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Case Series

Esophageal Metastatic Adenocarcinoma Diagnosed with Endoscopic Ultrasound

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Keywords

Esophageal metastatic adenocarcinoma · Endoscopic ultrasound ·

Abstract

Metastasis to the esophagus from a distant primary cancer is a rare manifestation in a patient with a history of oncological disease presenting with obstructive upper gastrointestinal symptoms. Computed tomography of the thorax or esophagogastroduodenoscopy can be non-diagnostic as the disease tends to be submucosal. In such a situation, endoscopic ultrasound (EUS) with fine needle aspiration (FNA) can be directed to characterize and sample the submucosal esophageal lesion. We present a case series of metastatic esophageal strictures diagnosed with EUS and FNA.

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Introduction

Esophageal strictures occurring due to metastases arising from distant organs are rare and difficult to diagnose owing to the submucosal nature of the lesions. Computed tomography (CT) imaging would typically detect thickening of the esophageal wall without any ex-

trinsic or endoluminal mass. Gastroscopy would reveal an esophageal stricture with smooth and apparently benign-appearing overlying mucosa from which superficial biopsies would prove undiagnostic of metastatic disease.

Endoscopic ultrasound (EUS) allows for the visualization of lesions in the submucosa or muscularis propria as well as enlarged para-esophageal lymph nodes. Fine needle aspiration (FNA) can be targeted to obtain cytological diagnosis of metastatic disease. Such an approach has been evaluated with success in metastatic breast cancer [1], but as of now is not a widely known or adopted practice in the evaluation of metastatic esophageal strictures. We present here a case series of 5 patients with metastatic esophageal disease of various primary tumor origins for which EUS and FNA greatly aided in their diagnosis.

We reviewed the patient database records at Singapore General Hospital, a tertiary hospital in Singapore, over a period from 1993 to 2016, for patients with metastatic esophageal disease diagnosed using EUS and FNA.

Case Series

Case 1

A 77-year-old woman with metastatic non-small cell lung carcinoma presented 8 months after the diagnosis of lung cancer with dysphagia to solids and odynophagia. Her pain caused her to consume less food, to the extent that she had lost 10 kg of weight over the past 4 months. CT thorax showed a dilated fluid-filled esophagus with transition point at the gastro-esophageal junction without evidence of extrinsic obstructing lesion. She underwent esophagogastroduodenoscopy (EGD) which showed a tight esophageal stricture about 5 mm in diameter above the gastro-esophageal junction without any overlying suspicious mucosal changes. The stricture prevented further passage of the scope. EUS was then performed which showed the disruption of tissue planes and mass effect at the level of the stricture. FNA of the submucosa at the stricture revealed atypical cells positive for thyroid transcription factor-1 (TTF-1) on immunohistochemistry, consistent with metastasis from lung adenocarcinoma. An 18 × 100 mm covered stent was endoscopically placed across the stricture providing some resolution of her symptoms.

Case 2

A 57-year-old man with non-small cell lung carcinoma presented with vomiting immediately after meals, dysphagia to solid food, and retrosternal chest pain 6 months after diagnosis. CT thorax did not show any esophageal dilatation or extrinsic compressing masses. EGD found a 9-mm stricture at the gastro-esophageal junction with normal overlying mucosa which was biopsied and negative for malignant cells. EUS performed showed concentric thickening of the esophagus and cardia with thickened submucosa and loss of architecture. FNA of the submucosa yielded malignant cells positive for TTF-1, supportive of primary lung origin. The stricture was dilated up to 12 mm with a controlled radial extension balloon, and later dilated further to 15 mm at another procedure, providing significant resolution of the patient's symptoms.

Case 3

A 62-year-old woman with breast cancer presented with vomiting after meals 29 months after her diagnosis. Her vomiting had been going on for the past 3 weeks, and usually occurred 10 minutes following ingestion of solid food. She had lost 5 kg of weight over that period and was severely dehydrated. CT thorax showed esophageal dilation and thickening of the lower esophagus at the gastro-esophageal junction. EGD revealed a nodular esophageal tumor with distal structuring, estimated to be about 10 mm in diameter and passable by gastroscopy. EUS revealed a hypoechoic mass within the muscularis propria at the stricture, from which guided biopsies yielded atypical cells which stained positive for estrogen receptor and progesterone receptor, consistent with adenocarcinoma of breast origin. She was initiated on palliative chemotherapy and without further endoscopic procedures thereafter.

Case 4

A 70-year-old woman with breast cancer presented with dysphagia to solids of 1 month duration, 18 years after her initial diagnosis. CT thorax showed soft tissue thickening of the esophagus at the level of the aortic arch without mediastinal lymphadenopathy. EGD showed a 9-mm stricture above the gastro-esophageal junction with normal-looking mucosa. EUS showed a hypoechoic mass, infiltrating the adventitia, from which FNA samples were taken. Immunohistochemistry analysis of the FNA cells showed malignant cells positive for estrogen receptor and progesterone receptor and negative for TTF-1 and caudal type homeobox 2, consistent with adenocarcinoma of breast origin. An 8-Fr feeding tube was endoscopically placed across the stricture to allow for feeding.

Case 5

An 84-year-old woman with newly diagnosed cervical cancer presented with vomiting immediately after meals for the past 4 months. CT thorax showed dilated proximal thoracic esophagus with transition at the subcarinal region, suggestive of circumferential wall thickening, without extrinsic mass compression or mediastinal lymphadenopathy. EGD showed a 10-mm esophageal stricture with benign-appearing smooth mucosa. EUS revealed a small hypoechoic area on adventitia and enlarged para-esophageal lymph node from which FNA was obtained. Cytology from the lymph node yielded malignant cells suggestive of poorly differentiated squamous cell carcinoma, similar to her previous cervical biopsy cells. The patient underwent serial controlled radial extension balloon dilatations of the esophagus and her vomiting significantly improved.

Summary of Cases

Of the 5 cases identified, 4 were female. Mean age at diagnosis was 70 years (range 57–84). There were 2 patients with lung primaries, 2 with breast primaries, and 1 cervical primary. Clinical presentation of esophageal disease was either with progressive dysphagia or post-prandial vomiting. Duration from diagnosis of primary tumor until onset of esophageal symptoms ranged from 1 month to 18 years, and tended to be longer in breast cancer patients (Table 1). All cases had similar CT thorax findings, demonstrating the lack of extrinsic

compressing extraesophageal lesion, and EGD findings of benign-appearing tight esophageal stricture without overlying mucosal changes (Fig. 1).

EUS studies of all the cases showed lesions within the submucosa or adventitia of the esophageal wall (Fig. 2). FNA of these lesions yielded cytology suggestive of metastatic disease from each respective primary cancer (Fig. 3). Patients with significant obstruction were treated with stenting, balloon dilation of the strictures, or with placement of feeding tubes to bypass the obstruction.

Discussion

Metastatic disease to the esophagus is an extremely rare and difficult diagnosis to make, although an autopsy series in Japan of 1,835 patients who had died of cancer showed esophageal metastasis in 6.1% [2]. Metastasis to the esophagus is spread via hematogenous or lymphatic dissemination from a distant primary cancer, and this should be made distinct from direct contiguous invasion from an adjacent organ which occurs more commonly. A radiological review of 62 cases of secondary esophageal involvement showed that direct extension accounted for 45.2% of the cases, 35.5% were spread via mediastinal nodes, and 19.3% were spread hematogenously [3].

Primary malignancies which metastasize to the esophagus are most commonly of breast and lung origin [2], although cases of endometrial, ovarian, colorectal, prostate, renal, and melanoma metastasis have been reported as well [2, 4–6]. Clinical presentation of patients is commonly with progressive dysphagia and time to onset dependent on the primary cancer. Esophageal disease from breast primaries tends to occur much later, with reports ranging between 7 and 10 years [7, 8].

Diagnosis is often difficult owing to the submucosal nature of the esophageal lesions. Simchuk et al. [9] described a series of patients with similar findings to ours, primarily the presence of a smooth benign-appearing stricture in the esophagus. The reason for the submucosal location of the metastatic disease is most likely facilitated by the extensive lymphatic plexus and found in the esophageal submucosa aiding dissemination from a distant primary. EUS would be the most appropriate study to identify submucosal tumors, and targeted biopsies can be stained for immunohistochemical correlation with their suspected primary cancer. Sobel et al. [1] described an EUS-guided approach to diagnose metastatic breast cancer esophageal disease, and we applied the same principle to our patients with varying disease primaries.

Our case series demonstrates that metastatic disease to the esophagus is a difficult entity to diagnose owing to its submucosal nature, and EUS is a very useful tool to be used on a background of a high clinical index of suspicion.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare no conflict of interest.

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Fig. 1. EGD showing esophageal stricture with smooth benign-appearing mucosa.



Fig. 2. Linear EUS probe demonstrating a hypoechoic tumor within the submucosa (circled).

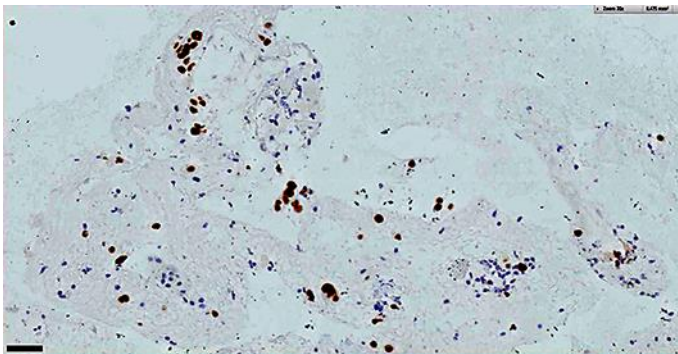


Fig. 3. TTF-1-immunostained cell block section shows the atypical cells to be TTF-1 positive, consistent with non-small cell lung carcinoma (stained brown).

Table 1. Patient characteristics, investigational findings, and treatment outcomes

| Age, years | Gender | Primary tumor | Presentation | Time since diagnosis of primary tumor | Computed tomography scan | Gastroscopy | Endoscopic ultrasound | Fine needle aspiration | Treatment and outcome |
|------------|--------|---------------|----------------------|---------------------------------------|---|--|--|--|--|
| 77 | Female | NSCLC | Dysphagia | 8 months | Dilated fluid-filled esophagus, transition point at GEJ, without extrinsic mass | Tight esophageal stricture with normal mucosa | Disruption of tissue planes with mass effect at level of stricture | TTF-1 positive, atypical cells of NSCLC origin | Placement of esophageal stent |
| 57 | Male | NSCLC | Vomiting after meals | 6 months | Circumferential esophageal thickening, without extrinsic mass | Tight GEJ stricture with normal mucosa | Concentric thickening of esophagus and cardia, thickened submucosa, loss of architecture | TTF-1 positive, atypical cells of NSCLC origin | Serial balloon dilatations of esophagus |
| 62 | Female | Breast | Dysphagia | 29 months | Circumferential esophageal wall thickening, distal to the level of carina, without extrinsic mass | Impacted food bolus in the upper esophagus, stricture with normal mucosa | Enlarged hypoechoic lymph nodes | Malignant appearing adenocarcinoma, suspicious of breast origin | Chemotherapy, dead 8 months after diagnosis |
| 70 | Female | Breast | Dysphagia | 18 years | Esophageal thickening at aortic arch, without extrinsic mass | Tight esophageal stricture with normal mucosa | Hypoechoic mass infiltrating the adventitia | Malignant cells, ER and PR positive, TTF-1 and CDX-2 negative, consistent with adenocarcinoma of breast origin | Endoscopically placed 8-Fr feeding tube past the stricture for feeding, dead 42 months after diagnosis |
| 84 | Female | Cervix | Vomiting after meals | 1 month | Dilated proximal thoracic esophagus, circumferential subcarinal esophageal thickening, without extrinsic mass | Tight esophageal stricture with benign-appearing smooth mucosa | Hypoechoic area on adventitia, enlarged para-esophageal lymph node | Poorly differentiated squamous cell carcinoma, similar to previous cervical cancer biopsy cells | Serial balloon dilatations of esophagus, dead 6 months after diagnosis |

NSCLC, non-small cell lung cancer; GEJ, gastro-esophageal junction; TTF-1, thyroid transcription factor-1; ER, estrogen receptor; PR, progesterone receptor; CDX-2, caudal type homeobox 2.