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CASE REPORT | ESOPHAGUS

Downhill Varices and Apical Lung Cancer Without Superior Vena Cava Syndrome

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ABSTRACT

A 75-year-old woman with hypertension, dyslipidemia, thalassemia trait, osteoarthritis of the knees, and hyperthyroidism presented with bloating, abdominal discomfort, and change in stool caliber underwent an esophagogastroduodenoscopy. The esophagogastroduodenoscopy revealed varices at the middle of esophagus, which were diagnosed to be downhill esophageal varices (DEVs). DEVs occur mainly from the superior vena cava (SVC) obstruction; however, in the absence of obstruction, angiogenesis and thrombosis could be the etiology. In our patient, computed tomography showed a pulmonary nodule located at periphery of the right upper lung without SVC contact nor obstruction. The nodule was later proven to be an adenocarcinoma. Thus, our patient showed the possibility that adenocarcinoma of the lung might associated with the DEV through a mechanism other than SVC obstruction. Recognition and differentiation of DEV from other benign venous blebs of the esophagus are important, and once detected, further investigation with computed tomography of the chest is recommended.

KEYWORDS: downhill varices; esophageal varices; varix; SVC obstruction; SVC syndrome; lung cancer

INTRODUCTION

The downhill esophageal varices (DEVs) are vertical longitudinal dilatation of the veins in the esophagus, which were different from the more rounded venous dilatations of blebs in the esophagus. The DEVs were similar in appearance to the more common uphill varices seen in cirrhosis, except for the fact that they appeared at the midesophagus and did not extend to the distal esophagus/esophagogastric junction, where uphill esophageal varices arise from. DEVs were first reported by Simchowitz et al in 1932.[1] Subsequent reports[2] revealed that the most common etiology for downhill varices is the obstruction of the superior vena cava (SVC). An increase in SVC pressure or obstruction of the SVC results in the retrograde blood flowing to the azygos vein, where the pressure transmits to the esophageal venous plexus, respectively. There are several etiologies of DEVs reported in the literature (Table 1), and most of them are caused by the SVC obstruction either from the direct compression of mass or secondary to various conditions. The downhill varices can be treated conservatively while treating the primary cause of the varices or treating the SVC obstruction with dilation of the SVC stricture by SVC stenting or angioplasty. In case of bleeding, which is rare, the treatment includes endoscopic variceal band ligation or systemic embolization through the brachiocephalic vein, injection of sclerosing agents, or balloon tamponade.[3,4]

CASE REPORT

A 75-year-old woman with the underlying hypertension, dyslipidemia, thalassemia trait, knee osteoarthritis, and hyperthyroidism presented with bloating, abdominal discomfort, and change in stool caliber for a couple days in the previous few weeks. For her bloating, she denied eating a fatty diet, alcohol consumption, nor frequent intake of the dairy products. She had no respiratory symptoms and no

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Table 1. The etiologies of DEVs reported in previous cases

Study	Age	Sex	Comorbidities	Endoscopic findings	Cause	Management
Lung cancer						
Tanaka et al[5]	68	Male	Unknown	Four striated DEVs (F1, CB, and RC)	Small-cell lung cancer at upper right lung filed completely obstructed SVC	Concurrent chemoradiotherapy
Tanaka et al[5]	55	Male	Unknown	Three striated downhill varices (F1, CW, and RC)	Squamous cell lung cancer narrowing SVC with good collateral pathways	Concurrent chemoradiotherapy
Subramaniam et al[6]	27	Male	No underlying disease	Marked varicosity of the esophageal veins over almost the entire length (necropsy finding)	Anaplastic bronchogenic carcinoma 2″ × 1½″ at the entire upper lobe, arised from the right upper lobe bronchus with SVC obstruction	Antimitotic drugs
Kokubo et al[7]	66	Male	Unknown	DEVs at the upper esophagus	Recurrence lung cancer	Upper lobectomy
Chauvin et al[8]	55	Male	Stage IIIb non–small-cell carcinoma status post chemotherapy and radiation therapy	Grade III varices 25–30 cm from the incisors with a visible fibrin clot	Stage IIIb non–small-cell carcinoma in the anterior mediastinum encasing brachiocephalic trunk and SVC occlusion	Band ligation
Nonlung cancer cause						
Berkowitz et al[9]	32	Female	ESRD MCTD	Esophageal varices in the upper and middle esophagus	SVC syndrome secondary to central venous dialysis catheters	Endoscopic band ligation of a proximal varix
Chakinala et al[10]	55	Male	ESRD Rheumatoid arthritis PAD Esophageal varices	Upper and middle esophageal varices	Chronic SVC and right brachiocephalic vein occlusion secondary to venous catheters	Esophageal band ligation Failed SVC stenting
Loudin et al[3]	22	Female	ESRD Henoch-Schönlein purpura	Large varices in the proximal esophagus with positive red wale sign	SVC syndrome secondary to central venous dialysis catheters	Balloon dilation of the stenotic SVC
Bédard and Deslauriers[11]	68	Female	Retrosternal goiter	Upper esophageal varices	Extrinsic compression of the right innominate vein secondary to retrosternal goiter	Thyroidectomy
Yaşar B, Kılıçoğlu G.[12]	31	Male	Behçet disease	Prominent esophageal varices in the upper half of the esophagus with an overlying clot	SVC syndrome secondary to Behçet disease	Conservative management DMARDs Steroids
Gholam et al[13]	87	Female	Cameron ulcers Aortic stenosis Pulmonary hypertension	Large varices in the upper third of the esophagus and Cameron lesions	Severe pulmonary hypertension secondary to aortic stenosis	Conservative management
Harwani et al[14]	55	Female	Liver cirrhosis Chronic rheumatic heart disease; severe mitral and tricuspid regurgitation Pulmonary hypertension	Upper and lower esophageal varices	Dilated SVC because of pulmonary hypertension	Variceal banding
Maton et al[15]	34	Female	Idiopathic vasculitis	Upper esophageal varices	Vasculitis	Conservative management
Serin et al[16]	60	Female	None	Upper esophageal varices	Increase blood drainage from the tumor into the esophageal veins	Tumor removal

Table 1. (***continued***)

Study	Age	Sex	Comorbidities	Endoscopic findings	Cause	Management
Shirakusa et al[17]	26	Male	Hepatitis	Upper esophageal varices	Excessive blood flow into the esophageal wall from a giant lymphoma	Thoracotomy
Yasar and Abut[18]	45	Male	Seminoma Pelvic radiotherapy	Varices in the upper third of the esophagus	Bilateral brachiocephalic truncus stenosis because of mediastinal fibrosis	Conservative management
Basar et al[19]	54	Male	AV block Epicardiac pacemaker	Upper esophageal varices	Bilateral subclavian veins DVTs secondary to pacemaker	Patient refused treatment
Ibis et al[20]	35	Female	History of subtotal thyroidectomy and multinodular goiter	Upper esophageal varices	Downhill varices secondary to recurrent multinodular goiter	Esophageal band ligation Inferior thyroid artery embolization Repeat subtotal thyroidectomy
Van der Veldt et al[21]	77	Female	COPD Multinodular goiter	Grade II–III upper esophageal varices	Right internal jugular vein compression secondary to multinodular goiter	Subtotal thyroidectomy

AV, atrioventricular; CB, blue varices; COPD, chronic obstructive pulmonary disease; CW, white varices; DEVs, downhill esophageal varices; DMARDs, disease-modifying antirheumatic drugs; DVT, deep vein thrombosis; ESRD, end stage renal disease; MCTD, mixed connective tissue disease; PAD, peripheral arterial disease; RC, red color sign; SVC, superior vena cava.

appetite loss nor cachexia. She was a life-long nonsmoker. Physical examination was unremarkable; she was breathing comfortably with normal breath sounds on auscultation; the abdomen was soft without tenderness nor guarding; and no lymphadenopathy, no hepatosplenomegaly, no abdominal mass, and no stigmata of chronic liver disease were found. Her medications were calcium carbonate, calciferol, and atenolol.

In view of her age, her medical attendance despite her usual habit of medical stoicism, and the previous change in stool caliber, she was investigated with the colonoscopy and esophagogastroduodenoscopy (EGD). Colonoscopy found multiple polyps, which were removed by biopsy forceps and cold snare.

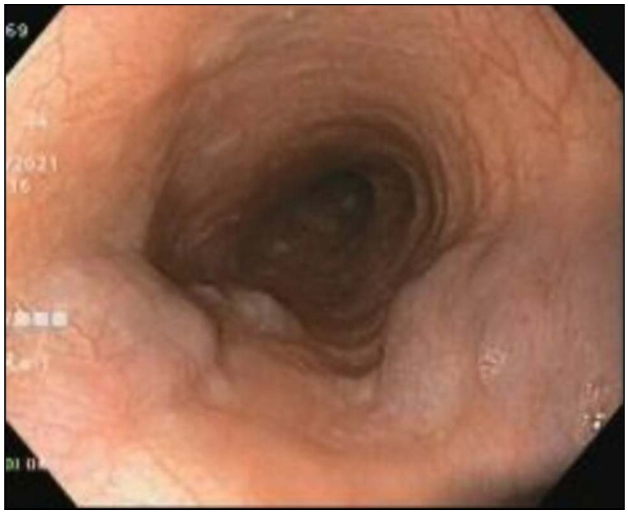

Figure 1. Downhill esophageal varices seen in the patient. Two F2 varices and 1 F1 varix were seen between 30 and 35 cm from the incisors.

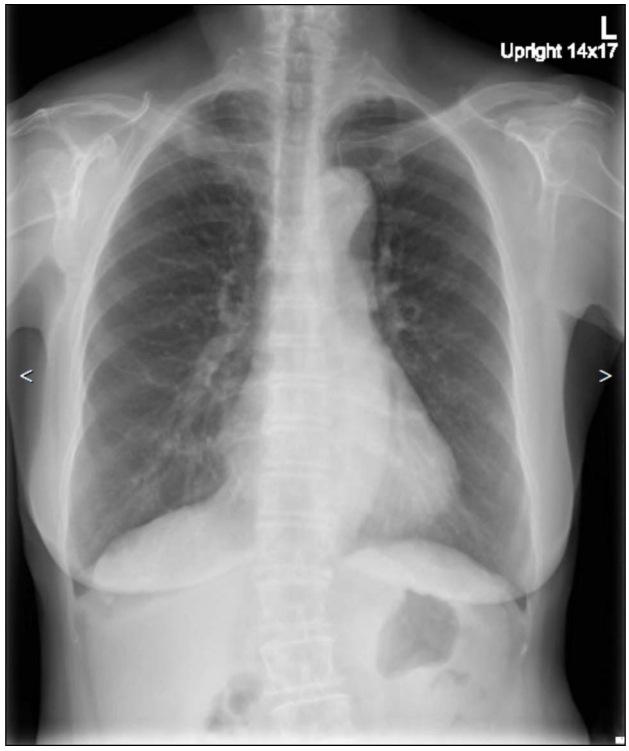

Figure 2. Chest x-ray posteroanterior upright showing a reticular-ground glass at right upper lung zone, which was barely detectable.

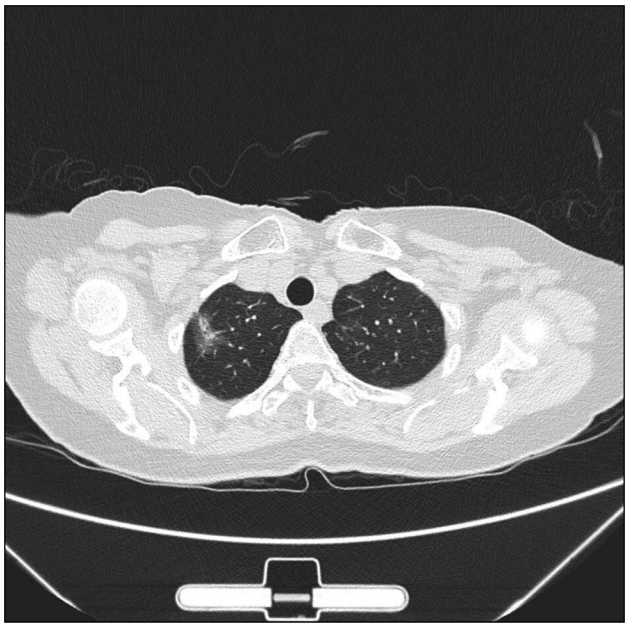

Figure 3. CT of the chest and mediastinum axial plane showing a 2.7-cm nodule at periphery of the right upper lung. CT, computed tomography.

These were found to be hyperplastic polyps on pathological examination. EGD found 2 F2 varices and 1 F1 varix between 30 and 35 cm from the incisors, both of which were in the mid-esophagus and did not extend to the esophagogastric junction (Figure 1). Below the varices, there were a few benign squamous papillomata, and a venous bleb at 39 cm from the incisors just proximal to the esophagogastric junction, but otherwise, the mucosa distal to the varices was normal. No gastric varices were seen. The varices were recognized to be DEVs from their appearance as vertical longitudinal dilatation of the veins in the esophagus, which were different from the more rounded venous dilatations of esophageal blebs, and the fact that they did not extend distally to the esophagogastric junction like the more common uphill varices seen in cirrhosis; thus, chest x-ray and computed tomography (CT) of the chest and neck were performed to evaluate the cause of varices. Although the chest x-ray (Figure 2) showed a barely detectable reticular-ground glass opacity in the right upper zone, the CT results (Figures 3 and 4) revealed a 2.7-cm pulmonary nodule located at periphery of the right upper lung, adjacent to the pleura and far superolateral to the SVC without SVC contact and obstruction, no neck mass, subcentimeter lymph nodes with internal microcalcification at left cervical IIb level, posterior to spinal accessory nerve and internal jugular vein. No thyroid nodules and no liver cirrhosis were found.

The patient underwent a lung biopsy, which revealed the lesion to be an adenocarcinoma.

After the pathology results, the patient underwent a video-assisted thoracoscopic surgery with right upper lobe lobectomy and lymph node biopsy. The pathological examination from the surgical specimen (Figure 5) showed a lepidic-predominant invasive adenocarcinoma, the total size of 2.7 cm, with an invasive tumor size of 1.1 cm in the greatest dimension, with acinar pattern at the periphery of the lung and close to pleura (as shown in Figure 5). Visceral pleural invasion was not identified in the additional elastic stain. Lymphovascular invasion and vascular thrombosis were not seen (as shown in Figure 6). The dissection of the lymph nodes of hilar, interlobar, right paratracheal, and subcarinal area showed no evidence of metastatic carcinoma. The vascular abnormalities associated with pulmonary hypertension were not detected. The epidermal growth factor receptor (EGFR) gene mutational analysis in the paraffin block revealed EGFR c.2573T>G (L858R) mutation. Clear resection margins were seen. In conclusion, the tumor staging was T1bN0M0.

The patient recovered postoperatively and remains well at 12 months. No further endoscopy was performed because there has been no clinical indication for a repeat endoscopy.

DISCUSSION

DEVs develop when the esophageal plexus has increased blood flow, and they are usually associated with venous obstruction from the SVC. The level of obstruction affects the formation of varices. Lesions proximal to azygous vein push the drainage through mediastinal collaterals and drain back to the azygous system below the obstruction. Varices that occur from lesions in this location are limited to the upper third of the esophagus. On

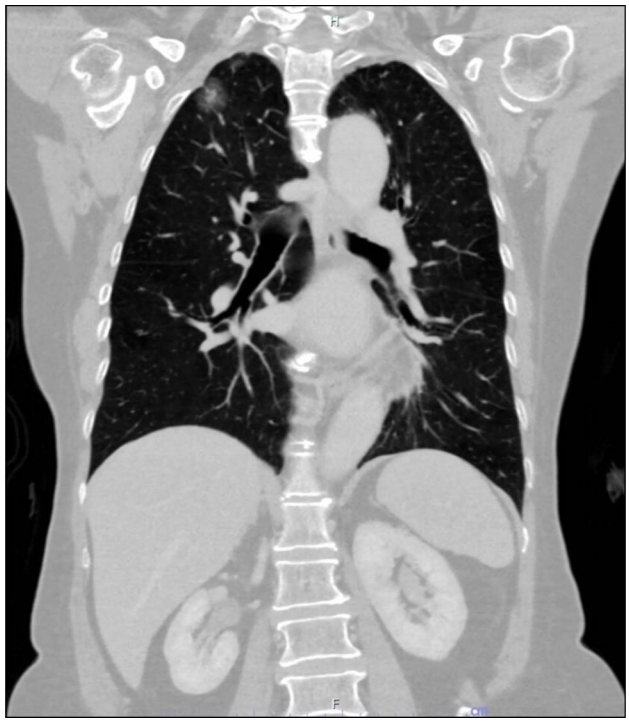

Figure 4. CT of the chest and mediastinum coronal plane showing a 2.7-cm nodule at periphery of the right upper lung. CT, computed tomography.

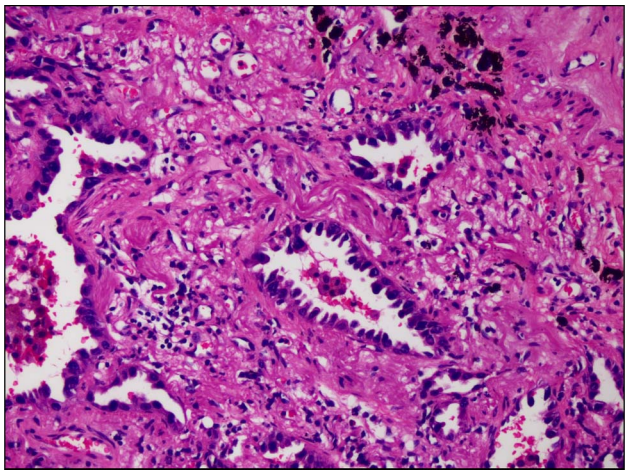

Figure 5. The histopathological specimen showing adenocarcinoma with acinar pattern.

the other hand, varices that are from obstruction distal to the azygos vein mostly expand along the entire length of the esophagus.

The etiology of downhill varices has been widely reported among case studies, most of which were from SVC syndrome and other vascular occlusions. The literatures describe other causes including mediastinal fibrosis,[18] Behçet disease,[22] catheter manipulation,[3,9,11] retrosternal goiter and other thyroid masses,[10,20,21] thymomas,[23] bronchial carcinomas,[6] metastatic mediastinal tumors,[7] pulmonary hypertension,[13,14] lymphomas,[17] or were idiopathic. The causal pathway for most of these etiologies is through venous obstruction in the paraesophageal/mediastinal area.

Our patient presented with asymptomatic downhill varices diagnosed incidentally on EGD. However, in this case, from the CT, there was no evidence of SVC obstruction. This is unlike most other cases of downhill varices with upper mediastinal/thoracic tumor, which often reported SVC compression from an extrinsic mass such as from small-cell lung carcinoma, lymphoma, or bronchial carcinoma. Downhill varices without SVC obstruction have also been mentioned in the literature and can occur from an increase in blood flow in the esophageal plexuses, eg, from Castleman disease, also known as angiofollicular lymph node hyperplasia, which is known to be hypervascular and cause downhill varices by increasing blood drainage to the esophageal veins.[16] Moreover, obstruction in some venous drainage other than SVC has also been reported as a cause of downhill varices. In thyroid disease, obstruction of the inferior thyroid vein can lead to the development of proximal esophageal varices.[21]

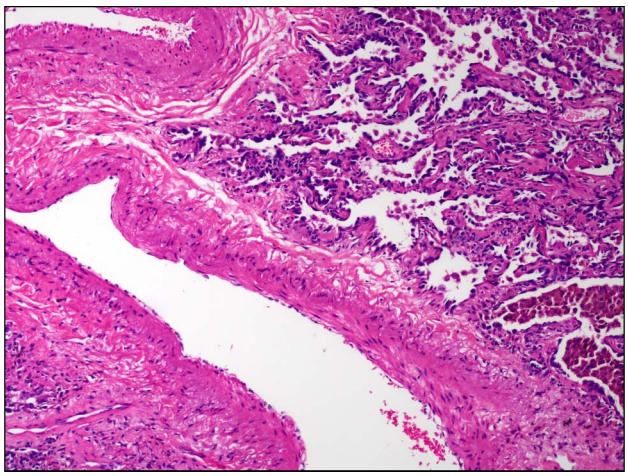

Figure 6. The histopathological specimen showing a lepidic adenocarcinoma, with pulmonary vein but no thrombosis.

From previous case studies,[5–8,24] all lung cancer patients with DEVs were associated with SVC syndrome, by the mechanism of venous obstruction. However, in our case, SVC obstruction was absent on CT, and no vascular invasion nor thrombosis was seen on the histopathological specimen; the varices might be hypothesized to have formed because of increased blood flow in the area as a result of tumor angiogenesis, given that tumor progression depends primarily on vascular supply. Non–small-cell lung cancer, particularly adenocarcinoma, is a highly vascularized tumor,[25] suggesting that a consequent increase in the blood flow to the tumor and surrounding vessels is likely.[26] In addition, the pathological specimen revealed EGFR gene mutation of the tumor, which have a critical role in tumor angiogenesis through upregulation of vascular endothelial growth factor and other angiogenic factors.[27,28] Alternatively, it is possible that thrombosis could have formed in the small vessels in the area because of the hypercoagulable state of cancer, causing a retrograde blood flow into the esophageal plexus and subsequent formation of new varices.

Downhill varices occur mainly from SVC obstruction, which could be caused by malignant or benign processes. The presence of DEVs should lead to a suspicion of lesions compressing venous drainage, including lung cancer, especially non–small-cell lung cancer at apex or the upper lung. However, without obstruction, aberrant blood flow, angiogenesis, or thrombosis may also be the etiology for DEVs. Recognition of downhill varices at endoscopy and its differentiation from other benign venous blebs of the esophagus is important, and once detected, further investigation with CT of the chest is recommended.

DISCLOSURES

Author contributions: N. Kitkarncharoensin, S. Catithammanit, and N. Chavanachinda: draft, edited the article, and reviewed the literature. B. Phruttinarakorn supplied, interpreted the pathology images, and edited the article. P. Cherntanomwong edited the article. T. Kitiyakara edited the article and is the article guarantor. All authors approved the final version of the manuscript.

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