

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2017 October 15; 9(10): 402-435





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World Journal of Gastrointestinal Oncology (*World J Gastrointest Oncol*, *WJGO*, online ISSN 1948-5204, DOI: 10.4251) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJGO covers topics concerning carcinogenesis, tumorigenesis, metastasis, diagnosis, prevention, prognosis, clinical manifestations, nutritional support, molecular mechanisms, and therapy of benign and malignant tumors of the digestive tract. The current columns of *WJGO* include editorial, frontier, diagnostic advances, therapeutics advances, field of vision, mini-reviews, review, topic highlight, medical ethics, original articles, case report, clinical case conference (Clinicopathological conference), and autobiography. Priority publication will be given to articles concerning diagnosis and treatment of gastrointestinal oncology diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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World Journal of Gastrointestinal Oncology is now indexed in Science Citation Index Expanded (also known as SciSearch®), PubMed, and PubMed Central.

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I-IV Editorial Board

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NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

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PUBLICATION DATE
October 15, 2017

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Primary esophageal diffuse large B cell lymphoma presenting with tracheoesophageal fistula: A rare case and review

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Author contributions: Teerakanok J and DeWitt JP contributed equally to this work and should be considered as co-first authors; Teerakanok J and DeWitt JP researched and reviewed literatures, wrote manuscript; Juarez E collected patient's data; Thein KZ reviewed and wrote manuscript; Warraich I reviewed tissues pathology and conducted critical review.

Institutional review board statement: This case report does not require Texas Tech University Health Sciences Center IRB review.

Informed consent statement: Patient's legal guardian provided verbal informed consent authorizing discloses and use his information.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

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Manuscript source: Unsolicited Manuscript

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Telephone: +1-806-7432155

Received: February 21, 2017

Peer-review started: February 23, 2017

First decision: May 7, 2017

Revised: May 30, 2017

Accepted: July 14, 2017

Article in press: July 17, 2017

Published online: October 15, 2017

Abstract

Primary non-Hodgkin lymphomas in the esophagus are rare. Tracheoesophageal fistulas mainly arise from solid esophageal carcinoma or mediastinal malignancies. Our patient presented with cough, dysphagia and weight loss, and upon initial computed tomography imaging and esophagogastroduodenoscopy, a malignant mass in the middle third of esophagus with tracheoesophageal fistula was found. The location of the mass and presence of malignant tracheoesophageal fistula were strongly suggestive of squamous cell carcinoma. However, tumor biopsy revealed diffuse large B-cell lymphoma. This case report details a rare incident of a primary diffuse large B-cell lymphoma presented as tracheoesophageal fistula and reviews previous literature.

Key words: Non-Hodgkin lymphoma; Tracheoesophageal fistula; Esophageal cancer; Esophageal lymphoma

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Core tip: Primary non-Hodgkin lymphoma of esophagus is a rare disease, and tracheoesophageal fistula secondary to this condition prior to treatment is extremely rare and fatal. However, it has better prognosis than fistulas secondary to solid tumor if patients receive timely treatment.

Teerakanok J, DeWitt JP, Juarez E, Thein KZ, Warraich I. Pri-

mary esophageal diffuse large B cell lymphoma presenting with tracheoesophageal fistula: A rare case and review. *World J Gastrointest Oncol* 2017; 9(10): 431-435 Available from: URL: <http://www.wjgnet.com/1948-5204/full/v9/i10/431.htm> DOI: <http://dx.doi.org/10.4251/wjgo.v9.i10.431>

INTRODUCTION

Lymphomas, the most common blood cancers, are characterized by proliferation of lymphocytes in the lymph nodes and of lymphoid tissue^[1,2]. Lymphomas are categorized into two groups: Hodgkin and non-Hodgkin lymphomas (NHLs). Among NHLs, diffuse large B-cell lymphomas (DLBCLs) account for 40% of all lymphoma cases worldwide^[3]. Primary gastrointestinal (GI) lymphoma is the most common extranodal presentation NHL; however, most cases involve the stomach, small intestine and colon. Esophageal involvement is the rarest. Malignant tracheoesophageal fistula (TEF) from NHL is uncommon and presents mostly as complication of radiation therapy or chemotherapy.

Here, we present a rare case of a primary esophageal NHL presented with malignant TEF. To the best of our knowledge, this is the first case of primary DLBCL with malignant TEF prior to cancer treatment.

CASE REPORT

A 60-year-old male with past medical history of diabetes mellitus type 2, hypothyroidism and chronic tobacco smoking presented with gradually worsening 3-wk dry cough, dysphagia and cough provoked with all oral intake. On review of systems, patient had unintentional 30-pound weight loss in the past 3 mo. On physical exam vital signs were unremarkable except for oxygen saturation of 91% on room air with respiratory rate of 18 breaths per minute. Moreover, the patient was not in acute distress; his breathing was non-labored; liver and spleen were not palpable; superficial lymphadenopathy was not found. The initial CBC revealed a white blood cell count of 21900/ μ L, 5% bands, 81% segmented neutrophils, 5% lymphocyte, and 8% monocytes. Lactate dehydrogenase was 223 units/L (normal value; 135-225 units/L), liver functions and renal functions were unremarkable and human immunodeficiency virus (HIV) was negative. A chest computed tomography (CT) imaging revealed a mid-esophageal wall thickening and enhancement, a fistulous connection between the membranous portion of the trachea and the anterior portion of the mediastinum, nonspecific mediastinal lymph nodes enlargement and some of ground glass opacity in posterior segment of the upper lobes and superior segments of the lower lobes bilaterally (Figure 1). Abdominal and pelvic CT imaging revealed multiple lytic lesions in pelvic bone, mild hepatic steatosis, normal spleen and no intraabdominal or pelvic lymphadenopathy. Our patient was started on levofloxacin for concern of aspiration pneumonia.

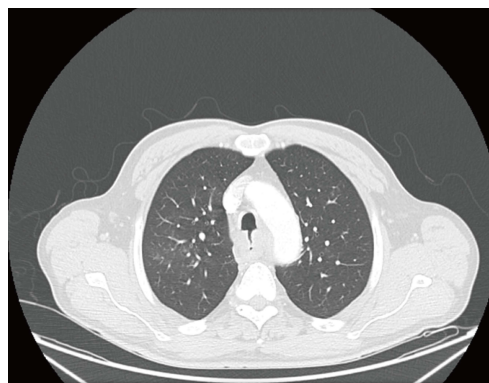


Figure 1 Contrasted chest computed tomography imaging showing tracheoesophageal fistula in a 60-year-old male patient.

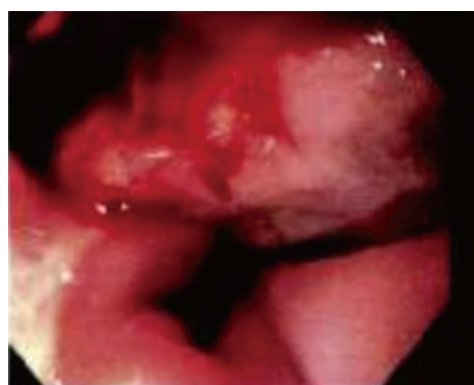


Figure 2 Esophagogastroduodenoscopy showing a partially obstructing mid-esophageal tumor and tracheoesophageal fistula in a 60-year-old male patient.

Esophagogastroduodenoscopy (EGD) found a large fungating and ulcerating mass in the middle third of the esophagus with partial obstruction, and TEF was found in the middle third of the esophagus with tracheal rings (Figure 2). Bronchoscopy revealed 3 cm TEF in the trachea and 1.5 cm bronchoesophageal fistula in left mainstem. The esophageal mass biopsy showed large, highly pleomorphic cells with diffuse growth pattern (Figure 3A). Various immunohistochemical staining were performed. Tumor cells had strong and diffuse expression for CD20 (Figure 3B), CD10, CD45, CD79a and bcl2. CD 3 and CD5 were negative. Cytokeratin (CK) AE1/AE3 was negative for the cells of tumor infiltrate (Figure 3C). Tumor cells did not show any expression for P40, a marker for squamous cell carcinoma (Figure 3D). These findings were consistent with diffuse large B-cell lymphoma diagnosis. Bone marrow biopsy was not performed because CT imaging suggested bone marrow involvement. Lumbar puncture was not done as well. Patient underwent for percutaneous endoscopic gastrostomy tube placement, esophageal stent placement and tracheobronchial stent placement. He received rituximab 375 mg/m² for 1 dose, and a week later he subsequently received complete first cycle of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP regimen). Patient completed 6

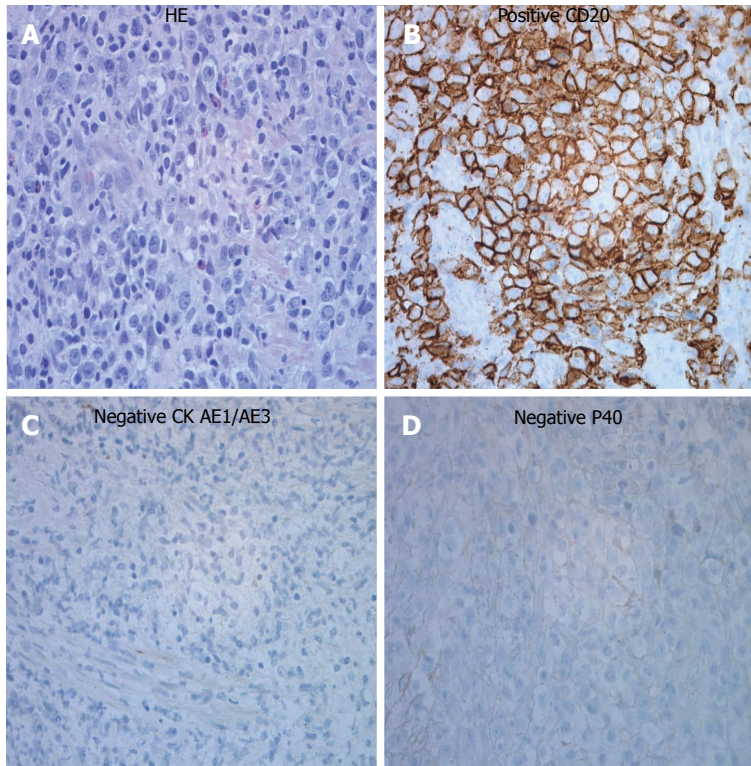


Figure 3 Histological features of primary diffuse large B-cell lymphoma in a 60-year-old male patient. A: HE staining shows highly pleomorphic large cell proliferation on sections of neoplasm; B: Immunohistochemistry shows tumor cells with a strongly diffused positive expression for CD20; C: Cytokeratin (CK) AE1/AE3 was negative for the cells of tumor infiltrate; D: P40 was negative for squamous carcinoma.

cycles of R-CHOP with good response in tumor but still has persistent TEF with intermittent aspiration. He lost 30 pounds during the course of treatment due to poor feeding intolerance.

DISCUSSION

GI lymphomas comprise 5%-20% of extranodal lymphomas^[4] and only 1%-4% of all GI cancers^[5]. Primary esophageal lymphoma accounts for less than 1% of GI lymphomas. The earliest reported primary esophageal NHL was in 1979^[6]. Heretofore, there have been less than 25 reported cases of primary esophageal cancer from NHL^[7-16]. Sometimes, it can be difficult to differentiate between primary GI lymphomas and lymphomas that disseminated to GI tract. Dawson *et al.*^[17] described the diagnostic criteria of primary GI lymphomas: (1) absence of peripheral lymphadenopathy; (2) absence of mediastinal adenopathy; (3) no involvement of liver and spleen; and (4) normal peripheral blood count. Majority of primary GI lymphomas are DLBCL^[18]. A major risk factor for primary esophageal lymphoma is immunosuppression, such as HIV infection^[19]. Radiologic features of primary esophageal lymphoma are ulceration, stenosis, polypoid masses, aneurysmal dilatation and TEF, which are non-specific^[19,20].

Malignant TEF is a serious late complication of cancers. Most malignant TEF cases are related to esophageal and lung cancers^[21]. TEF from primary esophageal lymphoma is an uncommon complication. TEF in lymphoma frequently develops during or after treatment

with radiation or chemotherapy, but it can occur due to the disease itself. Most of the reports were of Hodgkin lymphomas^[22-25]. Even though literature review reveals case reports of NHL with esophageal-tracheobronchial connection, the reported NHLs are not primary esophageal NHLs^[26-28]. Malignant TEF usually has very poor prognosis; however, if lymphomas are recognized and treated early, TEF repair and chemotherapy treatment will result in good prognosis^[29]. Standard treatment of DLBCL is R-CHOP regimen. Management of TEF is predominantly a non-surgical intervention because of the difficulty of and risk from surgery. Esophageal stent and/or airway stent is effective to prevent aspiration of GI contents and risk of pneumonia. In addition, general treatments, such as gastrostomy/jejunostomy tube, antibiotics and airway secretion prevention help reduce further risk of aspiration^[22,30].

Novelty of this case report is the co-presence of malignant TEF with primary DLBCL in the esophagus. Primary esophageal lymphoma-related TEF is extremely rare but fatal. Physicians should suspect it for timely diagnosis since NHL with TEF has better prognosis with interventions and chemotherapy alone than TEFs caused by esophageal cancer or lung cancer.

COMMENTS

Case characteristics

A 60-year-old man presented with worsening 3-wk dry cough, dysphagia and cough provoked with all oral intake.

Clinical diagnosis

Clinical examination was unremarkable.

Differential diagnosis

Stroke, esophageal spasm, esophageal tumor, tracheoesophageal fistula-related or pulmonary infection.

Laboratory diagnosis

Blood count showed leukocytosis suggested of infection or inflammation, but lactate dehydrogenase and liver function were unremarkable.

Imaging diagnosis

Chest, abdominal and pelvic computed tomography imaging revealed fungating and ulcerating mass in the middle third of the esophagus with partial obstruction and tracheoesophageal fistula (TEF) without significant lymphadenopathy.

Pathological diagnosis

Esophageal mass biopsy revealed diffuse large B-cell lymphoma.

Treatment

Patient received chemotherapy R-CHOP regimen and underwent to have PEG tube placement, tracheal and esophageal stents.

Related reports

Most primary esophageal lymphoma cases are the rarest among primary gastrointestinal lymphoma, and TEF is seldom found as a presenting symptom.

Term explanation

Tracheoesophageal fistula is an abnormal connection between the esophagus and trachea. Diffuse large B cell lymphoma is a subtype of non-Hodgkin lymphoma.

Experiences and lessons

Primary esophageal lymphoma is extremely rare, and malignant TEF is fatal. However, patients with this condition have better prognosis if they receive a proper management.

Peer-review

This case report is very interesting and rare. It is helpful to know if the patient has been immunologically investigated. The manuscript is well written and illustrations are informative.

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