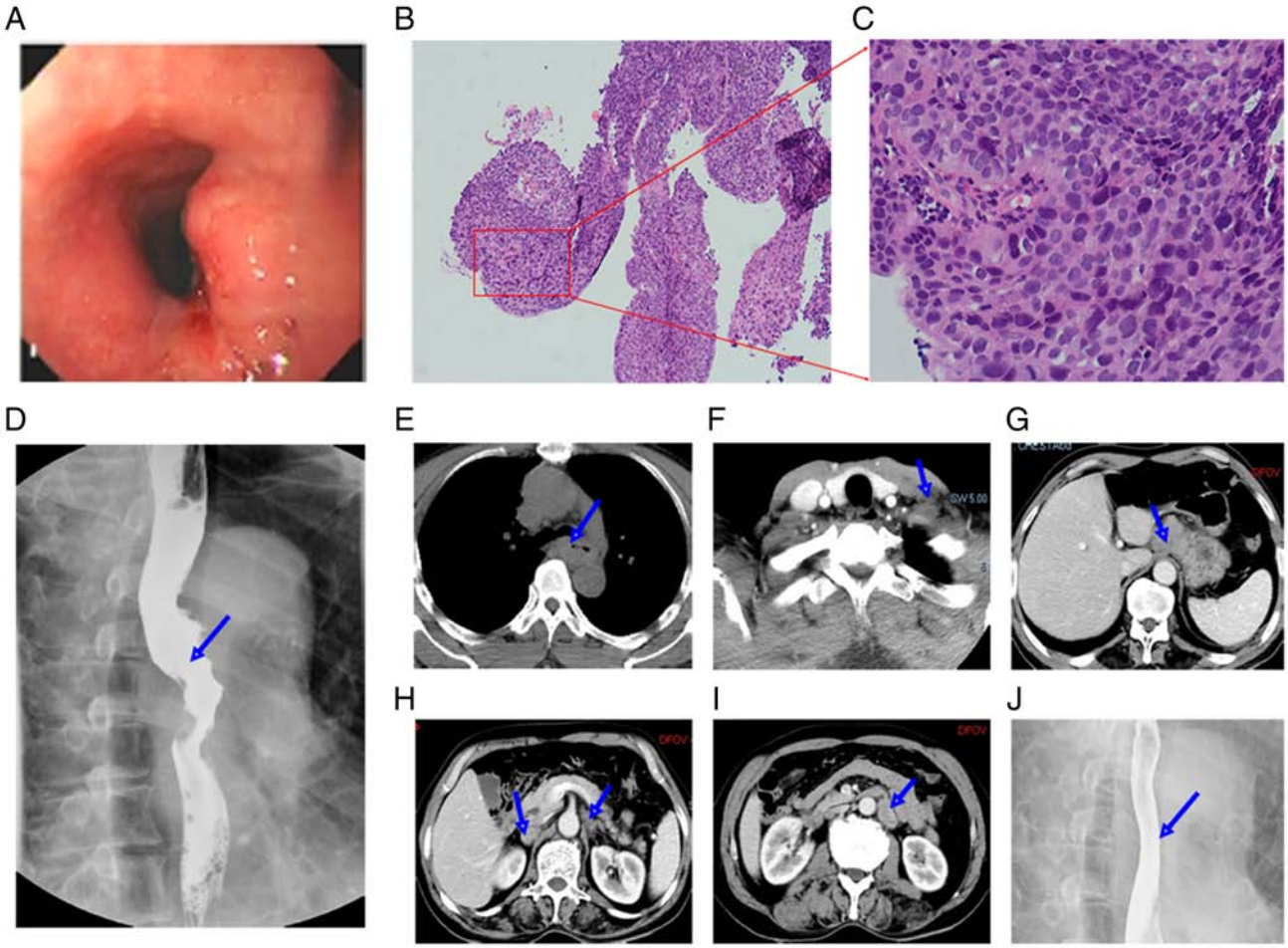

Figure 1. Esophageal squamous cell carcinoma with multiple lymph node metastases. (A) Endoscope showed a protrusion lesion of esophageal wall. Biopsy of esophageal lesions at a magnification of (B) x100 and (C) x400 showed middle differentiated squamous cell carcinoma (hematoxylin and eosin staining). (D) Barium esophagram demonstrated interruption and destruction of esophageal mucosa, and esophageal lumen stenosis. (E) Thickened esophageal wall on CT image. (F) An enlarged lymph node in station 104L. (G) Enlarged lymph node in station 7 on CT image. (H) Enlarged lymph nodes in station 13 and station 16a2 and (I) 16b1 on CT image. (J) Approximately normal esophageal mucosa after chemoradiotherapy. The arrows show the lesion locations. Lymph node stations based on Japanese Classification of Esophageal Cancer (4). CT, computed tomography.

and two cycles of chemotherapy with carboplatin and Tigeo capsule. Lymph node stations in the present study were based on the Japanese Classification of Esophageal Cancer of 11th edition (4).

The patient was not followed up regularly and returned to the hospital 8 months later. A mass in front of the rectum was found by a follow-up CT scan at the People's Hospital of Huoqiu County (Huoqiu, China). There were no symptoms of discomfort. A pelvic enhanced magnetic resonance (MR) scan revealed a mass in front of the rectum on the right side without invasion of the rectal mucosa (Fig. 2A-C). Serum tumor makers indicated that his carcinoembryonic antigen (CEA) level was slightly elevated (6.1 ng/ml). To make a definite diagnosis, a transrectal ultrasound-guided biopsy of the mass instead of colonoscopy was performed because the rectal mucosa was intact on MR images. Histopathological findings showed SCC with identical cytomorphology to the primary esophageal tumour (Fig. 2D and E). Immunohistochemical findings include positive CK5/6, p40 and p63 staining (Fig. 2F-H) and negative CK7, CDX-2 and Villin staining, which was consistent with a metastatic lesion from esophageal SCC. A CT scan of the neck, chest and abdomen demonstrated no obvious residual tumour. After a discussion with the patient, palliative IMRT with 36.0 Gy in 18 fractions and a cycle of concurrent chemotherapy with the Tigeo capsule was administered. Further treatment was refused because of diarrhea and a decrease in platelets ($32x10^9$/l). After discharge, the patient died 5 months later. The treatment timeline was shown in Fig. 3.

Discussion

EC is the seventh most common cancer and sixth most common cause of cancer-associated mortalities worldwide in 2020 (5). SCC and adenocarcinoma are the most common histological subtypes with quite different aetiologies (2). China has a high incidence rate, accounting for ~50% of the global total cases, and >90% of cases are SCC (1). Despite improvements in diagnosis and treatments, overall survival is still poor for EC. One important reason is that most patients are diagnosed at an advanced stage, making radical treatment difficult.

There are five main routes of metastasis for EC: i) Direct invasion; ii) lymphatic system; iii) hematogenous; iv) trans-peritoneal; and v) intraluminal implantation. The common

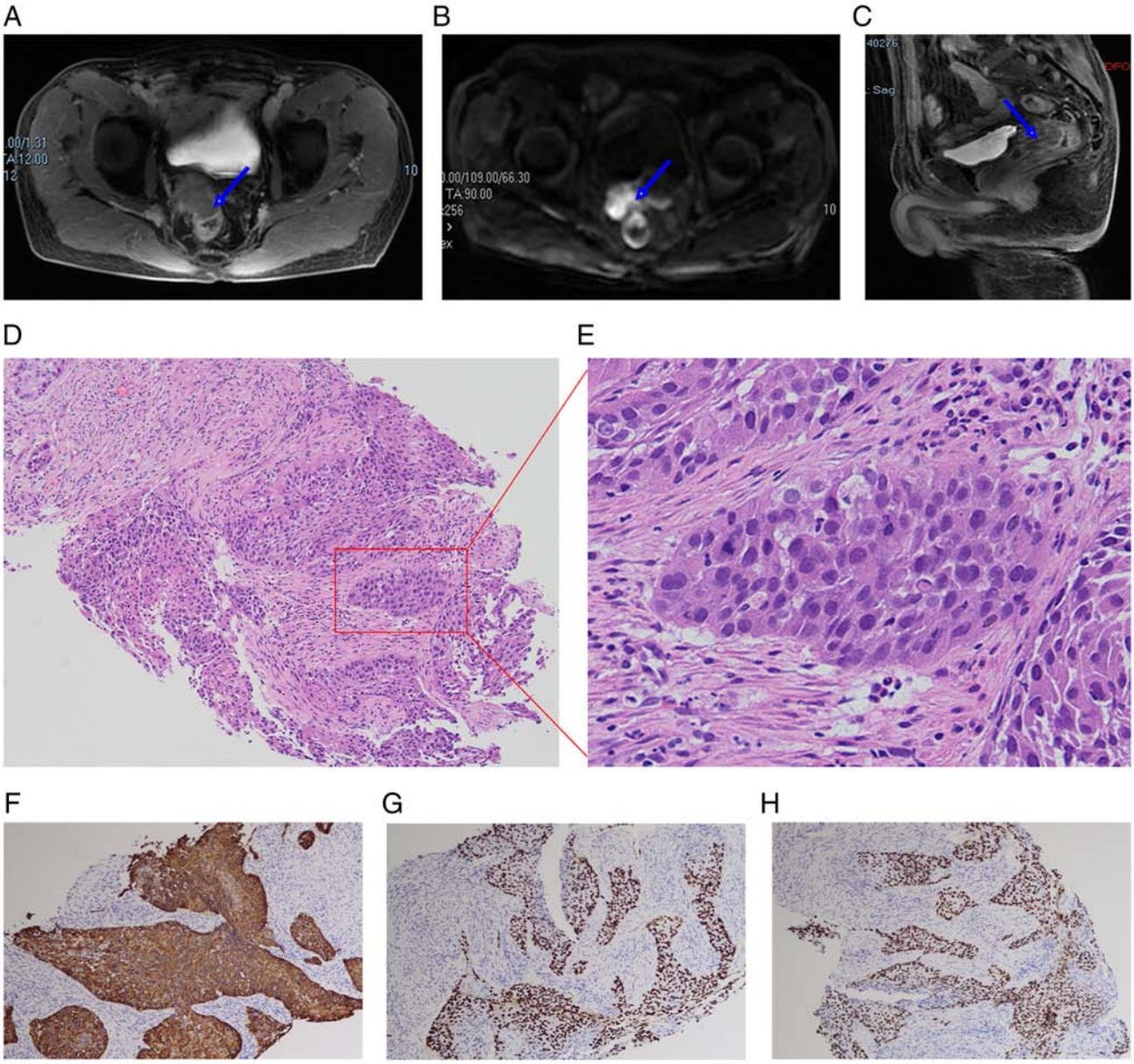

Figure 2. Magnetic resonance and histological results of the rectal mass. An irregular mass with intact mucosa anterior the middle rectum was shown on (A) transverse enhanced image, (B) transverse diffusion-weighted image and (C) sagittal enhanced image. The arrows show the lesion locations. Histopathological examination showed middle differentiated squamous cell carcinoma with identical cytomorphology to primary esophageal tumor at a magnification of (D) x100 and (E) x400 (hematoxylin and eosin staining). (F) Positive CK5/6, (G) p40 and (H) positive p63 staining. Magnification, x100.

metastatic sites are the lymph node, lungs, liver and bones. Occasionally, brain metastasis can be found in EC (6). Additionally, some unexpected sites have been reported, such as the skin, eyes, muscles and breasts (3). Table I summarizes the reported cases of colonic metastasis from esophageal SCC (7-14). To the best of our knowledge, rectal metastasis from esophageal SCC has not been previously reported.

Although it is rare, primary rectal SCC can also be found, accounting for ~0.3% of all rectal cancer (15). The etiology of primary rectal SCC remains unclear, and the most prominent theory is chronic inflammation leading to squamous metaplasia and subsequent carcinoma (16). To diagnose primary rectal SCC, four criteria were proposed by researchers (15,17): i) Absence of SCC in any other organ that may spread directly to rectum; ii) the affected rectum should not be involved in any squamous-lined fistula tract; iii) exclusion of the tumor being from proximal extension of anal SCC; and iv) confirmation of SCC by histopathology.

Given that rectal cancer can be SCC, metastatic rectal SCC should be discriminated from primary rectal SCC. Primary rectal SCC lesions usually have an appearance of lesions infiltrating from the mucosa gradually to the deep wall of the rectum. Histologically, it is not possible to determine whether it is of rectal or metastatic origin based on morphological characteristics. Features that led to classifying the present case as metastasis included the intact overlying mucosa of the rectum and histological features identical to those of esophageal tumour cells.

Metastatic involvement of the rectum out from pelvic tumors is rare. There are cases of metastatic rectal cancer from breast cancer (18), gastroesophageal adenocarcinoma (19) and gastric cancer (20). The hematogenous spread of circulating tumour cells

Table I. Published cases of colonic metastasis from esophageal squamous cell carcinoma.

Authors (year)	Age, years	Sex	Location	Symptom	Treatment	Survival from colonic metastasis	(Refs.)
Iwase *et al*, 2004	51	Man	Sigmoid	Bleeding	Chemotherapy	1 year	(7)
Shimada *et al*, 2014	64	Man	Transverse	None	Resection	2.5 months	(8)
Hasegawa *et al*, 2015	77	Man	Transverse	Pain	Resection	2 months	(9)
Garg *et al*, 2017	60	Man	Ascending	Bleeding	Radiation	6 months	(10)
Fang *et al*, 2017	63	Man	Sigmoid	Pain, nausea	Unknown	Unknown	(11)
Wiseman *et al*, 2020	71	Woman	Rectosigmoid	None	Radiation	6 months	(12)
Chen *et al*, 2022	68	Man	Ascending	None	Unknown	Unknown	(13)
Zhang *et al*, 2022	73	Woman	Transverse	None	Chemotherapy	Unknown	(14)

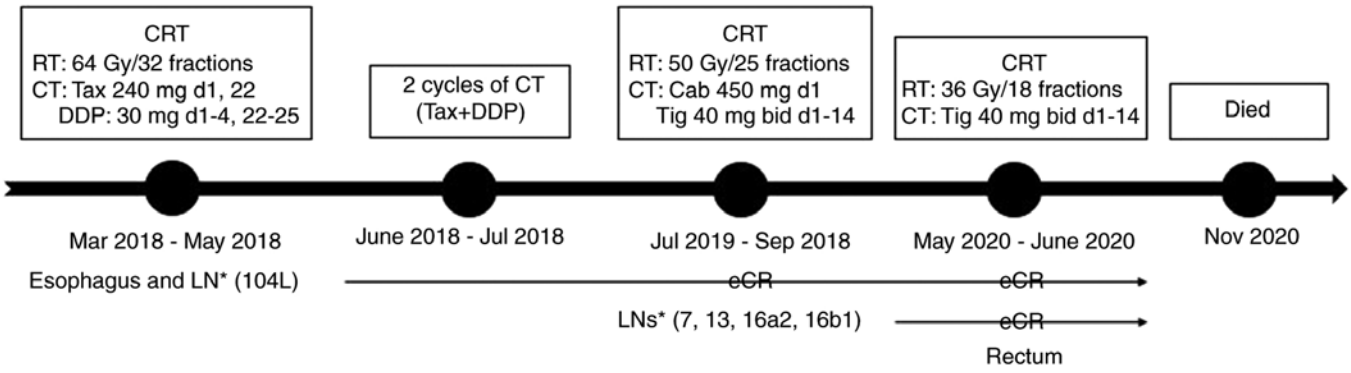

Figure 3. Timeline of treatments. *Lymph node stations based on Japanese Classification of Esophageal Cancer. Cab, carboplatin; cCR, clinical complete response; CRT, chemoradiotherapy; CT, chemotherapy; DDP, platinum; Tax, paclitaxel; Tig, tigeo; LN, lymph node.

is a plausible explanation for these distant metastases. Due to the complex lymphatic drainage of the esophagus, lymphatic spread may be another potential explanation (21). In the present case, there were extensive abdominal lymph node metastases without involvement of common distant organs. Therefore, retrograde lymphatic spread of cancer cells to the rectum should be considered, as has been proposed in cases of a Krukenburg tumor (22).

A pelvic examination is not usually a part of the workup for EC (23). The present case may heighten the awareness of unexpected metastasis to the pelvis, especially for patients with extensive abdominal lymph node metastases. Positron emission tomography (PET) may be helpful in detecting these unusual metastases (9,11). It is a limitation that PET was not performed in the present case report. For rectal tumors, MRI can help to find the tumour location and morphology and identify its relationship with surrounding structures (24). Biopsy is requested to determine the histological type and molecular markers of the tumour.

For patients with stage IV ESCC, systematic therapy or palliative care is recommended based on the Karnofsky performance in the National Comprehensive Caner Network (NCCN) guidelines (25). To improve quality of life and survival, a multidisciplinary approach is usually needed. The present patient received chemoradiotherapy to the rectum because the well-controlled tumor in other sites after chemoradiotherapy. In recent years, immunotherapy with PD-1 inhibitors has demonstrated promising activity in recurrent or metastatic esophageal SCC (26,27).

To the best of our knowledge, the present case is the first report of esophageal SCC with middle rectal metastasis. It is of utmost importance to take a biopsy of this unexpected lesion for histological analysis, which can help to discriminate metastatic from primary cancer. The goal of treatment with multidisciplinary approach is palliative therapy to improve quality of life and survival for this metastatic disease.

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Availability of data and materials

All data generated or analyzed during this study are available from the corresponding author on reasonable request.

Authors' contributions

YW contributed to the conception and design of the work. MK, LZ, SW and YZ collected the data and wrote the original

draft. MK, MY and YW contributed to the interpretation of data. YW revised the manuscript. SW and YW confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of First Affiliated Hospital of Anhui Medical University, Hefei, China (approval no. PJ2023-10-39).

Patient consent for publication

Written informed consent was obtained from the patient for the publication of anonymized data and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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